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Editorial

Developed countries, in recent times, are turning to the use of traditional medicines that involve the use of herbal drugs and remedies. According to a recent survey about 1400 herbal preparations are used widely and are popular in primary healthcare in several countries of the world. Also, amongst the poor, cures and drugs, derived from plants, constitutes the main source of healthcare products. This calls for the need to investigate the information on the therapeutic effects of herbs with more clinical, scientific and evidence – based approach in an effort to validate them and prove their medical efficacy and safety. It is in this context a large number of traditional drugs have been investigated in recent years for their pharmacological activity and bioactive constituents to discover new therapeutic agents of natural origin.

Unani system of medicine, although originated in Greece, is one of the recognized systems of medicine of the country. Although, the Unani medicine have been in use for centuries and are known for their therapeutic efficacies, there is a need to scientifically establish their efficacy and safety in order to achieve global acceptance. Organized research work in this system was, therefore, a need of the hour. In post independent era, Central Council for Research in Unani Medicine, through its clinical, drug research, literary research, survey & cultivation of medicinal plants programme is contributing significantly for last three decades. Vitiligo, Sinusitis, Filariasis, Eczema, Malaria, Infective Hepatitis, Asthma, are some of the conditions where Unani therapies have earned recognition after scientific validation.

The Council has been publishing the peer reviewed Hippocratic Journal of Unani Medicine (HJUM), mainly to bring out fundamental and applied aspects of Unani Medicine. The journal also publishes recent advances in other related sciences and traditional medicines as well as different streams of medical sciences, which have bearing on validation and scientific interpretation of various concepts and strengths of Unani medicine.

In view of an overwhelming response, the journal earlier published twice a year, its periodicity has now been changed to quarterly w.e.f. January 2008 to accommodate more articles for quick dissemination of research data among scientific community. The journal has sufficient room for invited articles from luminaries of modern medicine and sciences as well as scholars of Unani medicine. The broad areas being covered include clinical research on single and compound Unani drugs, validation of regimental therapy, Clinical and experimental pharmacological studies, standardization of single and compound drugs, development of standard operating procedures, ethnobotanical studies, experimental studies on medicinal plants and development of agro-techniques thereof, and literary research on classics of Unani medicine. The journal is also open for studies on safety evaluation of Unani and other herbo-mineral drugs, nutraceuticals, cosmotherapeutics, aromatics, oral health, life style disorders, sports medicine etc. and such other newer areas which are the outcome of modern day living.

The current issue of this journal provides 12 original and review papers in the areas of clinical research, drug standardization, pharmacology, ethnobotanical surveys and allied disciplines contributed by eminent scholars in their respective fields. It is hoped that data presented will contribute significantly in R&D sector of traditional drugs and prove to be an excellent exposition of current research efforts of scientists in this direction. Council acknowledges the authors for their contributions included in this issue and hope for their continued support in this endeavor. We wish to ensure the readers to bring out the future issues of the journal on time.

We at the CCRUM have been constantly striving to reach to higher standards and make HJUM the leading journal of Unani Medicine and related sciences. In this context, we thank our learned reviewers for their invaluable inputs in improving the manuscripts. We sincerely hope and trust that the mission can be accomplished with active partnership of quality-conscious individuals and institutions. Through these lines we seek your cooperation and support in materializing our dreams about the HJUM. In this regard, we request you for your as well as your colleagues' contributions for publication in and subscription to the journal. Further, we will appreciate if the journal is introduced far and wide. We would also welcome esteemed suggestions for achieving the highest standards of quality for the journal.

(Prof. S. Shakir Jamil)
Editor-in-Chief

A Clinical Study on Primary Hypertension (*Zaght al-Dam-Qawi Ibtidai)* and a Comparative Evaluation of *Qurs-e-Dawaushifa* with Amlodipine in its Management

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Abstract

Hypertension the "silent Killer" is considered to be a major health problem throughout the globe. This is due to high prevalence and its association with increased risk of cardiovascular complications. In spite of increasing public awareness and a rapid advancement of anti-hypertensive medications hypertension still remains one of the leading cause of cardiovascular morbidity and mortality.

The term hypertension or *Zaght al-Dam-Qawi* has not been mentioned in any of the classical unani literature. The term hypertension was first used by Harry Gold Ballet in 1934 and the term *Zaght al-Dam-Qawi* was used by Unani scholars contemporary to Indian period. But most of the Unani scholars were familiar to manifestation of hypertension, as they have described most of its symptoms such as headache, palpitation, vertigo and epistaxis, due to *imtala* (repletion). Some of them even described vascular pressure by increased blood volume in lumen of blood vessels.

To evaluate clinical efficacy of drugs in hypertension, *Qurs-e- Dawaushifa* was chosen which contains *Asrol* (*Rauwolfia serpentina* Linn) and *Filfil siyah* (*Piper nigrum* Linn.). This drug for hypertension is proposed keeping in mind the side effects that directly arise after the administration of the drug for relatively longer period. Hence, an attempt has been made to evaluate the efficacy of these drugs on modern parameters in patients with essential hypertension.

The study was concerned with comparison between *Qurs-e-Dawaushifa* and Amlodipine in the treatment of primary hypertension. Hence all the 50 patients were divided into two groups, control and test group. Each group consists of 25 patients. Control group was treated with amlodipine and test group was treated with *Qurs-e-Dawaushifa*. All the results were analysed statistically.

Key Words: *Zaght al-Dam-Qawi*, Hypertension, *Qurs-e-Dawaushifa, Asrol, Filfil Siyah*

Introduction

Hypertension the "silent Killer" is considered to be a major health problem throughout the globe. This is due to high prevalence and its association with increased risk of cardiovascular complications (Fauci *et al*., 2008).

In spite of increasing public awareness and a rapid advancement of anti-hypertensive medications, hypertension still remains one of the leading cause

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of cardiovascular morbidity and mortality. About 95% of cases of hypertension are idiopathic in nature and are labelled as essential or primary hypertension whereas remaining 5% have definite cause of the disease and are called as secondary hypertension (Boon *et al.*, 2006).

The term hypertension or *Zaght al-Dam-Qawi* has not been mentioned in any of the classical unani literature. The term hypertension was first used by Harry Gold Ballet in 1934 and the term *Zaght al-Dam-Qawi* was used by Unani scholars contemporary to Indian period. But most of the Unani scholars were familiar to manifestation of hypertension, as they have described most of its symptoms such as headache, palpitation, vertigo and epistaxis, due to *imtala* (repletion). Some of them even described vascular pressure by increased blood volume in lumen of blood vessels (Kantoori, 1896; Baqar, 1939).

After an in-depth study of Unani literature, one may be reached to the conclusion that hypertension is a manifestation of *Yabust-e-Mizaj* (dryness of temperament) (Ahmad, 1980). As described by various scholars of Unani Medicine, *Yabusat* (dryness) is the main cause of sclerosis. Dryness causes hardening and narrowing of blood vessels (Ahmad, 1983). Hypertension is a condition associated with headache (especially in the morning), palpitation, breathlessness, fatigue (especially in the evening), flushing of the face and sometimes epistaxis. These symptoms may or may not be present in all the cases (Tierrey *et al.*, 2005).

Need for the Study

The management of hypertension is a difficult problem in day to day practice. Western medicine drugs are effective but costly and have various adverse metabolic effects, these drugs when stopped cause rebound hypertension and also have various side effects. The antihypertensive drugs used in Western medicine seem to be good to control blood pressure, but on the other hand they fail to prevent the complications of hypertension and the complications brought out by them. Looking at this, a need was felt to explore the hidden potential of certain Unani medicines used for such conditions, which may prove more effective, safe and with least adverse effects.

In the treatment of hypertension, compound drugs in natural forms are preferred over single drugs. Because a compound formulation produces desired type of effects and cover many complexities of the disease, such as ischaemic heart disease, retinopathy, neuropathy and chronic renal disease. To evaluate clinical efficacy of drugs in hypertension, *Qurs-e- Dawaushifa*

was chosen which contains *Asrol* and *Filfil siyah*. This drug for hypertension is proposed keeping in mind the side effects that directly arise after the administration of the drug for relatively longer period. Hence on the ground of above mentioned properties of these two drugs, an attempt has been made to evaluate the efficacy of these drugs on modern parameters in patients with essential hypertension.

Material and Method

This was single blind non-randomised standard control trial. The aim of this study was to assess the efficacy, safety and tolerability of combination therapy in adults of established hypertension. In this prospective the study was carried out on 50 cases of hypertension of either sex in the Unani OPD and indoor section of Ajmal Khan Tibbiya College Hospital, Aligarh Muslim University, Aligarh. The trial was carried out after approval of departmental ethics committee and informed written consent from the patients between from 2006 to 2008. Only 50 cases that full filled the selection criteria (confirmed on two consecutive visits) between 25 to 75 years of age, were selected.

The study was concerned with comparison between *Qurs-e- Dawaushifa* and Amlodipine in the treatment of primary hypertension. Hence all the 50 patients were divided into two groups, control and test group. Each group consists of 25 patients. Control group was treated with Amlodipine and test group was treated with *Qurs-e-Dawaushifa*.

The patients with established hypertension were included in the study and all antihypertensive drugs were discontinued at least one week before starting the trial. The diagnosis was made on the basis of detailed history, clinical examination and investigations including complete haemogram, random blood sugar level, blood urea, serum creatinine, serum uric acid, serum cholesterol, triglycerides, VLDL, urine analysis and stool examination. The blood pressure was measured in the right arm with an appropriate cuff size. Two readings were taken after 5 minutes rest and higher one considered as hypertensive. Systolic blood pressure was recorded at phase I (appearance of korotkoff sounds) and diastolic blood pressure at phase V (disappearance of korotkoff sounds). Casual blood pressure was recorded in the seated position with a mercury sphygmomanometer. The same technique, but after 5 minutes rest and on subsequent visits, was used to made diagnosis. The cases of grade I hypertension i.e. systolic blood pressure 140-159 mm of Hg and diastolic blood pressure 90-99 mm of Hg (according to British Hypertension Society) were included in the study.

The cases of valvular or primary myocardial disease, cerebro-vascular accidents, Transient neurological deficits, malignant hypertension, renal failure, patient taking oral contraceptive pills (OCPs), hormone replacement therapy (HRT), pregnant women and lactating mothers were excluded from the study. All the signs were recorded on examination before the beginning of the study (0 day) and thereafter subsequently during the follow-up i.e. 7th, 14th, 21st, 28th, 35th and 42 days. Simultaneously, adverse effects of the drugs noted down at regular interval during follow up.

The test drugs used in the study were procured from Dawakhana Tibbiya College, Aligarh and identified them properly while drug of control group was procured from open market keeping in view the same batch and manufacturer. These drugs were given in the following fixed dosage to all 25 cases of test group in the tablet form irrespective of age, sex and severity of disease. Two tablets of *Qurs-e-Dawaushifa* were given twice a day in test group while in control group, Amlodipine (5 mg) once a day was used.

Table 1 : Distribution of patients according to Age and Sex

Total No. of Patients – 50

Age Group (in years)	Number and percentage of males	Number and percentage of females	Total number and percentage
25-35	2(4)	0(0)	2(4)
35-45	8(16)	10(20)	18(36)
45-55	9(18)	12(24)	21(42)
55-65	2(4)	4(8)	6(12)
65-75	1(2)	2(4)	3(06)
Total	22(44)	28(56)	50(100)

Table 2 : Distribution of patients according to occupation

Total No. of Patients – 50

Occupation	Number of patients	Percentage
Service class	10	20
Business class	14	28
House wives	26	52
Total	50	100

Table 3 : Distribution of patients according to food habits

Total No. of Patients – 50

Food habits	Number of patient	Percentage
Vegetarian	10	20
Non-vegetarian	40	80
Total	50	100

Table 4: Distribution of patients according to additional salt intake

Total No. of Patients – 50

History of added salt	Number of patients	Percentage
Present	12	24.00
Absent	38	76.00
Total	50	100

Table 5 : Distribution of patients according to physical inactivity

Total No. of Patients – 50

History of physical inactivity	Number of patients	Percentage
Present	45	90
Absent	05	10
Total	50	100

Table 6 : Distribution of patients according to history of alcoholism, smoking and tobacco chewing

Total No. of Patients – 50

Past history	Number of patients	Percentage
Alcoholism	01	02
Smoking	20	40
Tobacco chewing	13	26
No habit	16	32
Total	50	100

Table 7 : Distribution of patients according to family history of hypertension

Total No. of Patients – 50

Family H/o hypertension	Number of patients	Percentage
Present	32	64
Absent	18	36
Total	50	100

Table 8 : Distribution of patients according to Temperament

Total No. of Patients – 50

Type of Temperament	No. of Males (percentage)	No. of Females (percentage)	Total No. of Patients	Percentage
Sanguinous (Damwi)	20(4)	19(38)	39	78
Bilious (Safravi)	02(40	05(10)	07	14
Phlegmatic (Bhalghami)	00	04(08)	04	08
Melancholic (Saudavi)	00	00	00	00
Total	22(44)	28(56)	50	100

Table 9 : Distribution of patients according to low and high risk BMI

Total No. of Patients – 50

Low risk BMI (kg/m^2)		
BMI	Number of Patients	Percentage
18-20	03	07.5
20-22	07	17.5
22-24	05	12.5
24-26	13	32.5
26-28	12	30.5
Total	40	
High risk BMI (Kg/m^2)		
28-30	06	60
30-32	02	20
32-34	01	10
34-36	01	10
Total	10	

Table 10 : Effect of Drugs in Test group

Total No. of Patients – 25

Follow-up (in days)	Before Treatment	After Treatment					
	0 Day	14th Day		28th Day		42th Day	
Clinical Feature	Total No. of Patients	Total No. of Patients	Improved %	Total No. of Patients	Improved %	Total No. of Patients	Improved %
Headache	23	12	47	06	73	04	82
Palpitation	24	13	45	07	70	03	88
Fatigability	24	10	58	05	79	05	79
Dizziness	25	15	40	07	72	03	88
Dyspnoea on exertion	23	11	52	06	74	04	82
Nocturia	25	08	68	07	72	06	76
Sleeplessness	25	12	52	08	68	04	84
Mental stress	23	09	60	07	69	05	78

Table 11: Effect of Drugs in control group

Total No. of Patients – 25

Follow-up (in days)	Before Treatment	After Treatment					
	0 Day	14th Day		28th Day		42th Day	
Clinical Feature	Total No. of Patients	Total No. of Patients	Improved %	Total No. of Patients	Improved %	Total No. of Patients	Improved %
Headache	25	15	40	06	76	03	88
Palpitation	25	13	48	07	72	04	84
Fatigability	25	12	52	06	76	05	80
Dizziness	25	11	56	08	68	05	80
Dyspnoea on exertion	25	10	60	07	60	04	84
Nocturia	22	09	52	06	72	04	81
Sleeplessness	24	10	58	07	70	05	79
Mental stress	23	11	52	06	73	05	78

Table 12: Effect of drugs on cholesterol in both groups

Control Group N = 25		Test Group N = 25	
0 Day	42th Day	0 Day	42th Day
Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)
208.8 + 27.5	207.8 + 24.7	220.08+ 35.3	212.4 + 28.3

Table 13 : Effect of drugs on Triglycerides in both groups

Control Group N = 25		Test Group N = 25	
0 Day	42th Day	0 Day	42th Day
Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)
136.4 + 31.8	131.6 + 31.6	145.7+ 26.7	131.2 + 29.0

Table 14 : Effect of drugs on Blood Urea in both groups

Control Group N = 25		Test Group N = 25	
0 Day	42th Day	0 Day	42th Day
Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)
23.96 + 4.01	24.56 + 3.8	28.84+ 3.5	26.36 + 3.3

Table 15 : Effect of drugs on Serum Creatinine on both groups

Control Group N = 25		Test Group N = 25	
0 Day	42th Day	0 Day	42th Day
Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)
1.28 + 0.38	1.26 + 0.36	1.37+ 0.4	1.13 + 0.4

Table 16 : Effect of drugs on Serum Bilirubin in both groups

Control Group N = 25		Test Group N = 25	
0 Day	42th Day	0 Day	42th Day
Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)
0.71 + 0.19	0.75 + 0.12	0.79+ 0.14	0.78 + 0.14

Table 17 : Effect of drugs on SGOT in both groups

Control Group N = 25		Test Group N = 25	
0 Day	42th Day	0 Day	42th Day
Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)
27.4 + 9.81	26.04 + 9.4	27.52+ 9.7	26.96 + 10.0

Table 18 : Effect of drugs on SGPT in both groups

Control Group N = 25		Test Group N = 25	
0 Day	42th Day	0 Day	42th Day
Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)	Mean + S.D. (mg/dl)
29.84 + 8.08	30.8 + 7.7	31.28+ 6.8	30.6 + 7.7

Table 19 : Effect of drugs on Systolic Blood Pressure in both groups

Control Group N = 25		Test Group N = 25	
0 Day	42th Day	0 Day	42th Day
Mean + S.D. (mm of Hg)	Mean + S.D. (mm of Hg)	Mean + S.D. (mm of Hg)	Mean + S.D. (mm of Hg)
156.8 + 15.7	125.8 + 10.9	151.5+ 9.5	123.8 + 6.0

Table 20 : Effect of drugs on Diastolic Blood Pressure in both groups

Control Group N = 25		Test Group N = 25	
0 Day	42th Day	0 Day	42th Day
Mean + S.D. (mm of Hg)	Mean + S.D. (mm of Hg)	Mean + S.D. (mm of Hg)	Mean + S.D. (mm of Hg)
97.4 + 2.9	81.7 + 4.6	93.32+ 2.5	82.6 + 3.1

Results and Discussion

Due to shortage of space, we are discussing the finding of tests group only as observations of the group are given tabulated form. During the course of study, it was observed that maximum number of cases i.e. 21 cases (42.00%) belonged to age group 45-55 years. Among the total patients 22 cases (44.00%) were males, while 28 cases (56.00%) were females (Table 1).

In present study, house wives were more than service class and business class persons. Business class subjects have more mental stress. Apart from that women do also suffer from life stress. Women are often victims of domestic violence exacerbate vulnerability to anxiety. Service class also have mental stress but less than business class (Table 2).

Majority of patients were non-vegetarian or with mixed diet habit (Table 3). Recent evidences suggest that saturated fat increases blood pressure as well as serum cholesterol. High fat intake (i.e. dietary fat representing 40% or over of the energy supply and containing a high proportion of saturated fats) has been identified as a major risk factor (Kumar *et al.*, 1990). Fish oil is a main source of omega-3 fatty acids and vegetable oil (eg. Sunflower oil) lowers STG, LDL and total cholesterol level and the blood pressure possibly through generation of nitric oxide (vasodilator) and reduces the risk of CHD. Green leafy vegetables due to its fibre content increases the bowel motility and reduces re-absorption of bile salts. Vegetables also contain plant sterol (sitosterol) which decreases the absorption of cholesterol. So that diet advised was effective in reducing blood pressure.

About 24% patients of total 50 cases took added salt in our study and patients had physical inactivity except routine physical work (Table 4 & 5). Studies suggested that such moderate physical activity may lower SBP by 9 to 11 mm of Hg (Schmotz *et al.*, 2008). Additional benefits of regular physical exercise including weight loss enhanced sense of well being, improved functional health status and reduced risk of cardiovascular disease and mortality from all causes.

From the opinion of Unani scholars we deduced that environmental factors implicated in the causation of hypertension include *umoor-e*-nafsaniyah (Tabri, 1995) (stress, anger and anxiety), obesity, excessive consumption of alcohol, physical inactivity, lack of exercise and evacuation. In fact, lack of exercise may cause *imtela or imtialee marz* (congestive disease) like hypertension. Exercise helps to excrete deranged matter without any harm to the body. Regular isotonic exercises produce modest drop in blood pressure in mild to moderate hypertensive subjects.

In our study 40% and 26% patients were smokers and tobacco chewers respectively (Table 6). There is evident that the influence of smoking is not only independent of but also addition with other risk factor such as family history of hypertension, physical inactivity, added salt intake, saturated fat intake, mental stress, smokers have more atherosclerosis than non-smokers, particularly in the aorta (Dey *et al.*, 1980).

Unani scholars asserted that *imtela-e-urooq* occurs due to increased amount of blood which increases the tension in the vessels. Due to atherosclerosis (*salabat-e-sharaeen*) in old patients which reduces arterial compliance that's also increases *imtela* and produces features of *imtela* or hypertension (Ahmad, 1980; Ahmad, 1983). We can deduce that from above account hypertension is a sanguineous temperament in our study. It is proved that hypertension is *damvi marz* (Table 8).

In our study patients were divided into two groups' i.e. low risk BMI and high risk BMI. 32.5% patients fell into BMI group 24-26 kg/m^2 and 30.5% laid down in BMI 26-28 kg/m^2 in low risk BMI. While in high risk BMI, 60% patients fell into BMI group 28-30 kg/m^2, 20% patients in 30-32 kg/m^2, 10% in 32-34 kg/m^2 and 10% in 34-36% BMI group respectively (Table 9).

Symptomatic improvement is always difficult to be evaluated in hypertensive patients. Test drugs have definite sedative effect (Chopra *et al.*, 1956). The combination therapy subside the clinical features of hypertension. Headache, palpitation, fatigability, dizziness, sleeplessness, mental stress, dyspnoea on exertion and nocturia improved in 82%, 88%, 79%, 88%, 84%, 78%, 88% and 76% cases respectively (Table 10).

In the present study, all patients' pursued life style modification with concomitant drugs used. Patients followed this line of treatment. They used low fat diet, especially cessation of saturated fat, increased physical activity and low sodium intake. It revealed significantly the reduction in total cholesterol and serum triglyceride from 220.08 $\pm$ 35.3 to 212.4 $\pm$ 28.3 and 145.7 $\pm$ 26.7 to 131.2 $\pm$ 29.0 respectively (Table 12 & 13). On the other hand recommended high fibre diet also reduces cholesterol level, because it contains sitosterol, which reduces the absorption of cholesterol and it also improves bowel motility. Thus, decrease re-absorption of bile salts.

It was revealed that there is no deviation from the normal limits at the end of study but improved as compared to previous reading. On applying paired t test it was found that blood urea decreases significantly from 28.84 $\pm$ 3.5 to 26.36 $\pm$ 3.3 while reduction in serum creatinine was significant from 1.37 $\pm$ 0.4 to 1.13 $\pm$ 0.4 at the end of study (Table 14 & 15). It showed that range remained within the normal limits but improved from previous reading. Likewise, serum bilirubin, SGPT, SGOT was estimated before and after the study. It was observed that serum bilirubin, SGOT and SGPT reduced insignificantly at the end of the study (Table 16, 17 & 18). It revealed that the test drugs have no adverse effects on liver and kidney rather it may have improved the function of these organs.

At the end of clinical trial, it was found that systolic and diastolic blood pressure reduces significantly from 151.5± 9.5 to 123.8± 6.0 and 93.32 ± 2.5 to 82.6 ± 3.1 respectively (Table 19 & 20). This highly significant result may be most likely because of the following reasons:

1. *Asrol* has sedative, tranquilising, anaesthetic, antiarrythmic, haemostatic, blood purifier effect (Chopra *et al.,* 1958; Kritkar *et al.*, 1996; Baitar, 1999).

2. *Filfil Siyah* has diuretic (*mudir-e-baul*), digestive, resolvent (*muhilal-e-warm*), nervine tonic (*muqqavi asab*), local anaesthetic (*mukhadir*) and bioavailability enhancer of the drug (Kritkar *et al.*, 1996; Khan, ynm; Hakim, 1991).

The test drugs have good effect because Asrol is *triyaq-e-samoom* (antidote), *musaffi-e-dam* (blood purifier), *habis dam* (haemostatic). Symptoms produced due to deranged humor, results imtila-bi-hasbil quwa relieved by *Asrol* because of above cited properties.While *Filfil Siyah* has *mudir-e-baul* (diuretic) action, which reduce *imtala* thus, it is suitable for hypertension.

Conclusion

To conclude, it may be deduced that the effect of the drugs on various clinical and biochemical parameters was highly significant statistically. The drugs were well tolerated and have no serious ill effect. Further advanced studies and research for better drugs combination need to be carried out in this field.

Summarising the above finding, a highly significant reduction in high blood pressure as well as in atherogenic lipid fraction i.e. total cholesterol and serum triglycerides is due to effective drug combination. This underlines the importance of an effective antihypertensive treatment to prevent cardiovascular complications associated with hypertension. Drug treatment as well as life style modification recommendations should be emphasised upon.

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A Critical Review of Some Unani Topical Dosage Forms – With Special Reference to Their Bases and the Procedures Used to Formulate Them

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Abstract

Unani system of medicine has various dosage forms including topical drugs for effective delivery of drug substances. Although most of the drugs intended to be used orally have been found effective, but some of the formulations of dermal dosage forms especially, Marham (Ointment), Zimaad (Paste) and Tila (Liniment) at occasions fail to produce their expected pharmacological and therapeutic effect. The failure has been mainly attributed to the erroneous processing of crude drugs and inappropriate selection of the bases and excipients that sharpens the ability of drug to go deep into skin and produce the desirable effects. An attempt has been made to explore and elaborate the possible reason of expected failure of some of Unani dermal formulations and to find out the possible solutions so that their therapeutic objectives could be achieved.

Key words: Topical Dosage Forms, Marham, Zimad, Tila, Skin permeability, Excipient

Introduction

The practice of topical dosage forms, especially the use of *Marham* (ointment), *Zimaad* (paste) and *Tila* (liniment), in Unani System of Medicine has been in vogue since ancient time. Preservation of mummies with the help of certain liquid and semiliquid preparations may be taken as the evidence of the use of Marham, Zimaad and Tila as a customary and social practice in ancient period. Hakeem Sharif khan [d, 1763], in his book 'Ilaj-ul-Amraz', has cited the use of ointment from the Hippocratic period (Khan, 1896). A large number of dermal formulations, mentioned in classical Unani literature, have been found beneficial in the pathological conditions, they have been mentioned for, but some of the preparations failed to demonstrate desirable results. This failure may be attributed to the factors such as skin's anatomical structure, temperament and its physiological aspect which were not taken into consideration during pre processing and pre-formulation stage and also the inappropriate selection of ingredients of formulation intended for dermal or trans-dermal use. Besides these factors, certain other pharmaceutical factors that play a key role in the efficacy of therapeutically effective ingredients have been ignored to a great extent. There is no need of specific discussion on the pharmacological and therapeutic effect of drugs on the skin surface only or on detached skin because they will be governed as per the rule for enteral dosage form (Idson, 1976). Actual problem arises when pathology lies in the epidermis

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or beneath it and there is no skin detachment. In such circumstances, drug molecule is needed to reach the site of pathology via dermal route.

Technicalities of Topical Dosage Form

Externally, the human skin is packed with a tough and thickened layer known as stratum corneum. At the molecular level, it comprises of three major components; protein, fat and water, out of which water molecules are less in number as compared to lipid ones. This layer possesses diverse physiological function. It is responsible for the development and protection of human life and opposes the influx and efflux of substances. Efflux of sweat and sebum through glandular duct is ongoing process but not through stratum corneum (Tregear, 1964). Hence, the major problem is permeation and diffusion of different forms of drug designed for external use. If the active ingredients are capable of getting penetrated through stratum corneum, they can produce the effect at the pathological site after penetration. This problem is not common in case of dermal dosage forms of mineral origin drugs, but it is frequently encountered in case of the formulations of plant drugs. This is due to the fact that quantity of therapeutically active component in plant drugs is very little as compared to the drugs of mineral origin. Due to this fact, crude form of plant origin drugs, mostly taken through oral route, get digested under the influence of gastrointestinal fluids and their active components are released and absorbed resulting in desired pharmacological effect. Since, in crude drugs as such do not follow the same kinetics as that of the active ingredients and fail to exhibit the similar pattern of absorption, distribution and excretion over the skin which is consistent with active ingredients. Therefore, the effect likely to be produced by the active ingredient cannot be expected from crude drugs. Hence, it is mandatory that only active principles should be used in topical dosage forms for the therapeutic purpose so that the problem of permeation and absorption can be overcome and consequently their pharmacological effects can be established (Barry, 2007).

In Unani Pharmacopoeia of compound drugs, less space has been given to topical dosage forms although syrups, distillates, decoctions and calcinates extracted form of indigenous drugs have been accommodated appropriately. On the contrary, in cases of ointments, paste and liniments, usually crude drugs have been used in powder form not withstanding the complete release of the active principles from the plant cells for permeation through the skin seems to be a difficult.

The active principle permeation through the skin either indirectly by sweat duct, sebaceous duct and hair follicles or directly by stratum corneum of intact skin plays major role in the determination of efficacy of dermal dosage forms. Both the pathways mentioned above, allow permeation of components of specific type and of particular size under special circumstances. Lipid soluble drugs have great capacity to diffuse through stratum corneum. Though water soluble drugs can also penetrate stratum corneum indirectly but they can't diffuse directly through the stratum corneum (Barry, 2007). The problem of less permeability of water soluble drugs can be over come by including certain skin penetration enhancers in excipients and additives.

The second most important issue in pretext of drug permeation through skin is that, particle of ten micron or less can diffuse through indirect route i.e. hair follicles and duct of sebaceous glands while particles up to three micron only can diffuse through direct route i.e. through stratum corneum but only in a condition where skin loses its resistance and power (Idson, 1976). This is seen when natural property of skin is changed which allows increase in skin hydration to such extent that bio-molecules of skin especially water molecules increase from 5-15% to 25% where the passive diffusion which is one of the most important process required for transfer of drug substance could be possible (Idson, 1976). Rate of passive diffusion depends upon condition of skin; age, blood circulation, temperature and its metabolism and also on quantity of active principles. Minor variation in these factors can accelerate the rate of passive diffusion. But these factors are effective only if particle size of active principle is of less than 10 micron and could retain at the site of application for such a duration within which hydration of skin and the mechanical process of passive diffusion can pursue in such a manner where therapeutically active principles can exhibit their effects. (Barry, 2007). For this purpose, in case of ointment, paste and liniment, we need a suitable base commensurating with the purpose of permeation at the site of disease and the release of the active principles, so that they can hydrate the skin for drug permeation and hence can produce therapeutic effect.

In Unani medicine, commonly used bases for the said dosage forms are plain water, plant distillate, vinegar, vegetable oils, fat, honey, bee-wax and emulsions. Two or more bases in combination can be used considering the therapeutic objectives and site of application of the formulations, a wide range of formulations of ointment, paste and liniment do not have an appropriate base combination giving rise to the elements of doubt about such preparations.

Problems Consistent with Topical Unani Dosage Form and Their Possible Solution

Topical dosage forms which are prepared by using water or distillate of plant drugs as a base, instead of hydrating the skin, may absorb water molecule from skin due to atmospheric temperature even if there is mucilaginous or gummy substances in the formulation. As a result, the drug will not come in contact with skin leading to failure of drug to reach the stage of permeation and absorption in effective manner. The other cause of poor efficacy of such formulations lies in the fact that the presence of water or distillate of plant drugs allows release of water soluble particle only from crude drug, while the rate of diffusion of water-soluble particles in the skin is very low, as compared to lipid-soluble particle. For example "Zimaad Kabid" which is used in hepatitis, includes *afsanteen, haasha, nagar motha, baranjasif, iklilul malik, gul-e-babuna, balchad, mako khushk, jadwar, mur makk and rasot* as ingredients. *Mur makki* and *rasot* have been included as gummy substances while *aab- e-mako* has been used as the base for preparation of this formulation (Kabeeruddin, 1938). But unfortunately this pharmaceutical preparation will neither produce skin hydration nor cause permeation of active ingredients.

Experts of Unani pharmacy often use vinegar and alcohol as a base in some formulations for topical use, probably due to the fact that vinegar and alcohol act as better solvent for various active ingredients as compared to water. These are better solvents for resinous substances and most varieties of lipid, thus allowing better penetration. But this is possible only when these bases which are volatile in nature, could be retained on the site of application for sufficient period of time. It does not appear to be feasible unless the formulation is prepared in a form that allows minimum evaporation where applied over the skin only, then its efficacy can be speculated.

In certain cases, physicians use honey as a base for topical preparations, so that drug could remain adhered to the base and induce response gradually. But use of honey as a base does not appear to be rational. Honey itself is water soluble, its ability to dissolve / solubilize the active ingredients of drugs is not appreciable. Besides, honey is also not able to produce hydration of desirable degree. As a result, active ingredients in honey base won't be able to reach the stage of penetration and absorption and hence, it will not serve the purpose for which it was included in the formulation. For example, "Tila-e-Mulazziz", a compound formulation prepared by using honey as a base, has ingredients viz. *kafoor, aqarqarhah* and *suhaga khaam* (Kabeeruddin, 1938). Practically, *kafoor* is lipid soluble and *suhaga khaam* is water soluble. On the other hand,

Aqarqarhah is a plant origin drug having different chemical constituents. Whether active principles of drugs like kafoor, aqarqarhah and suhaga khaam are soluble in honey is doubtful. Honey will release and allow them to penetrate the skin? It is also not clear that what amount of active constituents will be released by honey to allow them to penetrate the skin. Both the possibilities i.e. chances of solubility and the release of active ingredients appear to fiddling.

To prepare ointment and liniment, physicians use bees wax along with some other bases. Most of the experts believe that bees wax as a single absorptive base has the ability to absorb water molecules and can attach the water molecules to about half of its own weight. In the light of this characteristic feature of bees wax, its use as base will put hindrance in hydration of skin, as it will absorb the moisture and thereby arrest the penetration of active principle through the skin. That's why physicians do not prefer use of beeswax alone (as a base) for intact and healthy skin. But, for the treatment of skin diseases like septic wounds, abraded and injured skin, its use is found to be beneficial as drying of exudates would be the main motive of treatment in all such cases and hydration of skin would not be required. The beeswax in such cases will absorb the exudates on one hand and release the drug molecules on the other and thus will promote the process of healing. But due to certain complexities the use of beeswax alone as a base, is not in practice rather it is commonly used along with some fixed oil which gives several other pharmaceutical benefits.

Dermatological dosage forms for pathologies on intact skin or within the skin which are prepared in lipids or oils, not only make the skin hydration better but also allow easy penetration and absorption of lipid soluble drug, thus promoting their actions. But this is possible only when active principles are soluble in lipid or oil to a large extent. But if the drug substances remain suspended in lipid or oil base, then the expected pharmacological action and therapeutic effect can not be ascertained. For example "Zimad Khadar Jadeed", a topical dosage form containing *filfil siyah, aqarqarhah, qaranfal, farfiyoon, shoneez, zanjabeel* is being prepared in base of *roghan-e-gul* (Kabeeruddin. 1938). The active constituents of crude plant drug will hardly dissolve in oil base, *farfryoon* is soluble in oil but only when the oil is hot, therefore there are lead chances that this formulation will be able to produce any pharmacological effect. A little modification in pharmaceutical procedure of this formulation will help it absorption through skin and assure its efficacy. Firstly, *farfiyoon* should be dissolved in hot *roghan-e-gul* and 50% alcoholic extract of remaining plant drugs should be incorporated in the same base; mixed well to make a homogenous paste. In this way, the active principle, will be in a state to diffuse the skin and hence will exert the optimum pharmacological effect.

Similar condition is seen with “Zimad Khwab Aawar” which is prepared from the following ingredients: *kafoor, afyoon, zafraan, tukhm kaaho, gul nilofar,* and is prepared by using *roghan-e-gul, sirka* and *aab-e-kishneez* as the base. *Kafoor* is soluble in *roghan-e-gul*, *afyoon* in vinegar and *zafraan* in *aab-e-kishneez*. Moreover, it makes a strong coating over the skin that facilitates the process of skin hydration (Kabeeruddin. 1938). Therefore, this formulation, due to the solubility of its active principles and the ability skin to hydrate the skin seems to be therapeutically effective as drug contents will permeate the skin and exert their pharmacological effect.

Nowadays, while selecting the base for paste, ointment and liniment, experts of pharmaceutics advocate the use of mineral oils such as soft and liquid paraffin, especially in cases where pathology lies under the skin or within the skin. This will form a thick layer over the skin which will melt because of body temperature and hydrate the skin. But the major problem associated with such a base is its non-penetrating ability in the skinwhen used singly as a base. That’s why other bases like beeswax, oil etc. are also included along with them for better skin hydration, easy penetration and good therapeutic effects (Barry, 2007).

In the light of above discussion, it can be said that use of single base in dermal dosage forms is not appreciable because of the problem of inconsistent permeation and absorption of active principles, associated with single base. That’s why experts have used different combinations of the bases. Oil with beeswax, water with oil and vinegar with oil and beeswax are few important combinations that are frequently used in preparation of certain dermal dosage forms.

Among these combinations, water in oil emulsion as a base is considered appropriate for specific benefits and for selected dermal dosage forms when the pathology is present at skin surface or abraded skin, or when intended to be used over oily skin. But for the pathology under or within the intact skin, these emulsions as base are less useful as they form only light coating over skin which is insufficient for proper hydration of skin. Therefore, emulsions are used as a base in those conditions where pathology exists on skin surface or the continuity breached, because penetration of active principles through breached skin is similar to penetration through stomach and intestine. Although bases like water in oil emulsion are less used in Unani Medicine, but cosmetic products like cold creams are prepared in these types of bases as these are designed for protection of skin surface and for treating the pathology of skin. “Zimaad-e-Jarab Deegar” of Bayaz Kabeer, is used for infective scabies

where skin surface gets inflammed and ulcerated. This formulation is based on "*henna*" and prepared in the base of linseed oil and plain water which presents a picture of water in oil emulsion (Kabeeruddin, 1938). Because of being processed in emulsion base, it seems to be effective for skin surface pathology. The active principle of the compound will interact with ulcerated surface and hydration of skin with further help in permeation and thereby inducing the pharmacological effect.

Some of the formulations on account of having better combination of bases produce desirable pharmacological and therapeutic actions. For example, "Marham Nasoor" based on z*ard chob* and m*urdaar sang* is prepared by using beeswax and *roghan-e-gul* as base. It is used in the management of open and septic wounds (Kabeeruddin, 1938). This appears to be a complete and excellent ointment for the pathological condition, it is recommended for the beeswax contained in it will absorb the oozing exudates of ulcerated skin and *roghan-e-gul* will help in skin hydration that will ultimately result in better drug delivery and better therapeutic effect. Similarly, "Marham-e-Rusul" that contains *zangaar, murdaarsang* and *zarawand* is prepared by using *jausheer, behrozah, mur makki, kundur, muqil, ushq, rateenaj* with beeswax and olive oil as base (Khan, d. 1763, p. 1896). These gummy substances along with bees wax constitute a potent base for absorbing the exudates of ulcerated wound, while olive oil facilitates drug permeation hydrating in skin. That is why this formulation seems to be very useful in condition of ulcerated or septic wounds. The gunny substances have added value owing to possessing healing property.

Conclusion

In the light of above discussion, it may be concluded that the successful treatment through dermal dosage forms; ointment, paste and liniment, depends mainly on physicochemical properties of bases which will be selected by taking into account the site of disease, type of disease and type of ingredients. Permeation, absorption and metabolism of these forms are totally different from those of oral dosage forms. In case of dermal dosage forms, only active principles of ingredients are able to penetrate the skin. So, it would be better if only their active principles are used in the form of extracts. Bases should be selected on the basis of the site of disease and the nature pathological condition because skin hydration plays a major role in drug permeation. Therefore, use of fixed oil along with some suitable bases would be a preferred option. It seems essential to formulate or develop the formulation of topical

dosage forms in view of the solubility of active ingredients so that permeation and absorption of drugs could be speculated. With the condition of skin, intact or ulcerated, alteration in the bases is to be made as it will accelerate the absorption of exudates and promote the healing. Therefore, a critical review and thereafter editing and compiling of pharmaceutical methods and processing of ointment, paste and liniments is necessary in order to get the complete benefit from ancient Unani topical dosage forms which are mentioned in Classical Unani literature.

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Clinical Efficacy of a Unani Formulation in the Treatment of *Saman-e-mufrat* (Obesity)

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Abstract

randomized single blind placebo controlled trial was designed to evaluate the efficacy of Unani formulation viz *Ajwain desi/ Nankhwah* (*Trachyspermum ammi* L.), *Tukhme Suddab* (*Ruta graveolens* L.*), Zeera Siyah/Kamoon* (*Carum carvi* L.), *Marzanjosh* (*Origanum majorana* L.), *Bura Armani (Armeniac bole)* in the patients of *Saman-e-Mufrat* (Obesity). Total 30 patients were allocated randomly to Test and Control groups and were treated with Unani formulation and with placebo respectively for the period of 60 days. All the Patients were advised planned diet and 30 minutes brisk walk daily for the same duration and they were assessed for subjective and objective parameters. The data was statistically analyzed by Repeated Measures ANOVA with post test and Tukey-Kramer multiple comparison test, One-way ANOVA and Friedman test.

A significant improvement in intra group comparison was noted in objective parameters, (Body weight, Body Mass Index, Upper Arm Circumference, Waist Hip Ratio, Skin fold thickness). In inter group comparison the effect on UAC and WHR were significant while effect on body weight, BMI and Skin fold thickness was statistically not significant. The study revealed that the test drug is safe and effective for the management of obesity.

Key word: Obesity, *Saman-e-mufrat,* Body Mass Index, *Trachyspermum ammi* L.*, Ruta graveolans* L.*, Carum carvi* L.*, Origanum majorana* L.*, Arminiac bole.*

Introduction

Saman-e-mufrat (obesity) is one of the commonest and most prevalent diseases of affluent society of the world. The prevalence of obesity is consistently increasing day by day. It has become global epidemic and contributes to increasing burden of type-2 diabetes mellitus, cardiovascular diseases, hypertension, stroke, and eventually causing premature death worldwide. (Humes *et al.,* 2000; Mohan, 2005; Bray, 2004) Nevertheless, obesity epidemic is an actual and potential public health problem and possesses pronounced economic health consequences. Earlier, it was considered a state of excess adipose tissue mass or characterized by excessive accumulation of fat in the subcutaneous and deep tissue of the body, usually 20% or more of an individual's ideal body weight. (Longo *et al.,* 2012; Longe, 2005) But it is now defined in terms of the body mass index (BMI = weight in kilograms divided by height in meters square) and if BMI is

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greater than 25 kg/m^2, the person is considered to be overweight and if it is greater than 30 kg/m^2 the patients is called obese. (Longo *et al.,* 2012; Longe, 2005; Humes *et al.,* 2000; Neinstein, 2002; Souhami *et al*., 2002; Siegenthaler, 2007) over weightness/Obeseness (*Saman-e-mufrat*) result from an imbalance between energy intake and its expenditure. (Ferri *et al.,* 2012; Warner, 2003)

Historically, Greco Arab Physicians like *Buqrat* (Hippocrates), *Jalinoos, Ibn sina, Zakariya Razi, Ibn Nafis, Daud Intaki* and *Akbar Arzani* were well acquainted with *Saman-e-mufrat* and they have mentioned it in their treatises enormously in terms of its etiological factors, symptoms, signs, and complications. (Ibn Sina, 1929; Halim, 2005; Razi, 1991; Jurjani, 1996; Chandpuri, 1998; Antaki, 2010)

Ibn Sina especially pointed out that obese people are more prone to develop cardiac and cerebral complication like stroke, syncope, coma, palpitation, breathlessness, concealed haemorrhage and sudden death. (Ibn Sina, 1929; Halim, 2005) As per Unani philosophy *Saman-e-mufrat* develops due to increased *barid Akhlat* (cold humors) leading to imbalance in body humours resulting tendency to accumulate the *Akhlate fasida* particularly *maddae balghamiya* on different parts of the body. (Kabeeruddin, 2001)

The aim of treatment of obesity is to reduce body weight, Modification in risk factors such as decreasing daily calorie intake, increase physical activity and behavioural therapy are the non-pharmacological measure to achieve the goal. Indeed, life style modification is helpful for most obese patients, but in several circumstances pharmacological management of obesity is inevitable. Sibutramine (Fetergil/Leptos) Orlistat (Cobese/Lipocut), Rimonabant (Riomont/ Zimult), Diethylepropion (Anorex/Tapanil), are widely prescribed drugs in main stream of medicine. (Laurence *et al.,* 2006) But the long term use of these drugs produce several side effects. Sibutramine produces hypertension, tachycardia, headache, insomnia, constipation and dry mouth etc. Orlistat are reported to produce incontinence of urine, flatulence, and vitamins malabsorption and Rimonabant is reported to demonstrate adverse effects like nausea, dizziness, anxiety, and depression. (Laurence *et al.,* 2006). Therefore, long term use of these drugs could not possible. Bariatric surgery is recommended for the patients of morbid obesity but it also exhibited several post operative complications such as malabsorption, malnutrition and vitamins deficiency etc. Furthermore, it is quite painful procedure and associated with risks of infection, large disfiguring skin, depression and formation of blood clots eventually lead to dangerous circulatory problem and kidney failure. (Townsend, 2008)

Owing to high prevalence, multi factorial causes and life threatening complications of the disease and most importantly, the inability of contemporary system of medicine to deliver safe and effective drug management of obesity, warrants search of alternative treatment to alleviate such complex diseases of serious complications.

Unani system of medicine has a large number of single and compounds drugs which possess actions like *muhazzil* (Emaciatic), *muhallil* (Resolvent)*, mudir* (Diuretic)*, musakhkhin* (Endothermic) are being in use to the management of *Saman-e-mufrat* since ancient period. Some studies carried out in recent past demonstrated promising result and explored the potentiality of Unani drugs to be used as effective anti obesity agent. Now a days, the researchers have taken interest to investigate drugs with an aim to provide better alternate in the currently available drugs.

In view of above facts, a compound formulation which is recommended by *Ismail Jurjani* in *Zakhira khawarzam shahi* for the treatment of obesity, containing *Ajwain desi* (seed of *Trachyspermum ammi* L.), *Tukhme Suddab* (seeds of *Ruta graveolens* L.)*, Zeera siyah* (seeds of *Carum carvi* L.), *Marzanjosh* (*Origanum majorana* L.), *Bora Armani* (*Armeniac bole*) has been selected for study. (Jurjani, 1996) The ingredients of test formulation are endowed with *haar yabis* temperament and possess properties like *Mohazzil, Musakhkhin*, *Hazim, mushile balgham, Mulattif, and Mudir* etc. and it ameliorate the derangement of temperament leading to minimize *fasad* in *maddae bhalghamia* and is being effective in obesity.

As this combination appears to be quite rational in term of ingredient having actions warranted in the treatment of obesity, and has been in use by Unani physicians since long time but the efficacy of this time tested formulation has not been scientifically evaluated so far. Therefore, a single blind placebo controlled study was envisaged to find out efficacy of combination in the management of obesity on scientific parameters.

Methodology

The present clinical study was conducted in Department of Moalajat, National Institute of Unani Medicine Bangalore, from September 2010 to February 2012. Prior to the beginning of clinical trial, the research protocol was submitted to Ethical committee of National Institute of Unani Medicine and Ethical clearance was obtained from the committee. During screening a total of 44 patients were registered for the study but 7 patients did not fulfil inclusion criteria hence

excluded from the study and remaining 37 patients were randomly allocated into test and placebo groups. Four patients from test group and three patients from placebo group were lost to follow up, leaving behind 20 patients in Test and 10 patients in Placebo group who completed the course of treatment.

Patients fulfilling the inclusion criteria were provided an information sheet having details concerning the nature of the study, the drug to be used with the mode of administration and method of treatment. Patients were given sufficient time to go through the contents of informed consent sheet. The patients were left free to ask whatever the query regarding the study and if they agreed to be enrolled in the study, they were requested to sign the informed consent form. The patients who did not fulfil inclusion criteria were excluded from the study.

The blue print of the study was conceptualized in material and methods which can be described under few headings for convenient comprehension.

1. Criteria for selection cases

   a) Inclusion criteria

   - Patients with *Saman-e-mufrat* (Obesity) of either sex.
   - Patients belonging to 15-60 years of age.
   - Patients having BMI between 25- 35kg/m^2.
   - Patient able to participate in the study and ready to follow the instructions and sign the consent form.
   - Obese patients having associated symptoms like restricted movement, joints pain, Weakness and letharginess, Dyspnoea, and Palpitation.

   b) Exclusion criteria

   Physiological status

   - Patient below the age of 15 and above the age of 60.
   - Pregnant and lactating women.

   Pathological status

   - Patients having cardiovascular disease, severe renal disease and severe hepatic disease and hypothyroidism.
   - Patients having BMI > 35 kg/m^2.

- Patients who refuse to give the written informed consent for the study.

2. Selection of subjects

Known cases of *Saman-e-mufrat*, having the symptoms like increasing body weight, restricted movement, joints pain, breathlessness and palpitation etc. were taken up from OPD and IPD section of NIUM hospital and subjected to lab investigations.

3. Investigations

Investigations like Lipid Profile, Haemoglobin percent, Total Leucocyte Count, Differential Count, Kidney and Liver function tests were done in all patients before starting the trial and also after completion of the study. However thyroid profile, Fasting & Post Prandial blood sugar and ECG were done prior to start the trail to exclude the patients suffering from other diseases.

4. Study design

The study was designed as a randomized single blind placebo controlled clinical study.

5. Sample size

The sample size was fixed as 30 patients.

6. Duration of protocol therapy

The treatment period in both Test and Placebo groups was fixed as 60 days.

7. Test drugs

The ingredients of test drugs are as follows:

1.	*Ajwain desi* (*Trachyspermum ammi* L.)	1 part
2.	*Tukhme Suddab* (*Ruta graveolens* L.)	1 part
3.	*Zeera siyah* (*Carum carvi* L.)	1 part
4.	*Marzanjosh* (*Origanum majorana* L.)	4 parts
5.	*Bora Armani (Armeniac bole)*	4 parts

8. Method of preparation, dosage and mode of administration of Test drug

Good quality single drugs were obtained from the pharmacy of National Institute of Unani Medicine, Bangalore. Before preparing the formulation, the drugs were properly identified to ascertain their originality. The ingredients were cleaned by weeding out unwanted material and separated impurities, and then powdered.

9. Administration of Test drug &placebo

The Test drug was administered orally in Group-A in the dosage 5gm once a day with cane vinegar 7.5ml just after breakfast for the period of two months. The placebo (containing wheat floor) was given in Group B in the dosage of 5 gm once a day just after breakfast for the period of two months. Along with the drugs, all the patients (in both groups) were recommended 1200-1800 k cal/day diet and also advised moderate physical exercise (20-30 minutes brisk walk) during the course of the study. (Longo *et al.,* 2012)

10. Follow up during treatment

Sixty days study was divided into 4 visits as follow up which were made at an interval of 15 days each. At every visit, patients were asked about the progression or regression in their symptoms and were subjected for examination to assess clinical findings.

11. Efficacy assessment

The assessment of efficacy in the test and placebo groups was based on subjective and objective parameters. Subjective parameters include symptoms like, restricted movement, joints pain, weakness & letharginess, dyspnoea and palpitation. Objective parameters are anthropometric measurements and laboratory investigations of the patients suffering from *Saman-e-mufrat*. Both subjective and objective parameters were assessed at every visit, while lipid profile was carried out before and after the completion of trial.

As subjective parameters differ in severity from patient to patient, therefore an arbitrary grading scale Total Sign and Symptom Score (TSSS) were adopted for appropriate assessment and statistical evaluation. The severity of 5 different signs and symptoms (Restriction of movement, Joints pain, Weakness & letharginess, Dyspnoea, Palpitation) were rated on a 4 point scale (0, absent; 1, mild; 2, moderate; 3, severe).

After the completion of treatment, the pre and post treatment values or scores of different parameters (subjective and objective) were assessed and were subjected to comparison and statistical analysis.

12. Objective Parameters

- Weight in kilogram
- Body mass index (BMI)
- Skin fold thickness.
- Upper arm circumference.
- Waist and hip ratio.
- Lipid profile.

13. Withdrawal criteria

a) Patients who fail to follow the protocol

b) Any adverse reaction or adverse event noticed by the patients/ investigators

c) Patients who were drug defaulters.

14. Safety Assessment

In order to assess safety of test drug LFT, RFT, Haemogram (Hb%, TLC, DLC & ESR) were carried out before and after treatment in both groups.

(a) Criteria for safety evaluation

No occurrence of any adverse effect or reaction during the treatment period.

(b) Adverse drug reaction documentation

Any adverse event or reaction appearing during the study either in Test or Placebo group was recorded.

15. Documentation

The case report forms and consent forms properly documented throughout the study and were submitted to the Deptt. of *Moalajat* after completion of the study.

16. Statistical analysis

At the end of study all the results were tabulated and statistically analyzed by Friedman test,

Kruskal-Wallis test with Dunn's multiple comparison tests repeated major ANOVA, one-way ANOVA with post test, Tukey-Kramer multiple comparison test and paired t test.

Results

Demographic data and effect of Test drug and Placeboon subjective parameters are depicted in Table (1) & (2).

Body weight

The mean score of body weight, in placebo group was 77.12 kg on 0 day, 76.86 on 15th day, 76.41 kg on 30th day, 76.13 kg on 45th day and 75.76 kg on 60th day, whereas in test group it was 80.5 kg on 0 day, 79.36 kg on 15th day, 78.44 kg on 30th day, 77.34 kg on 45th day and 76.37 kg on 60th day of treatment. (Table 3) In placebo group it was significant on 30th day with respect to day 0 ($p<0.01$), on 45th day with respect to day 15 ($p<0.01$) and on 60th day with respect to day 30($p<0.05$) and in Test group it was extremely significant on 15th day ($p<0.001$) with respect to 0 day, whereas it was not significant in inter group comparison ($p>0.05$). However, the body weight was reduced in both groups.

Body Mass Index

The mean of BMI of Placebo group was 31.08 kg/m^2 on baseline, 30.98 kg/m^2 on 15th day, 30.80 kg/m^2 on 30th day, 30.68 kg/m^2 on 45th day and 30.52 kg/m^2 on 60th day, whereas in Test group it was 30.56 kg/m^2 on 0 day, 30.11 kg/m^2 on 15th day, 29.77 kg/m^2 on 30th day, 28.9 kg/m^2 on 45th day and 28.97 kg/m^2 on 60th day of treatment (Table 3). In placebo group it was significance 30th day ($p<0.05$) with respect to day 0, on 45th day ($p<0.05$) with respect to day 15th and on 60th day ($p<0.05$) with respect to day 30th. In Test group it was significant on 45th day ($p<0.001$) with respect to test day 0, on 45th day ($p<0.001$) with respect to day 15th, on 45th day ($p<0.05$) with respect to test day 30th. The Inter group comparison was not significant ($p>0.05$).

Upper Arm Circumference

The mean UAC of placebo group was 31.28 cm. on baseline, 31.25 cm. on 15th day, 31.0 cm on 30th day, 30.75 cm. on 45th day and 30.6 cm. on 60th

day. Whereas, in test group UAC was 32.3 cm. on 0 day, 31.75 cm. on 15th day, 31.01 cm. on 30th day, 30.46 cm. on 45th day and 29.85 cm. on 60th day of treatment (Table No.-3). In placebo group it was significant on 45th day ($p<0.05$) with respect to day 0, on 60th day ($p<0.01$) with respect to day 15th, In test group significant on 15th day ($p<0.01$) with respect to test day 0, on 30th day ($p<0.001$) with respect to test day 15th, on 45th day ($p<0.01$) with respect to test day 30th, on 60th day ($p<0.01$) with respect to test day 45th. The Inter group comparison was also significant ($p<0.05$).

Waist Hip Ratio

The mean of WHR in placebo group was 1.01 on baseline, 1.01 on 15th day, 1 on 30th day, 0.99 on 45th day and 0.98 on 60th day. Whereas, in Test group, mean WHR was 1.02 on 0 day, 1 on 15th day, 0.97 on 30th day, 0.94 on 45th day and 0.93 on 60th day of treatment (Table No.-3). In placebo group it was significant on 45th day ($p<0.01$) with respect to placebo day 0, on 45th day ($p<0.05$) with respect to placebo day 15th, In test group significant on 30th day ($p<0.01$) with respect to test day 0, on 45th day ($P<0.001$) with respect to test day 15th, on 60th day ($p<0.01$) with respect to test day 30th. The Inter group comparison was also found significant ($p<0.05$).

Skin Fold Thickness

The mean of skin fold thickness in placebo group was 96.9 mm on baseline, 96.4 on 15th day, 94.8 mm on 30th day, 93.1 mm on 45th day and 91.6 mm on 60th day. Whereas, in test group skin fold thickness was 105.67 mm on 0 day, 102 mm on 15th day, 97.62 mm on 30th day, 94 mm on 45th day and 91.42 mm on 60th day of treatment (Table No.-3). In placebo group it was significant on30th day ($p<0.05$) with respect to placebo day 0, on 45th day ($p<0.001$) with respect to placebo day 15th and on 60th day ($p<0.001$) with respect to placebo day 30th. In test group, it was significant on 15th day ($p<0.001$) with respect to test day 0, on 30th day ($p<0.001$) with respect to test day 15th, on 45th day ($p<0.001$) with respect to test day 30th, and on 60th day ($p<0.001$) with respect to test day 45th. The Inter group comparison was not significant ($p>0.05$).

Serum Cholesterol

The baseline mean value of serum cholesterol was 185.95 mg/dl in test group and 180.8 mg/dl in placebo group. After completion of treatment mean value of serum cholesterol was observed 192.55 mg/dl in test group and 196.8 mg/dl in placebo group. For statistical analysis paired t test for intra group comparison

was done, significant ($p<0.05$) improvement was observed in placebo group with respect to day 0, but in test group it was found not significant. ($p>0.05$) Kruskal-Wallis post test with Dunn's Multiple pair comparison test was done for inter-group comparison, no significant improvement ($p>0.05$) was observed in test group. (Table No.-4)

Serum Triglycerides

The baseline mean value of serum triglycerides was 147.35 mg/dl in test group and 151.3 mg/dl in placebo group. After completion of treatment mean value of serum triglycerides was observed 128.35 mg/dl in test group and 159.9 mg/dl in placebo group. For statistical analysis paired t test for intra group comparison was done, no significant ($p>0.05$) improvement was observed in placebo group but it was not quite significant in test group ($p=0.057$). Kruskal-Wallis post test with Dunn's Multiple pair comparison test was done for inter-group comparison, no significant improvement was observed ($p>0.05$) (Table 4).

HDL-Cholesterol

The baseline mean value of HDL-Cholesterol was 41.25 mg/dl in test group, and 40.2 mg/dl in placebo group, after compilation of treatment mean value of HDL-Cholesterol 41mg/dl in test group and 39mg/dl in placebo group. For statistical analysis paired t test for intra group was done, no significant improvement was observed in placebo group and test group ($p>0.05$). One-way ANOVA comparison test was done for inter group comparison, no significant improvement was observed ($p>0.05$) (Table 4).

Safety Studies

In the study safety parameters (Haemogram, TLC, DLC, ESR, LFT & RFT) were also assessed before and after the treatment. The safety markers were remained normal before and after treatment. (Table 5)

Table 1 : Demographic Data of patients in Test and Placebo group n = 30

	n	Fp%		N	Fp%
Age group			Dietary Habit		
15-29	15	50%	Vegetarian	5	16.6%
30-44	14	46.6%	Mixed Diet	25	83.3%
45-60	1	3.3%			
Gender			Family History		
Male	19	63.3%	Positive	19	63.3%
Female	11	36.6%	Negative	11	36.6%
Marital status			Duration of Illness		
Married	29	80%	0-4 years	22	73.3%
Unmarried	6	20%	5-8 years	4	13.3%
			9-12 years	4	13.3%
Socioeconomic Status*			Mizaj		
Grade-I	1	3.3%	Balghami	24	80%
Grade-II	10	33.3%	Damvi	6	20%
Grade-III	19	63.3%	Safravi	0	0%
Grade-IV	0	0%	Saudavi	0	0%

(*According to Kuppa Swami Scale)

Table 2 : Effect of Test drug and Placebo on Subjective Parameters

(Test group n = 20, Placebo group n = 10)

Parameters	Group	0 day	15 days	30 days	45 days	60 days
Restriction of movement	Placebo	2 (0,2)	2 (0,2)	2 (0,2)	2 (0,2)	1 (0,2)
	Test	2 (1,3)	2 (1,3)	1(1,2)	1(0,2) a, b	0 (0,1) a, b, c, d, e, f, g
Joints pain	Placebo	2 (1, 3)	2 (1, 2)	2 (1, 2)	1 (1, 2)	1 (0, 2)
	Test	2 (1, 3)	2 (1, 3)	2 (1, 2)	1 (0, 2) a, b, d	0 (0,1) a, b, c, d, e, f
Weakness and lethargy	Placebo	2 (1, 3)	2 (1, 3)	2 (1, 3)	1 (1, 2)	1 (1, 2)
	Test	2 (1, 3)	2 (1, 3)	2 (1, 3)	1 (0, 2) a, b, c	1 (0, 2) a, b, c, d, e, f
Dyspnoea	Placebo	1.5 (1,3)	1.5 (1, 3)	1 (1, 2)	1 (1, 2)	1 (0, 2)
	Test	2 (1, 3)	1 (1, 2)	1(0, 2)	1 (0, 1) a	0 (0, 1) a, b, c, d, e, f, g
Palpitation	Placebo	1 (0, 2)	1 (0, 2)	1 (0, 2)	1 (0, 2)	0 (0, 1) a
	Test	1 (1, 2)	1 (1, 2)	1 (0, 2)	(0, 1) b, c	(0, 1) b, c, d, e

P<0.01 with respect to test day 0, b- P<0.01 with respect to test day 15,
P<0.01 with respect to test day 30, d- P<0.001 with respect to placebo day 0,
P<0.001 with respect to placebo day 15, f- P<0.001 with respect to placebo day 30,
P<0.001 with respect to placebo day 45.

Table 3 : Effect of Test Drug Formulation on Objective Parameters

(Test group n = 20, Placebo group n = 10)

Parameters	Group	0 day	15 days	30 days	45 days	60 days
Weight	Placebo	77.12 ± 2.01	76.86 ± 1.98	76.41 ± 2.03a	76.13 ± 2.08a, b	75.76 ± 2.15a, b, c
	Test	80.5 ± 2.51	79.36 ± 2.54d	78.44 ± 2.50d	77.34 ± 2.46d	76.37 ± 2.49 d
BMI	Placebo	31.08 ± .67	30.98 ± .68	30.80 ± .69a	30.68 ± .69a, b	30.52 ± .67a, b, c
	Test	30.56 ± .41	30.11 ± .42	29.77 ± .43	28.9 ± .60d, e, f	28.97 ± .42d, e, f
UAC	Placebo	31.28 ± .53	31.25 ± .53	31 ± .48	30.75 ± .52a	30.6 ± .55a, b
	Test	32.3 ± .46	31.75 ± .45c	31.01 ± .46c, d	30.46 ± .48c, d, e	29.85 ± .48c, d, e, f, g
WHR	Placebo	1.01 ± .02	1.01 ± .02	1 ± .02	0.99 ± .02 a, b	0.98 ± .02a, b
	Test	1.02 ± .02	1 ± .017	0.97 ± .016c	0.94 ± .016c, d	0.93 ± .015c, d, e, f
Skin fold thickness	Placebo	96.9 ± 4.018	96.4 ± 4.13	94.8 ± 4.07a	93.1 ± 4.04a, b	91.6 ± 4.03a, b, c
	Test	105.67 ± 3.54	102 ± 3.42d	97.62 ± 3.4d, e	94 ± 3.53d, e, f	91.42 ± 3.46d, e, f, g

a. <0.05 with respect to placebo day 0,
b. P<0.01 with respect to placebo day 15,
c. <0.01 with respect to test day 0,
d. P<0.001 with respect to test day 15,
e. P<0.01 with respect to test day 30,
f. P<0.01 with respect to test day 45.
g. P<0.001 with respect to test day 45.

Table 4 : Effect of Test drug and Placebo on Lipid profile

	Group	B.T.	A.T.
Serum Cholesterol	Placebo	180.8±6.79	196.8±9.48a
	Test	185.95±6.76	192.55±7.22b
Serum Triglyceride	Placebo	151.3±20.81	159.9±22.76a
	Test	147.35±11.23	128.35±8.59b
HDL- Cholesterol	Placebo	40.2±1.51	39±1.19a
	Test	41.25±1.34	41±1.59b

a. P<0.05 with respect to placebo day 0, b. P<0.001 with respect to placebo day 15

Table 5 : Safety Assessments for Test

(n = 20) Placebo group (n = 10), Baseline vs. 60th day

Parameters		Test group		Placebo group	
		BT	AT	BT	AT
		Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM
Hb%		12.86 ± 0.48	12.92 ± 0.45	13.03 ± 0.586	11.9 ± 0.735
TLC		12302 ± 3840.8	8457.5 ± 388.54	9160 ± 708.04	8240 ± 384.19
DLC	P	57.1 ± 1.478	56.6 ± 2.65	58.1 ± 2.04	58.1 ± 2.04
	L	36.75 ± 1.515	37.2 ± 2.37	35.9 ± 1.88	35.9 ± 1.88
	E	3.75 ± 0.279	4 ± 0.333	3.6 ± 0.221	3.6 ± 0.221
	M	2.4 ± 0.245	2.3 ± 0.36	2.4 ± 0.16	2.4 ± 0.16
	B	0 ± 0.00	0 ± 0.00	0 ± 0.00	0 ± 0.00
ESR		22.2 ± 2.88	22.7 ± 3.68	20.3 ± 2.82	18.2 ± 4.96
AST		30.4 ± 3.59	26.2 ± 2.23	27.2 ± 4.69	26.8 ± 3.88
ALT		24.4 ± 1.93	20.9 ± 1.13	21.5 ± 2.40	21.4 ± 2.36
S. Creatinine		0.835 ± 0.031	0.835 ± 0.027	0.81 ± 0.03	0.82 ± 0.02
Blood Urea		21.3 ± 1.138	22.5 ± 1.087	23.1 ± 1.64	24.7 ± 1.96

Discussion

Obesity is a disease of imbalance between energy intake and energy expenditure resulting in fat deposition inside the body which is responsible for various pathological changes and eventually causes ischemic heart disease, hypertension, diabetes mellitus, mild exertional dyspnoea, osteoarthritis etc. The treatment of obesity therefore mainly revolves around the management of weight reduction. According to Unani philosophy the main culprit of *Saman-e-mufrat* is *ijtemae akhlate ghleeza* (accumulation of morbid humours) leading to derangement of temperament particularly due to *ghalbae balgham*.Hence, any drug which possesses properties like *Muhallil, Muhazzil, Mullattif, Mudir, Qatae bhalgham, Qatae Akhlate ghaleeza* can ameliorate the derangement of temperament by evacuating *fasid maddae bhalghamia* and thereby effective in the management of obesity.

The administration of Test drug brought about significant reduction in the subjective and objective parameters consorted with the patients of obesity, demonstrating that the test combination is effective in relieving the symptoms associated with obesity and reducing body weight. These effects are

probably due to the diverse action of ingredients of Test formulation. Some of the ingredients of the test drug have been reported to possess important pharmacological actions that directly or indirectly support our contention regarding efficacy of test drug. *Ajwain desi* (*Trachyspermum ammi* L.), *Tukhme Suddab* (*Ruta graveolens* L.*), Zeera siyah* (*Carum carvi* L.), *Marzanjosh* (*Origanum majorana* L.), *Bora Armani* posses diverse pharmacological action like *Muhallil, Muhazzil, Mullattif , Mudir, Qatae bhalgham and Qatae akhlate ghaleeza* and endowed with *haar yabis* (hot & dry) (Ibn Baitar, 2000; Ibn Sina, 1929; Najm-ul-Ghani, 1927; Kabeeruddin, 2010; Ibn-ul-Quff, 1986). Thus these drugs act in the same line that has been mentioned above, in ameliorating symptoms of obesity.

It appears that the combined effect of the different constituents of the test drug produced anti obesity effect and or the combined effect of the constituents of the test drug modified the disease process, consequently improved various symptoms of obesity. As a result body weight, body mass index, upper arm circumference, skin fold thickness and waist hip ratio showed improvement up to some extent. An improvement in almost all the subjective as well as objective parameters clearly indicated anti obesity effect of Test drug. It is likely that, the different properties of ingredients of the test drug may have complemented each other to make suitable changes in the adipose tissues to improve its functioning. The effect on reducing body weight in placebo group may be due to strict dietary restriction and moderate exercise which was advised in both groups. Further, in test group more significant improvement was due to action of ingredients of test formulation, particularly the *Muhazzil*, and *Qatae balgham* effect of *zeera siyah*, (Najm-ul-Ghani, 1927; Ghulam Nabi, 2007) *Muhallil* effect of *tukhame suddab* (Ibn Sina, 1929; Ibn Ibrahim Magharibi, 2007), *Mulattif* action of *Marzanjoosh* (Ibn Hubal Baghdadi, 2005, Najm-ul-Ghani, 1927) and *Qateh akhlate ghaleeza* properties of *Bora Armani* (Ibn Baitar, 2000; Ibn Sina, 1929; Kabeeruddin, 2007; Najmul Ghani, 1927; Ibn-ul-Quff, 1986). The varied properties of above drugs complement each other and facilitate the anti obesity effect of test formulation.

Conclusion

In the present study, test drug exhibited overall improvement in the symptoms of the disease and was found effective in the management of Obesity without demonstrating any adverse effects as the safety markers (Haemogram, LFT and RFT) were remained within limit after completion of the course of the treatment.

On the basis of above result and discussion, it can be concluded that Unani formulation *Ajwain desi* (*Trachyspermum ammi* L.), *Tukhme Suddab* (*Ruta graveolens* L.)*, Zeera* siyah (*Carum carvi* L.), *Marzanjosh* (*Origanum majorana* L.), *Bora Armani* (*Armeniac bole*) is quite effective and safe in the treatment of *Saman-e-mufrat*. However, other aspect of Test formulation should also be explored, so that untapped potential of the test drug could be utilized to provide complete and safe remedy for treatment of *Saman-e-mufrat* (Obesity).

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Clinical Evaluation of a Unani Pharmacopoeial Formulation, Khameera Sandal Sada, in Zaght al-Dam Qawi Ibtidai (Primary Hypertension)

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Abstract

Zaght al-Dam Qawi (Systemic Hypertension) is a clinical condition characterized by persistent rise in arterial blood pressure. It is the commonest cardiovascular disorder, posing a major public health challenge to population in socioeconomic and epidemiological transition. In Unani system of medicine the term hypertension has not been described as such and the term *Zaght al-Dam Qawi* is adopted as a translation of hypertension. In classical literature of Unani medicine most of the clinical features of *Zaght al-Dam Qawi* (hypertension) are mentioned under the heading of *Imtala bi hasbil auiya.* The objective of the present study is to evaluate the efficacy of Unani formulation, Khameera Sandal Sada, in the management of *Zaght al-Dam Qawi Ibtidai* on modern parameters. The study was a single blind randomized standard control trial with the test and control drug treatment.

Key words: *Zaght al-Dam Qawi*; Hypertension; Khameera Sandal Sada, Unani Medicine*, Imtala bi hasbil auiya.*

Introduction

Zaght al-Dam Qawi (Systemic hypertension) is the most common cardiovascular disorder. It is a chronic condition of concern due to its role in the causation of coronary heart disease, stroke and other vascular complications. It is one of the major risk factors for cardiovascular mortality, which accounts for 20-50 percent of all deaths (Park, 2005).

In classical literature of Unani medicine, the term hypertension has not been used as such by Unani physicians and the term *Zaght al-Dam Qawi* was adopted by the Unani authors as a translation of hypertension. Ancient Unani scholars used a term *Imtala* to describe a condition in which normal or abnormal fluids are too much accumulated in the body producing certain type of symptoms.

The eminent physicians of Unani system of medicine like Abbas Majoosi in Kamilus Sana and Ibne Sena (980-1037AD) in his most famous medical text Al-Qanoon give a comprehensive description of this condition (Majoosi, 1889; Ibn-Sina, 1930).

Ibne Sena and Abbas Majoosi have described the *Imtala* in this way that excess of food, alcohol, rest, and lack of exercise result in accumulation of waste products in our body, whether *Mahmooda* (Beneficial) or *Ghair-mahmooda* (Non beneficial), both are toxic for the body. The accumulation of

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these waste products results in increase in blood volume, Tamaddud urooqi (Vascular distension) and increase in intravascular pressure. The Unani scholars had mentioned the types of imtala as: *Imtala bi hasbil auiya* and *Imtala bi hasbil quva.* The clinical symptoms of *Imtala bi hasbil auiya* described by the Unani physicians are very similar to that of hypertension. Literally '*Imtala'* means engorgement and fullness of the body with madda (material). (Kabeeruddin, 1938) Technically, it means there is accumulation of normal or abnormal fluids in the body.

The prevalence of hypertension varies considerably among and within population. In general, societies in which adulteration and industrialization are advanced have a higher prevalence of elevated blood pressure than less developed societies (Myron, 1989). In western countries, nearly 50 percent of all persons develop hypertension some time in their span of life and one-fourth of all deaths in the elderly are due to one of the complications of hypertension. In India the overall incidence of hypertension in the population is stated to vary from 1 to 4 percent (Prasad, 1997).

The idiopathic hypertension is called as essential or primary hypertension whereas with a specific is called as secondary hypertension. About 95% of cases are of the primary hypertension and about 5% cases belong to secondary hypertension. (Cotran *et al.,* 1989; Mac Sween *et al.,* 1992)

The clinical features usually associated with *Zaght al-Dam Qawi Ibtidai* are headache, especially in the morning, fatigue in the evening, palpitation, breathlessness, sleeplessness flushing of the face and sometimes epistaxis. These symptoms may or may not be present in all the cases. The complications of hypertension affect the heart, kidney, eye and nervous system. Hypertensive patients are prone to renal failure, peripheral vascular diseases. Cerebrovascular diseases and coronary artery diseases are the most common causes of death in hypertension (Kumar & Clark, 2002).

Methodology

The present study has been undertaken in the department of Moalejat and patients were selected from Hospital, National Institute of Unani Medicine, Bangalore, Karnataka, India. Patients were clinically examined and required hematological, biochemical investigations were carried out. A written informed consent was obtained from all the patients. The duration of study was two years and the patients were enrolled from 2006 to 2007.

Selection Criteria

Patients of both sexes selected randomly, in the age group of 18-70 of years with all grades (mild, moderate, severe) of Primary hypertension were enrolled in the study. Patients with severe anaemia, lactating mothers, pregnant ladies, Patients with chronic Renal failure, Myocardial Infarction, Ischemic Heart Disease, valvular Heart diseases, neurological disorders and cases of malignant hypertension were excluded from the study.

Study Design

The study was a single blind randomized standard control trial with the test and control drug treatment. Total 60 patients randomly selected were divided into two groups i.e Group A composed of 30 patients who were treated with test drug, Khameera Sandal Sada, in dosage of 7 gm twice a day for two months. Group B also consists of 30 patients and was treated with standard control drug "Atenolol" in the dosage of 50 mg once a day for two months. All the patients were assessed for subjective and objective parameters.

Statistical Analysis

The results were analyzed statistically using student't' test and wilcoxon matched pair test.

Selection of Test Drug

The best quality drugs were provided by the pharmacy of National Institute of Unani Medicine. Before preparing the test drug formulation, all of the ingredients were properly identified to ascertain their originality. The sandalwood powder was soaked in rose water for about 24 hours. This mixture then boiled up to the time it become half, than sugar was added and boiled and stirrer the substance with pastel till it becomes in the form of khameera 7 g of drug twice a day was given for two months.

Findings of effectiveness of test and control drugs were recorded on a specially designed case report form and the inference was made by appropriate statistical analysis.

Composition of Khameera Sandal Sada

Ingredients	*Used as*	*Quantity*
Sandal Safaid (*Santalum album* L.)	(Burada or Fine powder)	75 gm
Gul-e-Surkh (*Rosa damascena* L.)	(Arq or Distillate)	500 ml
Sugar		1 kg

(Kabeeruddin, 1938)

Observations

It was observed that the incidence of hypertension is higher in age groups between 49-78 years and least common in the age group between 18-28 years. (Fig. 1)

The disease was found more common in females than in males. As there was more number of female patients registered which were above the age of 50 years, the data show high incidence in females. (Fig. 2) The data shows the highest incidence of hypertension in damvi mizaj patients followed by balghami mizaj, sudavi mizaj and safravi mizaj (Fig. 3) which is supported by (Majoosi, 1889; Ibn-Sina, 1930; Ibn-e-Rushd, 1980; Jurjani, 1903).

The data reveals the high incidence of hypertension in middle income group followed by low income group and high income group (Fig. 4) which is supported by Pai and Halani (Pai and Halani, 1980). The data shows that incidence of hypertension is high in stressed subject (58.3%) than in otherwise (41.7%) (Fig. 5).

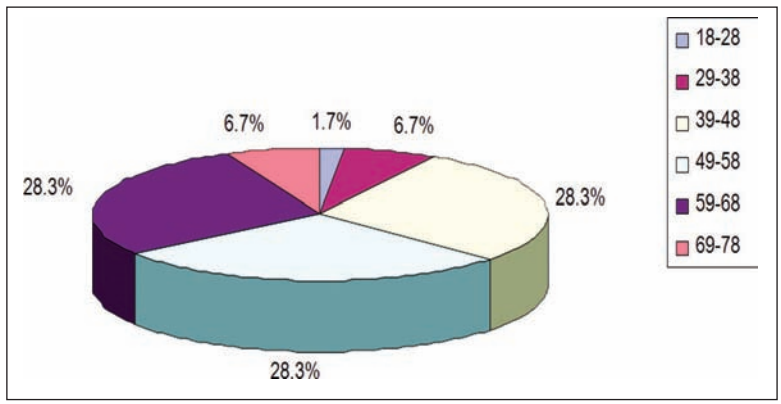

Fig. 1 : Distribution of Patients according to Age

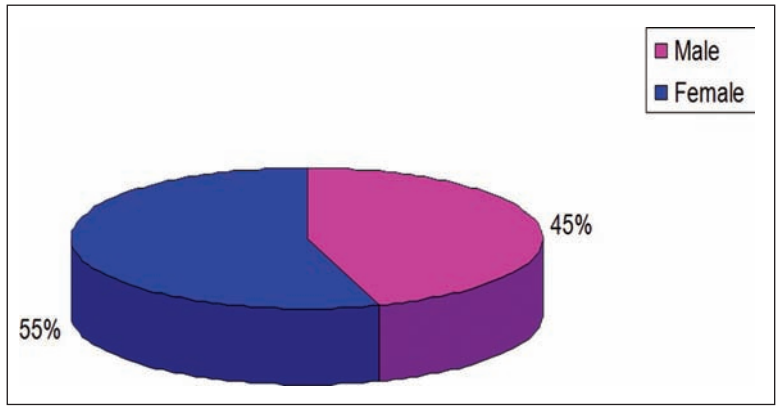

Fig. 2 : Distribution of Patients according to Sex

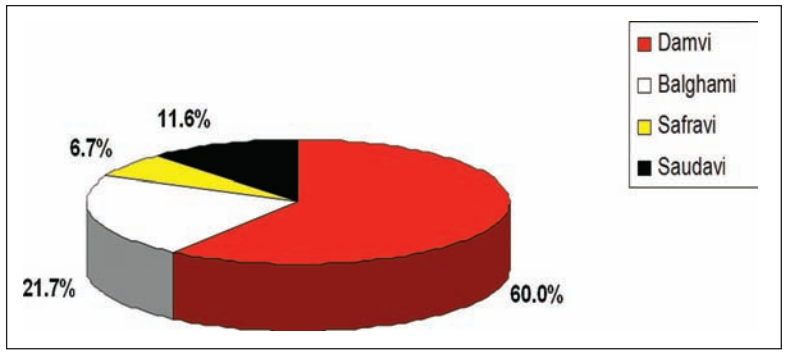

Fig. 3 : Distribution of Patients according to Mizaj

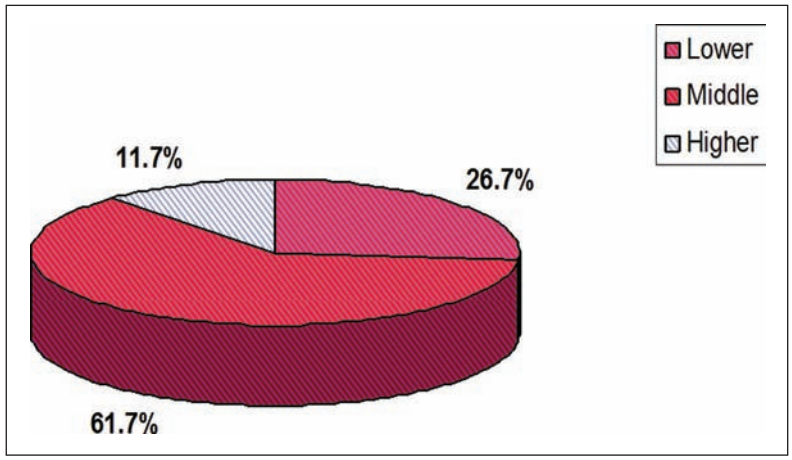

Fig. 4 : Distribution of Patients according to socio-economic status

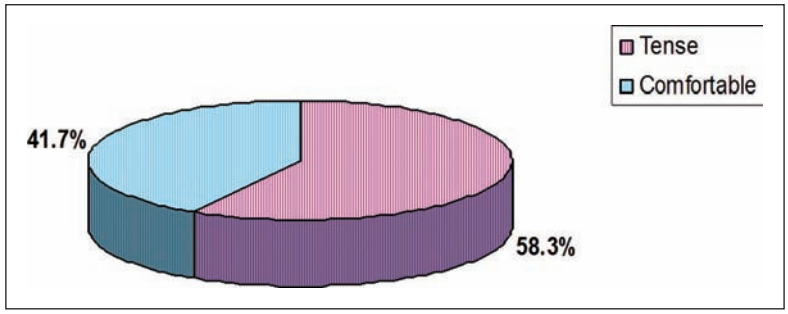

Fig. 5 : Distribution of Patients according to mental status

Table 1 : Effect of treatment on mean blood pressure

Mean Blood Pressure (in mm Hg)								
Blood Pressure	Test Group (n = 30)				Control Group (n = 30)			
	BT	AT	Reduction in BP	% Imp.	BT	AT	Reduction in BP	% Imp.
Systolic	161.8	147.4	14.4	8.89%	165.7	135.7	30.0	18.10%
Diastolic	100.9	91.7	9.2	9.11%	101.1	85.7	15.4	15.23%

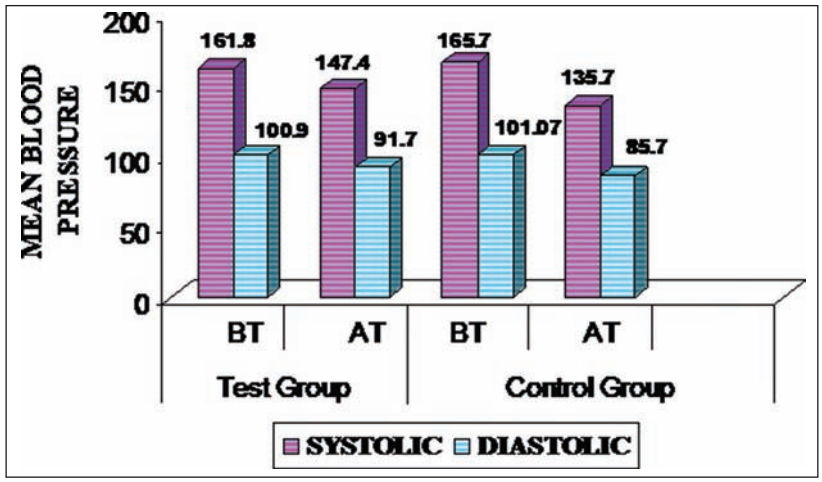

Fig. 6 : Effect of treatment on mean blood pressure

Table 2 : Statistical analysis of effect of treatment on mild hypertension using student 't' test

Blood Pressure	Test Group (n = 15)			Control Group (n = 13)		
	Mean blood pressure (mm Hg)			Mean blood pressure (mm Hg)		
	BT	AT	tc value	BT	AT	tc value
Systolic	154.1 + 0.883	142.4 + 1.11	11.39*	152.2 + 1.25	126.6 + 1.93	13.09***
Diastolic	96.5+ 0.363	90.1+ 0.925	7.91**	93.5+ 0.82	82.4+ 2.22	5.59****

* P. value < 0.05 in systolic BP as compared to pre-treatment in test group.
**P. value < 0.001 in systolic BP as compared to pre-treatment in control group.
***P. value < 0.05 in diastolic BP as compared to pre-treatment in test group.
****P. value < 0.001 in diastolic BP as compared to pre-treatment in control group.

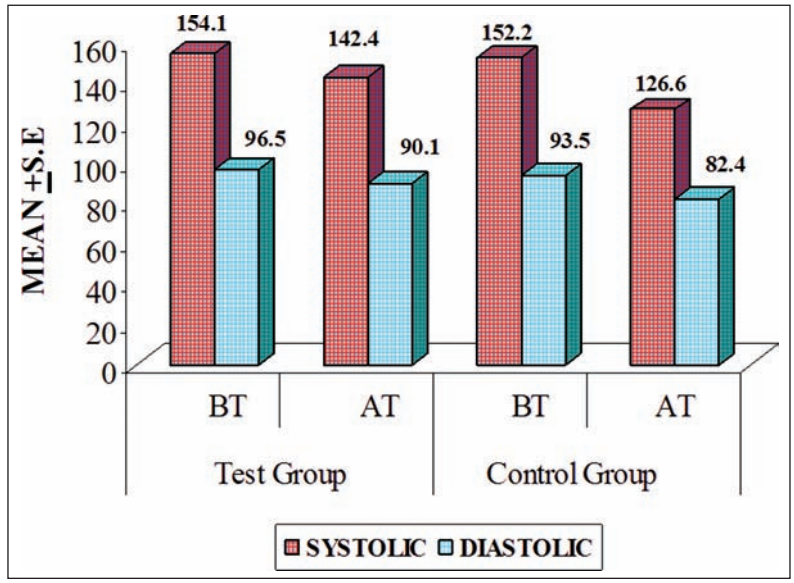

Fig. 7 : Statistical Analysis of effect of Treatment on Mild Hypertension

Table 3 : Statistical analysis of effect of treatment on moderate hypertension using student 't' test

Blood Pressure	Test Group (n = 13)			Control Group (11)		
	BT	AT	tc value	BT	AT	tc value
Systolic	166 + 1.84	149.3 + 2.04	13.86*	165.7 + 1.72	148.9 + 2.08	13.63***
Diastolic	103.8 + 1.09	92 + 1.07	13.62**	103.1 + 0.985	85.3 + 1.45	17.38****

* P. value < 0.05 in systolic BP as compared to pre-treatment in test group.
**P. value < 0.001 in systolic BP as compared to pre-treatment in control group.
***P. value < 0.05 in diastolic BP as compared to pre-treatment in test group.
****P. value < 0.001 in diastolic BP as compared to pre-treatment in control group.

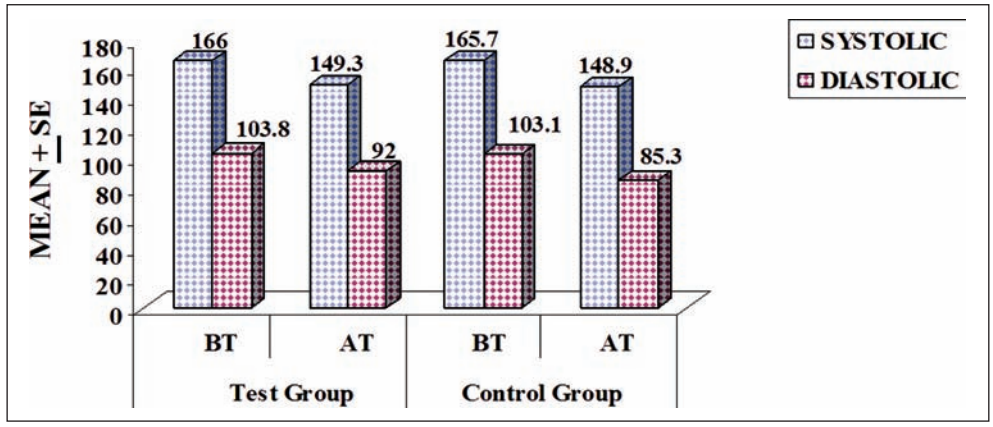

Fig. 8 : Statistical Analysis of Treatment on Moderate Hypertension Using Student 't' Test

Table. 4 : Statistical analysis of effect of treatment on severe hypertension using student 't' test

Blood Pressure	Test Group (n = 3)			Control Group (n = 6)		
	BT	AT	tc value	BT	AT	tc value
Systolic	183.3 + 1.76	162.6 + 3.71	7.11*	187.7 + 2.98	155.3 + 2.35	11.96***
Distolic	111.3+ 0.667	98.7+ 0.667	19.00**	113.7+ 1.58	93.3+ 3.49	5.72****

* P. value < 0.05 in systolic BP as compared to pre-treatment in test group.
**P. value < 0.001 in systolic BP as compared to pre-treatment in control group.
***P. value < 0.05 in diastolic BP as compared to pre-treatment in test group.
****P. value < 0.001 in diastolic BP as compared to pre-treatment in control group.

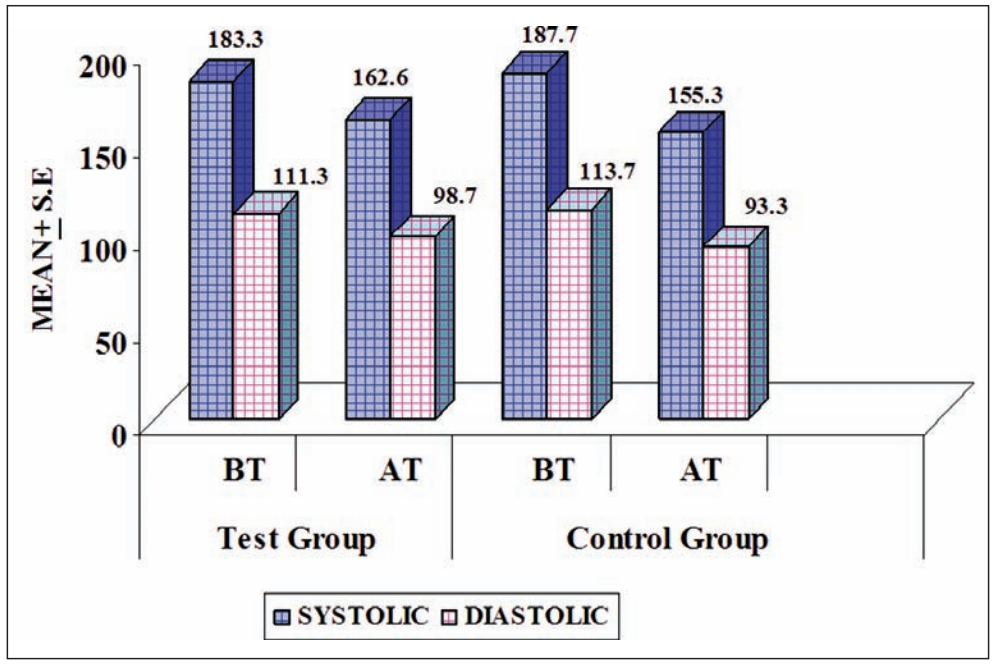

Fig. 9 : Statistical Analysis of Effect of Treatment on Severe Hypertension

Table 5 : Data Analysis of Test and Control drug on Symptoms

Symptoms	Test Group				Control Group			
	BT	AT	Improvement		BT	AT	Improvement	
	No. of Cases	No. of Cases	No. of Cases	%	No. of Cases	No. of Cases	No. of Cases	%
Headache	24	5	19	79.2	18	12	6	33.3
Palpitation	22	5	17	77.3	19	14	5	26.3
Nervousness	20	6	14	70.0	18	13	5	27.8
Dizziness	21	8	13	61.9	18	13	5	27.8
Weakness	17	7	10	58.8	16	12	4	25.0
Insomnia	17	4	13	76.5	15	11	4	26.7
Breathlessness	12	8	4	33.3	11	8	3	27.3
Fatigability	19	10	9	47.3	15	10	5	33.3
Chest Pain	10	5	5	50.0	7	4	3	42.8
Loss of Libido	5	5	0	0NS	2	2	0	0NS

Wilcoxon matched pair test

Results and Discussion

In mild, moderate and severe hypertension groups, the test drug showed significant (P<0.05) result in reducing both systolic and diastolic blood pressure after the treatment while the control drug showed highly significant (P<0.001) result in reducing both systolic and diastolic blood pressure after the treatment. The test drug has given good response on general symptoms than control drug. By using wilcoxon matched pair test, the results in group A are significant (p<0.001) as compared to group B (p<0.01) in relation to symptometology of hypertension.

Analysis of effect of Test and Control drug on Mean B.P. of 30 patients

When observed, the mean systolic B.P. from a level of 161.8 mmHg, came down to normal B.P. level of 147.4 mmHg likewise, the mean diastolic B.P. from a level of 100.9 mmHg, came down to the normal diastolic B.P. level of 91.7 mmHg after the eight weeks of the treatment with the test drug. Thus the average reduction in mean systolic and mean diastolic B.P. was recorded as 14.4 mmHg and 9.2 mmHg respectively (Fig.6). This significant reduction in blood pressure is due to diuretic, sedative and coolant properties of Sandal safaid which is supported by (Anonymus, 2003; Ghani, 1927; Rafeequddin, 1985; Anonymous, 2001).

In control group, the mean systolic blood pressure from a level of 165.7 mmHg, came down to normal blood pressure level of 135.7 mmHg. The mean diastolic blood pressure, from a level of 101.1 mmHg came down to 85.7 mmHg. Thus the average reduction in mean systolic and mean diastolic BP was recorded as 30.0 mmHg and 15.4 mmHg respectively (Fig.6).

Effect on Mild, Moderate and Severe hypertension

Out of total patients suffering from mild hypertension in test group, the improvement in mean systolic blood pressure was 7.59% and in mean diastolic blood pressure was 6.63% (Fig.7). In moderate hypertension the improvement in mean systolic blood pressure was 10.06 % and in mean diastolic blood pressure was 11.36% (Fig.8). In severe hypertension of test group the improvement in mean systolic blood pressure was 11.29 % and in mean diastolic blood pressure was 11.32% (Fig.9). The effect of Unani formulation in all grades of hypertension group after the treatment was found significant (P < 0.05). This significant effect is due to diuretic, sedative and coolant properties of Sandal safaid which is supported by (Anonymus, 2003; Ghani, 1927; Rafeequddin, 1985; Anonymous, 2001).

Effect on Symptoms

The test drug shows significant response in the symptoms of primary hypertension. The compound formulation, Khameera Sandal Sada may particularly be effective in symptoms of high blood pressure due to its sedative, hypnotic, diuretic and cooling effects and this is the unani formulation which has been successfully used in the treatment of palpitation, headache and nervousness, the symptoms commonly found in hypertension (Table.5). The improvement in headache is due to sedative properties of Sandal safaid. The rose has also the properties of relieving head pain due to anxiety, stress. The anxiety and stress may be the causes of primary hypertension. Hence the Sandal Safaid and Arq Ghulab are beneficial in headache, palpitation and nervousness. The data is supported by (Anonymous, 2003; Ghani, 1927; Rafeequddin, 1985; Anonymous, 2001).

Conclusion

The study revealed that test drug has given good response on general symptoms than control drug while the control drug found to be highly significant in lowering the elevated blood pressure than the test drug. Collectively, Khameera Sandal Sada (test drug) can be recommended for reducing the symptoms in general and mild to moderately elevated blood pressure as well.

On the basis of above results it can be concluded that Khameera Sandal Sada is effective and safer in the management of symptoms of Primary hypertension. In this preliminary clinical trial Khameera Sandal Sada was found to be safe and effective. However it can be further taken up on large scale for conduction of phase second and third clinical trial for further establishment of its therapeutic efficacy.

Acknowledgement

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Clinical Evaluation of Efficacy of Asal-us-Soos,Alsi,Irsa, Barg-e-Adoosa and Honey on Chronic Bronchitis: A Preliminary Study

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Abstract

In the present study, efficacy of a Unani drug preparation (Asal-us-Soos, Alsi, Irsa, Barg-e-Adoosa and Honey) has been assessed on 70 cases of chronic bronchitis. Among these 60 completed the course of study, the results were found to be highly significant. Further investigations are suggested.

Keywords: Chronic Bronchitis, Sual Muzmin, Unani Medicine.

Introduction

Chronic bronchitis is a cough phlegm syndrome. The term was introduced into the medical literature early in the 19th century and was recognized as an inflammatory disease of the airways (Sidney, 2006). The Ciba Guest Symposium published in 1959 provided definition of chronic bronchitis as "chronic or recurrent excessive mucous secretion in the bronchial tree". The definition of chronic bronchitis was quantified by epidemiologists as "the presence of chronic productive cough for at least three consecutive months in two consecutive years with other causes of chronic productive cough ruled out" such as pulmonary tuberculosis, carcinoma of the lung, bronchiectasis, cystic fibrosis and congestive heart failure (Chabra, 2009; Fauci, 2008; Fishman, 2007; Fletcher, 1984; Robert, 2005).

In developed countries, cigarette smoking is responsible for 85 to 90% cases of chronic bronchitis (Robert, 2005; Cohen, 1980; Goel, 2007; Jindal, 2006; Sharma, 2005).

Cigarette smokers have a higher prevalence of respiratory symptoms and lung function abnormalities, a greater annual rate of decline in FEV_1, and a greater COPD mortality rate than nonsmokers (Mannino, 2006; Anthoney, 2005). Ancient Unani physicians have described chronic bronchitis under the heading of *SualMuzmin* (chronic cough) (Khan, 1983; Khan, 1939; Jurjani, 1902; Arzani, 1955).

According to the report of National Heart, Lung, and Blood Institute US Department of Health and Human Service, March 2003, 9.2 million adults aged 25 and older reported being diagnosed with chronic bronchitis and about 24 million adults have impaired lung function. About 119, 054 adults ages 25 and older died from COPD in 2000 (Anonymous 2003).The total estimated cost of COPD treatment in 2002 was $ 32.1 billion. A survey conducted by the

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Copenhagen City heart study showed the prevalence of chronic bronchitis at around 10 percent in Copenhagen (Peter, 2003).

The most consistent pathologic correlate is the hypertrophy of the bronchial mucosa. Chronic cough, expectoration and breathlessness are the cardinal symptoms of the disease (Anthony and Douglas, 2005).

In Unani medicine, *Muhallil Auram* (anti-inflammatory), *Munaffis Balgham* (expectorants) and *Mulattif* (mucolytics) are given in the treatment of chronic bronchitis (Khan, 1983; Khan, 1939; Jurjani, 1902; Arzani, 1955).

In allopathic system of medicine, corticosteroids & bronchodilators are used in the treatment of chronic bronchitis (Mannino, 2006). Corticosteroids have serious side effects when used for a long period and bronchodilators are not the permanent solution. So there is a need for a permanent remedy which the patients can take for a long period safely.

Unani system of medicine, a traditional system, has a successful treatment of chronic bronchitis. Unani literatures show that *Asal-us-Soos, Alsi, Irsa, Barg-e-Adoosa*and Honey are effective in chronic bronchitis (Alam, 2011; Khan, 1933; Baitar, 1999). Holy Quran described the honey as, a drink of varying colors, wherein is healing for mankind. Verily, in this is indeed a Sign for people who think (Qur'ân 16:68-69). In addition, the Prophet Mohammad said: "Honey is a remedy for every illness and the Qur'ân is a remedy for all illness of the mind, therefore I recommend to your remedies, the Qur'an and honey" (Qur'ân 16:68-69, Bukhari, 2000; Ilahi, 2010). Hence an attempt was made to test their efficacy clinically.

Material and Method

The present study was a simple observational study conducted in OPD/IPD of Ajmal Khan Tibbiya College Hospital, under the Department of Moalajat, Aligarh Muslim University, Aligarh. Acomprehensive protocol was chalked out and was put forth for ethical clearance from the ethical committee of the Department. 70 subjects were randomly selected amongst the patients provisionally diagnosed to be suffering from chronic bronchitis and after fulfilling all the inclusive and exclusive criteria as mentioned below, among them 60 cases completed the course of study. 10 (14.2%) cases were dropped from the study as theycannotfollow the protocol.

Inclusion Criteria

1. Patients in the age group of 30 to 65 years.

2. Patients presenting cough with expectoration, on most days of at least three months of two consecutive years.
3. Patients with the history of smoking.
4. Patients with the history of smoke exposure.
5. Patients with harsh vesicular breathing with prolong expiration and/or bilateral rhonchi on clinical examination.
6. Patients with positive radiological diagnosis of chronic bronchitis.
7. Patients with FEV_1 < 80% of predicted value.
8. Patients with FEV_1/FVC ratio < 70%
9. Patients who were clinically stable.

Exclusion Criteria

1. Patients below 30 years and over 65 years.
2. Patients having evidence of cor-pulmonale.
3. Patients in acute exacerbation of COPD.
4. Patients with other associated diseases like left ventricular failure, mitral stenosis, other cardiac diseases and peptic ulceration etc.
5. Patients with previous documented response to oral steroids or who had been on oral and or inhaled steroids in the past 3 months.
6. Patients with personal or family history of allergy.
7. Patient having Hb% less than 10.
8. Patients having AFB positive.
9. Patients having wastage of muscles.
10. Patients having compromised immunity.

Selection of Drugs

All the ingredients of the test combination singly or, as a constituent of many pharmacopeal compound drugs, are in use in bronchitis and other diseases of chest and respiratory system since long past in Unani system of medicine. Physicians at Ajmal Khan Tibbiya College (AKTC) Hospital are frequently prescribing this combination in chronic bronchitis. Further, a combination containing all the ingredients except Berg-e-Adoosa is prepared by the hospital pharmacy for distribution of the OPD/IPD patients. The hospital data suggest

that the drug is effective in cases of chronic bronchitis. In view of its successful practice by the physicians at AKTC hospital who have described its promising effects in bronchitis and other respiratory diseases are 'age old' practice of the ingredients of the combination of Unani medicine (Mannan, 1999). This combination was selected to study its efficacy and safety in cases of chronic bronchitis.

Identification of Drugs

Identification of test drugs i.e. *Asal-us-Soos, Alsi, Irsa, Barg-e-Adoosa* was done by Professor S. H. Afaq, eminent pharma-cogonist, Department of Ilmul Advia, Ajmal Khan Tibbiya College, Aligarh Muslim University, Aligarh, while pure honey was purchased from Agro Honey, Gramudhyog Seva Samity, Malic Enclave, Nakasia, Bareilly, U.P. *Asal-us-Soos, Alsi, Irsa* and *Barg-e-Adoosa* were purchased from Dawakhana Tibbiya College, AMU, Aligarh.

The drugs also processedin pharmacy section of the Ajmal Khan Tibbiya College Hospital forthe removal of impurities and made them *Neemkoob Shuda* (semi grinded form) for joshanda preparation. The Joshanda was prepared by drugs in equal quantity of 4 grams each in 100 ml of water. The joshanda was boiled till the water remained half in quantity. The filtrate was superadded with 20 ml of honey. Patients were given the prepared joshanda twice a day on an empty stomach. No concomitant treatment was allowed during the study.

The duration of the study was 42 days. The weekly follow up of the cases was scheduled for the assessment of efficacy of the drugs.

Safety assessment: The safety of the drugs treatment was assessed through non-occurrence of any toxic or adverse effect during the treatment period on the following parameters:

Complete Haemogram, RFT, LFT, Blood Sugar.

Efficacy assessment: The assessment of the efficacy was determined on the subjective and objective parameters as follows:

Subjective Parameters:

Decrease in the cough	Decrease in sputum expectoration
Improvement in breathlessness	Disappearance of rhonchi
Improvement in general condition	

Objective parameters:

Increase in FEV_1 of predicted value	Enhancement of the FEV_1/FVC ratio

Statistical analysis: The observations and data collected were tabulated and statistically analyzed by applying paired t test for objective parameter and non-parametric values were calculated with applying Kruskal Wallis test.

Table 1: Effects of test drugs on the cough during follow up. n = 60

Follow up (in days)															
Group	Severity	Before treatment	After treatment												
		0 Day	7th		14th		21st		28th		35th		42nd		Net Improvement %
		No. of Patients	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	
Test Drug	Mild	15	15	0	12	20	9	40	6	60	0	100	0	100	66%
	Moderate	33	33	0	30	9.1	24	27.3	15	54.4	12	63.4	9	73	
	Severe	12	12	0	12	0	12	0	9	25	9	25	9	25	
Kruskal Wallis Value (KW)		8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	

Table 2 : Effects of test drugs on Sputum during follow up. n = 60

Follow up (in days)															
Group	Severity	Before treatment	After treatment												
		0 Day	7th		14th		21st		28th		35th		42nd		Net Improvement %
		No. of Patients	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	
Test Drug	Mild	15	15	0	12	20	9	40	6	60	0	100	0	100	59.8%
	Moderate	33	33	0	33	0	27	18.2	24	27.3	18	45.5	15	54.4	
	Severe	12	12	0	12	0	1	0	9	25	9	25	9	25	
Kruskal Wallis Value (KW)		8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	

Table 3 : Effects of test drugs on breathlessness during follow. n = 45

Follow up (in days)															
Group	Severity	Before treatment	After treatment												
		0 Day	7th		14th		21st		28th		35th		42nd		Net Improvement %
		No. of Patients	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	
Test Drug	Mild	12	12	0	12	0	9	25	6	50	3	75	0	100	61.1%
	Moderate	24	24	0	24	0	24	0	18	25	12	50	12	50	
	Severe	9	9	0	9	0	9	0	9	0	6	33.3	6	33.3	
Kruskal Wallis Value (KW)		8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	

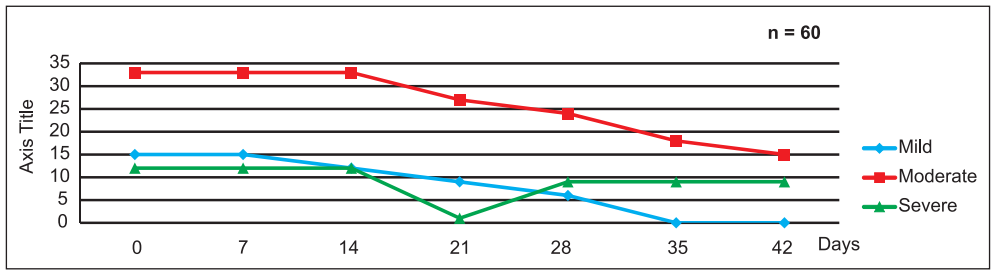
Table 4 : Effects of test drugs on Wheezes during follow up. n = 45

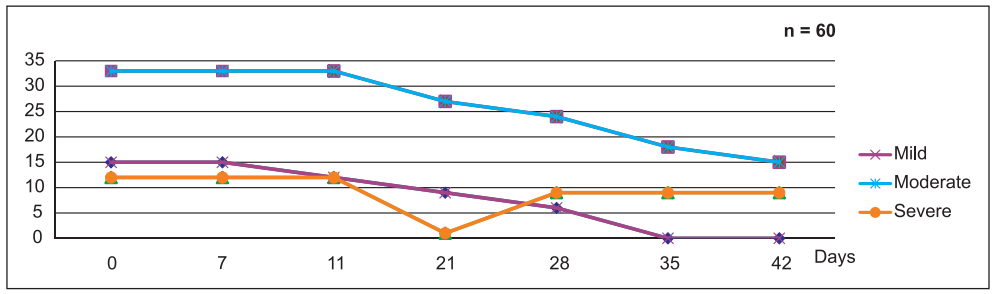
Follow up (in days)													
Group	Before treatment	After treatment											
	0 Day	7th		14th		21st		28th		35th		42nd	
	No. of Patients	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %	No. of Patients	Improvement %
Test Drug	45	45	0	45	0	39	13.3	30	33.3	24	46.7	18	60

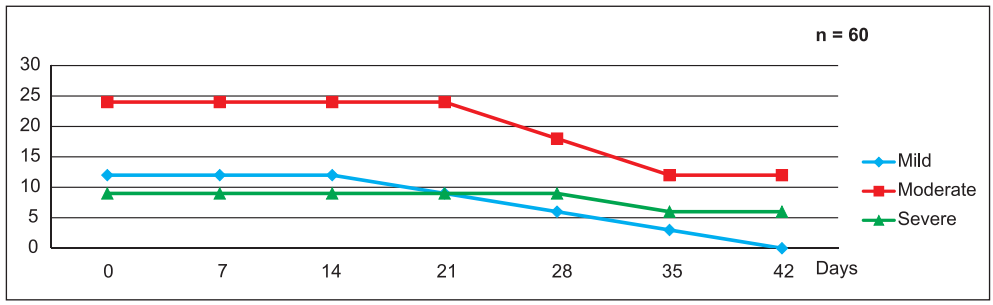
Table 5 : Effect of Drugs on FEV1 Predicted value n = 60

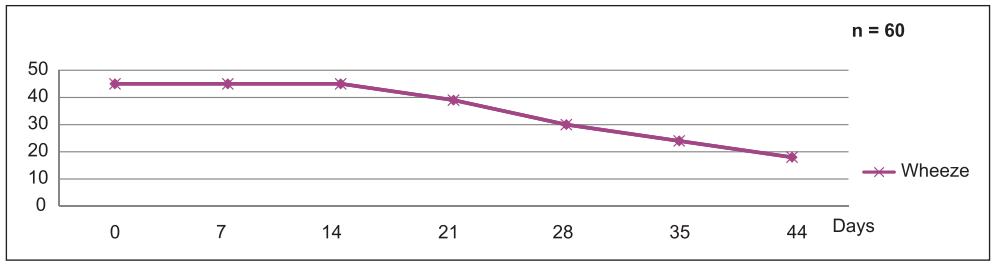
FEV1	No. of Patients	Mean FEV1 Predicted value		t value p value	Overall Mean Predicted value n = 20		t – value p – value
		Before Treatment	After Treatment		B.T	A.T	
70-79 (Mild)	15	75.0 + 3.4	86.4 + 5.7	t = 5.60 p < 0.001	62.1 + 6.9	80.6 + 5.1	t = 9.5 p< 0.001
60-69 (Moderate)	30	63.0 + 2.3	87 + 5.4	t = 3.25 p < 0.01			
50-59 (Moderately Severe)	15	55.0 + 3.9	75 + 3.0	t = 2.77 p < 0.05			

Applying paired t test for the observations recorded before and after the treatment.









Results and Discussion

The effect of the drugs on three sub groups of cough, i.e. mild, moderate and severe was observed as 100%, 73% and 25% improvement respectively. Average improvement was 66% of cases (Table and Graph 1). The important drugs in the formulation which directly suppress the spell of cough are Irsa*(Iris ensata)*, Asal-us-Soos*(Glycirrhiza glabra)* and Adoosa*(Adhatoda vasica).*They have a stabilized effect, but in combination, their cumulative effect is more important and potent then their individual effect. The base of the formulation is honey which has several properties including being demulcent, mucokinetic and having cough suppressant action on bronchoalveolar mucosa. Most probably the presence of essential oils, vacicinol, vacicinine and adhatine in Adoosa, glycyrrhizin, asparazines and a glycoside anthoxacin in Asl-us-sooos as well as the tonic and respiratory epithelium regenerator effect of honey are factors responsible for improving the drug efficacy (Rastogi *et al*., 1960-1969; 1980-1984; 1990-1994). The effects of the drug on three sub groups of sputum i.e. mild, moderate and severe were observed as 100%, 54.4% and 25% respectively. Overall improvement was 59.8% of cases (Table and Graph 2).

A remarkable improvement of 60% was noted in the severity of sputum expectoration in different categories at the end of the study (Table and Graph 2). The improvement may be contributed by mucolytic, mucokinetic and expectorant actions of *Asal-us-Soos, Irsa*and*Alsi,* as well as broncho-dilatory effects of *Adoosa*, *Alsi,* and *Irsa. Irsa* consists of vanalic and P- hydroxylenoic acid, which has anti-allergic and anti-histamic properties. It also suppresses the mucus to the mucus production (sputum). The Embinin present in *Irsa*acts as deobstractant effect besides having anti-dotal properties at various toxins and allergens (Rastogi *et al*.,1960-1969; 1980-1984; 1990-1994).

There was 100% aptness in mild cases, 50% correctness in moderate cases and 33.3% recovery in severe cases of breathlessness. Total improvement was 61.1% of cases (Table and Graph 3).

Breathlessness is due to impaired airflow in bronchial passage which is in the lumen of bronchioles due to hypertrophy of bronchial mucosa in chronic bronchitis. Also there is defective mucociliary clearance due to inactivation of cilia. The accumulation of mucous takes place and ultimately there are breathing difficulties i.e. breathlessness, hypoxemia etc. In our formulation, *Adoosa*is a known bronchodialator having bromhexin as alkaloid which is a potent mucolytic agent (Rastogi *et al*., 1960-1969; 1980-1984; 1990-1994). The mucolytic as well as bronchodilatory effect improves mucociliary clearance action and facilitates the air conductance. The *Irsa*, due to its membrane stabilizing action, along with honey, makes the lumen healthier and helps in rejuvenation process of bronchoalveolar epithelium. Breathlessness was categorized as mild, moderate and severe according to the Modified Medical Research Council questionnaire(Bestall,1999). The average improvement in breathlessness was 61% of cases(Table and Graph 3).

Wheeze or rhonchi were present in all the 45 cases and there was 60% improvement in them at the end of the study (Table and Graph 4).

The concept of Munzij is very vital in the expulsion of all viscid humours. The test drugs bear Munzij properties for khiltebalgham (phlegmatic humour) and KhilteSawdawi (melancholic humour) which spawn noxious pathological changes leading to chronic bronchitis. The expelling effect on abnormal MawadwaAkhlat is the significant action in relieving the pathology of bronchial mucosa and bronchus contents.

The mean FEV_1 percentage predicted values recorded prior to the study were 75.0 $\pm$ 3.4, 63.0 $\pm$ 2.3, 55.0 $\pm$ 3.9 and 62.1 $\pm$ 6.9 in mild, moderate, moderatelysevere respectively. Remarkable increments of 86.4 $\pm$ 5.7, 87.0 $\pm$ 5.4, 75.0 $\pm$ 3.0 and 80.6 $\pm$ 5.1 were achieved in mild, moderate and moderately severe respectively. The difference is significant statistically ($t = 5.60$ and $p < 0.005$, $t = 3.25$, and $p < 0.01$ and $t = 2.77$ and $p < 0.05$ and $t = 9.5$ and $p < 0.001$ (Table 5). Due to the aforementioned effect of the formulation the improvement in the objective parameter was significant statistically. $t = 9.5$, $p < 0.001$) (Table 5)

Conclusion

The subjected drugs formulation showed significant preiminary results in alleviating the symptoms, signs and physical findings along with improvement in FEV_1 and FEV_1/FVC ratio without any observable side effects.

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Nephroprotection: Meaning and Scope in Unani System of Medicine

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Abstract

The concept of protection and tonicity of an organ as described in Unani medicine has a specific notation that can be understood through the theories philosophies that govern the system. This will help understand the significance of the theory and its practical application and also the nature and mechanism of drugs action and thereby their actual therapeutic value. Evidences are accumulating to demonstrate that the drugs described to be useful in various renal disorders because of their nephroprotective and nephrotonic effect as described in Unani or other traditional medicines, have even more wide and diverse therapeutic uses than that depicted by the modern medicine practitioners. Many scientific studies have demonstrated that Unani medicine have ample potential to become an important source of managing many renal diseases and their complications. This paper gives a brief account of the concept of nephroprotection and explores the potentiality of Unani drugs that can be used to treat the renal diseases or at least arrest their progression to chronic or end stage renal disease.

Key words : Nephroprotection, Nephrotoxicity, Unani System of Medicine.

Introduction

The complex nature of renal diseases and their progression to renal failure (both acute and chronic) and end stage renal disease (ESRD) makes their management quite difficult. The majority of cases of renal disease remain unnoticed unless they progress to advance stage when the conventional therapeutic interventions are usually not sufficient to cure them completely. But the major problem with kidney disease is its progression to a stage when virtually no option works at all except the renal replacement therapy (RRT).

Two major components of RRT viz. dialysis and kidney transplantation are highly sophisticated and thereby too costly to be affordable for the patient of average income group. Only small chunk of elite class can take the luxury of such a regimen, that too subject to the availability of the facility in its reach. That is why most of the patients of kidney disease are left to die mainly in developing and poor countries, because of non-availability of RRT facilities in their region or their inability to pay for it. About 100 countries have been identified not to possess such facility at all (Lameire et al., 2005). In India the projected number of deaths due to chronic kidney diseases (CKD) is on a rise. In 1990 it was 3.78 million and is expected to become 7.63 million in 2020

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(WHO, 2005). Availability of kidneys for transplantation is another important problem consistent with RRT. Although, expenditure on RRT is costing about 1 trillion dollar, annually but the substantial percentage of patients in need of it, still remains untreated and consequently untreated patients have out-numbered those who are receiving the treatment. In nut shell therefore, it can be said that it is almost next to impossible to provide replacement therapy to all patients requiring it. The next option left with the physicians is to think of alternatives and the best way to come out of such a situation or at least scale down the prevalence and consequently the financial burden to a significant level, is to protect the kidney function, slow the progression of disease and delay the need of RRT (Remuzzi *et al.*, 1993 Hanneman *et al*., 1991). This second option actually paved the way for envisaging a concept that is broadly termed as nephroprotection. It aims at protecting the kidney from noxious stimuli, treating the kidney diseases or at least checking the progression of renal diseases and delaying the need of RRT. However the concept of nephroprotection in modern medicine is relatively new and can hardly be traced before eighties whereas traditional medicines especially Unani medicine offers various protective and curative options of management.

Concept of Nephroprotection in Unani System of Medicine

The concept of protection of an organ, and the *quwa* (faculty) consistent with it, so as to maintain its structure and function has been a distinguishing feature of Unani system of medicines since ancient times. Drugs that are supposed to be tonics and protective for particular organ are used for this purpose and are also combined with other drugs having related pharmacological effects, with an aim to strengthen the organ and its *quwa* to make them efficient enough to fight the noxious stimuli and protect the organ from aversive effect or at least minimize the harmful effects of various untoward elements. Thus, the protective approach to prevent, treat are slow down the progression of disease is the main stay in Unani system of medicine. The concept of nephroprotection in Unani system of medicine is meant to invigorate and strengthen the kidney and help the preservation of its *quwa* involved in maintaining the normal function of the kidney. Thus, when impairment in renal function and structure takes place protective agents help to bring the normalcy back by improving the inherent protective and defensive abilities of the organ.

The faculties at their equilibrium are poised inherently to maintain the normal functions of that organ / system and make it strong enough to fight and remove the untoward elements that come to its contact. That is why for every organ/

system a group of tonic drugs has been proposed that safeguards its larger interest and bring it near to its equilibrium, if some derangement in its function or structure has taken place. If the normalization does not take place then the drugs possessing specific actions are used to treat the disease or inhibit its progression. Thus, we can say that simultaneous protective and curative approach to prevent, treat or slow the progression of disease is the hallmark of Unani System of Medicine.

According to Unani system of medicine all the organs have been endowed with four faculties which work in coordination to maintain the function and the structure of the organ. These faculties are:

- *Quwwat-e-Hazimah*
- *Quwwat-e-Jazibah*
- *Quwwat-e- Masikah*
- *Quwwat-e-Dafeah*

Apart from these four faculties that are responsible to maintain the normal functioning of all the organs, kidney has also been bestowed upon with an additional faculty namely q*uwwat-e- mumayyizah* (separating and distinguishing faculty), by virtue of which kidney separates the blood from impurities and wastes which are the sequels of the ongoing metabolic process in the body or come from the deliberately administered drugs and chemicals for therapeutic purposes, or passively ingested toxicants from the environmental pollution and exposure to various hazardous toxic substances. When the process of separation completes, *quwwat-e- dafeah* helps the wastes excrete out, as early as possible. It suggests that a number of forces that complement each other, operate continuously in a synchronized way to maintain the functioning of kidney and also to protect it by not allowing the wastes and toxins which the kidney is constantly exposed to, to stay for sufficient period of time to cause local injury. The renoprotection by view point of Unani Medicine comprises of the protection of the various faculties the kidneys are imbibed with, to maintain its functioning. In case of mild degree of kidney disorder the drugs categorized to be kidney tonics, are sufficient enough to deal with the situation to bring the normalcy. However, when gross impairment in kidney function or it matrix takes place anyhow, because of the high toxic effect of a substance or because one of the natural faculties are undermined owing to some local or systemic disease of the body, then the drugs having other pharmacological actions along with the tonic one, are used. Drugs ascribed to

possess diuretic, anti-inflammatory, antioxidant, cathartic etc along with tonic effect are frequently used with an aim to treat the pathology and invigorate the kidney to bounce back to its normal state to perform its assigned work. Further, in case of progression of kidney diseases some other drugs are included in the regimen along with the drugs mentioned above, to directly ameliorate the compromised condition by promoting the healing of injured tissue, removal of toxins and reducing the pressure of work on kidney by diverting the wastes to some other system or organs of the body (Arzani, 2006; Ibn Hubal, 2007). However, despite a comprehensive approach of treatment described in literature and being practiced by the physicians it has been accounted by the practitioners that the treatment of renal injury itself is very difficult because of several reasons such as:

(a) Kidney is the passage of urine and other waste product therefore the drugs intended to be effective do not stay at the site of action for sufficient period of time.

(b) The matrix of kidney is too hard therefore the drugs did not diffuse easily to the site of action.

(c) The waste material excreted by kidney is usually noxious and corrosive in nature which delay or partially hamper the process of healing.

(d) Kidney always remains busy in its work, while healing process requires a degree of rest (Khan, 2003; Ibn Rushd, 1987).

The kidney disease also occurs due to change in *mizaj* (temperament), *Amraze Aliah*, (compound disease) or weakening of the any of five faculties. When the faculties become weak, kidney does not get sufficient nutrition from fluids and following diseases may occur:-

- *Sou-e-Mizaje Kulyah*
- *Waram-e-Kulyah*
- *Hasat-e-Kulyah*
- *Waj'-e- Kulyah*
- *Huzal-e-Kulyah*
- *Iltehab-e-Hauze kulyah*
- *Sudad-e-Kulyah* (Tabari, 2006; Khan, 2003; Ibn Rushd, 1987)

However, despite recognition of drug induced nephrotoxicity and concerted efforts directed towards developing therapeutic or prophylactic agents to induce protection against chemically induced nephrotoxicity, conventional therapeutic options available are still very limited. In the absence of reliable and effective modern nephroprotective drugs efforts are currently canalized toward exploring drugs from alternative and complementary medicines to treat and/or prevent the disease.

In modern medicine Antigiotensin Converting Enzyme (ACE) inhibitors and Angiotensin II Receptor Blockers (ARBs) are mainly used to induce renoprotection, however these agents are neither the drugs of choice for this purpose nor can be used exclusively to produce renoprotective effects, rather they are mainly effective in nephropathies associated with blood pressure and diabetes etc (George *et al*., 2000) It implies that by treating a patient with the above mentioned drugs it is obligatory to induce a pharmacological effect that may not be necessarily needed by him. The associated toxicities of these agents also limit their use to a great extent. Although, ARBs are comparatively safer than ACE inhibitors but some of the side effects are common to both the drugs such as neutropenia, proteinuria, angioneurotic edema, hyperkalemia especially in patients with renal impairment etc. (George *et al*., 2000), which undermine the therapeutic utility of these agents. A drug categorized to be effective specifically as a nephroprotective agent without having liability to produce some serious side effects will be the obvious choice for the patients suffering from renal dysfunction or failure.

In view of the limitations of Western medicine and the alarmingly increasing cases of renal disorders, development of effective and safe drugs to treat renal disorders has become the priority area of research. Unani system of medicine possesses many effective and safe diuretics and nephroprotective drugs which are in use since hundreds of years in renal disorders. However, these drugs have been neither described with necessary details for their role in renal disorders nor scientifically investigated for various pharmacological activities; therefore, in order to evaluate their different pharmacological effects concerning kidney ailments a comprehensive scientific study is inarguably inevitable.

Further, since the Western medicine as described above still doesn't have satisfactorily effective and safe drugs which can cure renal disorders completely, therefore the study of Unani drugs gains importance in respect of characterizing and identifying a better group of drugs that can fill this lacuna.

It is being appreciated that Unani System of Medicine can offer some effective drugs from its treatise to be useful in diverse pathological conditions of kidney and thus can be used to protect the renal function and prevent/slow the progression of renal diseases to CKD or ESRD. A number of drugs from herbal sources have been shown to possess promising nephroprotective and related effects in some recent studies and researchers are making it a point to concentrate seriously on the development of nephroprotective agents from traditional sources.

A number of poly herbal formulations and single drugs mentioned in Unani literature and being practiced by physicians have been demonstrated to produce some important effects such as diuretic, anti-inflammatory, antioxidant nephroprotective etc against known toxicants. Some of the drugs such as Jawarish zarooni sada (Afzal *et al.*, 2004), Banadequl buzoor (Anwar *et al.*, 1999), Bisehri Booti (*Aerva lanata* Juss) (Shirwaikar *et al.*, 2004), Revand Chini (*Rheum officinalis*) (Yokozawa *et al.*, 1991), Zanjabeel (*Zingiber officinale*) (Narora *et al.*, 1992), Asgand (*Withania somnifera*) (Panda *et al.*, 1997)**,** Khare khasak (*Tribulus terrestris*) (Nagarkatti *et al.*, 1942), Haleela (*Terminalia chebula*) (Yokozawa *et al.*, 1995), Sahajna *(Moringa olifera)* with a little opium, (*Papaver somniferum),* Giloo (*Tinospora cordifolia*) are useful in the inflammation of kidney (Sevanand *et al.*, 1996) have been shown to possess nephroprotective and related effect of varying degree.

The protective effect of Asgand (*Withania somnifera*) on cadmium induced toxicity in mice kidney has been studied to demonstrate a promising result (Panday *et al.*, 1997). Similarly, curcumin isolated from turmeric has been reported to produce protective effect against adriamycin induced nephrotoxicity (Venkatesan *et al.*, 2000). A Unani drug Kabab chini (*Piper cubeba)* was investigated for nephroprotective activity in chemically induced nephrotoxicity showed significant nephroprotective effect against gentamicin and cisplatin induced nephrotoxicity (Zaid *et al.*, 2012). These reports are although of preliminary nature but showing great potential of Unani Medicine to deliver promising agents that can be used to treat the kidney diseases or at least, preserve its function and slow the progression of diseases. Therefore, the study of Unani diuretics, tonics and nephroprotective drugs gains importance as one of the means of characterizing and identifying a better group of drug that can be used as nephroprotective agent. Some of the important studies showing interesting results are being presented in the table given below:

Table 1 : Unani drugs which are scientifically evaluated for nephroprotective effect

S. No.	Herbs	Protective effect
1.	*Tribulus terresteris*	Possess protective effect against the gentamicin induced nephrotoxicity in both structural and functional terms. (Nagarkatti *et al.*, 1942)
2.	*Boerhavia diffusa*	Clinically proved to be useful and safe drug in patients of nephritic syndrome (Singh *et al.*, 1972)
3.	*Withania somnifera*	Significantly reduced toxicity caused by cadmium (Panday *et al.*, 1997)
4.	Banadequl Buzoor	The formulation was found to decrease the serum urea and serum creatinine levels significantly (Anwar *et al.*, 1999)
5.	Jawarish Zarooni Sada	The formulation was found to decrease the serum urea and serum creatinine levels significantly (Afzal *et al.*, 2004)
6.	*Piper cubeba*	Showed significant protective effect against cisplatin and gentamicin induced nephrotoxicity (Zaid *et al.*, 2012)
7.	*Moringa oleifera* and *Tinospora cordifolia*	Useful in the inflammation of kidney (Melookunnel, 1996).
8.	*Ficus racemosa*	Significantly protects the toxicity produced by Cisplatin (Gowda *et al.*, 2011).
9.	*Aegle marmelos*	Normalized the serum creatinine, urea and blood urea nitrogen levels in gentamicin toxicity (Kore *et al.*, 2011).
10.	*Moringa oleifera*	Showed moderate protection in both curative and prophylactic models against Cisplatin induced toxicity (Sreedevi *et al.,* 2011).
11.	*Carica papaya*	Owed nephroprotective effect on CCl4 induced nephrotoxicity (Olagunjua *et al.* 2009).
12.	*Cassia auriculata*	Reduced the blood urea and serum creatinine level effectively in both the curative as well as the preventive regimen (Shirwaikar *et al.*, 2005).
13.	*Eruca sativa*	A potent antioxidant and renal protective activity and preclude oxidative damage inflicted to the kidney (Alam *et al.*, 2007).

14.	*Hemidescus indicus*	Showed nephroprotective activity against gentamicin induced nephrotoxicity (Magala *et al.*, 2004).
15.	*Allium sativum*	Showed dose dependent reduction in the elevated blood urea and serum creatinine levels and normalized the histopathological changes in the curative regimen. (Maldonado *et al.*, 2000).
16.	Glycyrrhizin	Offered protective effect against gentamicin induced toxicity (Sohn *et al.*, 2003).
17.	*Pongamia pinnata*	Demonstrated protective effect against cisplatin and gentamicin induced renal injury (Shirwaikar *et al.*, 2003).
18.	*Solanum nigrum*	Exhibited significant hydroxyl radical scavenging potential, thus suggesting its probable mechanism of cytoprotection (Prasanth Kumar *et al.*, 2001).
19.	*Terminalia chebula*	Reduced the serum concentrations of urea nitrogen, creatinine, methyl guanidine and guanidinosuccinic acid significantly (Yokozava *et al.*,1995).

Conclusion

It can be concluded that the concept of nephroprotection as described in Unani literature, is comprehensive and can be used to understand the subject matter in its entirety. The concept of quva and maintenance of the equilibrium in the body and specific organs may be used as a theoretical model to understand the physiopathology of many pathological conditions of many diseases including the renal disorders. Further, a number of drugs used in the management of renal disease by the Unani physicians have been validated by modern scientists who have reported very interesting effect possessed by these drugs. These drugs may be developed as a better substitute of ARBs and ACE inhibitors which have failed to produce the desired response.

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Biological and Pharmaco-logical studies on Asgand (*Withania somnifera* Dunal) – A Review

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Abstract

sgand consists of the dried roots of *W. somnifera* (L.) Dunal. Various important medicinal values of this plant are described in the classical literature of Indian systems of medicine. This led the researchers to carry out pharmacological and biological evaluation to unravel its therapeutic potential as also to provide scientific basis of use of the plant. Results of some of the pharmacological/biological activities on the root, the most important part reputed for its medicinal value have been reviewed in this article.

Keywords: Asgand, *Withania somnifiera,*Pharmacology, Biological studies.

Introduction

Asgand is one of the promising herbal drug used in all Indian systems of medicine. Since ages Asgand being used in Uniani, Ayurveda, Siddha, Homeopathy etc. It is attributable to *Withania somnifiera* L. (Hooker, 1973) Synonyms: *Physalis somnifera*Linn., *Physallis flexuosa* Linn., *Physalis arborescens* D. C**.** In Unaniit is known as Asgand, in Ayurveda it is popularly known as Ashwagandha, in Siddha it is called Amukakara and its common english name is Winter Cherry. The plant has been historically credited to various properties like immunomodulatory, rejuvenating, anti-ageing, health promoting and reported to be used in treatment of various ailments.

Geographical Distribution: Asgand is a widespread species disseminated from the Southern Mediterranean area to the different parts of Africa and from Palestine upto North India, covering Israel, Jordan, Egypt, Sudan, Iran, Afghanistan, Sind, Morocco, Spain, Island, Srilanka and Pakistan. In India the plant grows well throughout the drier parts *viz*. Maharashtra, Gujarat, Madhya Pradesh, Rajasthan, Uttar Pradesh, Haryana, Andhra Pradesh, Karnataka and Punjab, extending to Uttranchal, Himachal Pradesh and Jammu & Kashmir from plains to a height of 1700 m. This species has been under domestication since long in Central India. Asgand is cultivated in more than 5000 hectare area in the northwestern regions of Madhya Pradesh in Mandsaur, Neemuch, Jawad and the parts of Rajasthan. (Anonymous, 1976; Atal and Schwarting, 1961; Atal *et al*., 1975; Hooker, 1973; Jaffer*et al.,* 1988; Jain *et al.,* 2007; Patra *et al.,* 2004; Purohit and Vyas, 2004).

History: The use of Asgand in Indian Systems of Medicne dates back 3000-4000 years to the teachings of the famed ayurvedic scholar Punarvasu

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Atreya. Subsequently, it was included in the writings of Charaka, Sushruta, and many other ayurvedic scholars throughout the centuries. Asgand, derived from the Sanskrit *ashva* meaning “horse” and *gandha* meaning “smell”, describes the strong aroma of the root which is considered to be reminiscent of a horse’s skin, sweat, or urine, depending upon to which authority one refers. The species name *somnifera* refers to the Latin *somnus* meaning “to sleep”, apparently alluding to the use of Asgand as a nervine and sedative. In the Unani tradition, the root was considered as a tonic, aphrodisiac and emmenagogue.Asgand is being used in the treatment (Anonymous, 2007) of Sailan-ur-Rahem (Leukaria), Jiryan (Spermatia), Riqqat-e-Mani (Attenuated Semen), Waj-ul-Qutn (Backache), Waj-ul-Mafasil (Arthraliga), Zof-e-Bah (Sexual Debility). Historically, Asgand was widely used throughout India as a tonic, especially for emaciation in people of all ages, including infants, and for enhancing reproductive function in both men and women. In one text, it was stated that Asgand taken for a fortnight with milk, ghee, oil, or warm water promotes development in an emaciated body “as rains do for younger crops”. It is classed among the “rasayanas” (rejuvenative tonics), the most highly regarded of all medicinal substances in Ayurveda. The ayurvedic scholar Charaka (100 BC) wrote of rasayanas, “One obtains longevity, regains youth, gets a sharp memory and intellect and freedom from diseases, gets a lustrous complexion, and strength of a horse”. Charaka described various uses for Asgand, including its effectiveness for treating hiccups and female disorders.Asgand historically was used for inflammation, to reduce abdominal swelling, as a mild purgative, and for the treatment of swollen glands. Asgand has been used in traditional herbal healing practices of Africa. The Southern Sotho prepared a decoction of the roots for colds and chills. The Transvaal Sotho used the root to tone the uterus in women who habitually miscarry, a use commonly employed in India as well. It has also been used to facilitate expulsion of the afterbirth. An infusion of the root bark has been used for asthma. In India it is highly regarded as a tonic and is used in formulas for a wide range of imbalances. It is cited in National formulary of Unani medicine vol. part. 1, 3, 4 and 5 (Anonymous, 2001; 2006; 2006 a; 2008), as per The Unani Pharmacopoeia of India Vol. 1 Asgand is being used in various formularies like Majoon-e-Sohag, Sonth, Majoon-e-Salab, Zimad-e-Mohallil, Kushta-e-Gaodanti(Anonymous, 2007).The Ayurvedic Pharmacopoeia of Indiain which it is cited as a strengthening tonic, aphrodisiac, and for the treatment for arthritis (Anonymous, 2001 a). It is the primary component of numerous traditional ayurvedic tonic and anti-aging compounds (Atal and Schwarting, 1961; Tripathi *et al.,* 1998; Watt and Breyer-Brandwijk, 1962).

Pharmacology

(a) Experimental Pharmacology

Antioxidant: *W. somnifiera* extract given orally for 15 days exhibited potent antioxidant defense by significantly increasing the enzymes; superoxide dismutase, catalase and ascorbic acid and showed a significant decrease in lipid peroxidation (Bhatnagar *et al*., 2005; Chaurasia *et al*., 2000). Root powder of Asgand also possessed similar kind of free radical scavenging activity (Panda *et al*., 1997) In another study, Asgand extract reduced oxidative damage in both brain regions (hippocampus and cerebral cortex) as marked by a significant decline in both lipid peroxidation and protein carbonyl in diabetic mice (Parihar *et al*., 2004). An aqueous suspension of root extract of Asgand prevented the rise of experimentally induced lipid peroxidation in rabbits and mice (Dhuley, 1998). It has decreased the activity of glutathione peroxidase (GPx) in the spinal cord from adult to aged mice and inhibited lipid peroxidation and protein oxidative modification induced by copper (Gupta *et al*., 2003). Methanolic extract of *W.somnifera* showed a dose-dependent free radical scavenging capacity and a protective effect on DNA cleavage induced by H_2O_2 UV-photholysis (Russo *et al.,* 2001). Oral treatment with Asgand root extract resulted in a significant improvement in the mice's behavior and brain antioxidant status, along with a significant reduction in the level of lipid peroxidation. Pretreatment with *W.somnifera* rootextract prevented motor impairment and significantly decreased the raised levels of malondialdehyde compared with vehicle-treated rats in the middle cerebral artery occlusion model of stroke. The protection afforded by *W. somnifera* could be due to its anti-oxidant effect (Chaudhary *et al*., 2003). Glycowithanolides of *W.somnifera* root induced a dose related increase in super oxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX) in frontal cortex and striatum of rats (Bhattacharya *et al.,* 2001; Bhattacharya *et al.,* 2000).

Anti-tumor: *W. somnifera* exhibited anti-tumor effect in urethane-induced lung adenomas in adult male albino mice (Singh and Singh, 1986). The alcoholic extract of the dried roots of *W. somnifiera*as well as the active component withaferin A isolated from the extract showed significant anti-tumor and radiosensitizing effects in experimental tumors *in vivo*, without any noticeable systemic toxicity. Withaferin A gave a sensitizer enhancement ratio of 1.5 for *in vitro* cell killing of V79 Chinese hamster cells at a non toxic concentration of approximately 2 µM (Devi *et al.,* 1992). The growth inhibitory effect of Asgand was also observed in Sarcoma 180 (S-180), a transplantable mouse tumor. Ethanol extract of Asgand root (400 mg/kg and up, daily for 15 days) after intra-

dermal inoculation of 5 x 10^5 cells of S-180 in BALB/c mice produced complete regression of tumor after the initial growth. A 55% complete regression was obtained at 1000 mg/kg; however, it was a lethal dose in some cases. Asgand was also found to act as a radio and heat sensitizer in mouse S-180 and in Ehrlich ascites carcinoma (Devi *et al.,*1992; Devi *et al.,* 1995). Anti-tumor and radiosensitizing effects of withaferin (a steroidal lactone of WS) were also seen in mouse Ehrlich ascites carcinoma *in vivo*. *W.somnifera* hydroalcoholic root extract possessed potential chemopreventive activity on 7, 12-dimethylbenz[a] anthracene (DMBA) induced skin cancer in Swiss albino mice and the findings were supported by histopathological studies (Prakash *et al.,* 2002).The hydroalcoholic extract of the roots *W.somnifera* was screened against human laryngeal carcinoma (Hep2) cells by microculture tetrazolium assay (MTT) for anti-proliferative activity. The findings suggest that it possess cell cycle disruption and anti-angiogenic activity, which may be a critical mediator for its anti-cancer action (Mathur *et al.,* 2006). The effect of ethanolic root extract of *W. somnifiera* (REWS) against Dalton's Ascitic Lymphoma has been evaluated in Swiss albino mice. A significant increase in the life span and a decrease in the cancer cell number and tumour weight were noted in the tumour-induced mice after treatment with REWS (Christina *et al.,* 2004). *W.somnifera* (200 mg/kg, p.o.) when administered for 4 days before paclitaxel treatment and continued for 12 days caused significant reversal of neutropenia of paclitaxel in mice. The findings of the study suggest the potential of *W.somnifera* as an adjuvant during cancer chemotherapy for the prevention of bone marrow depression associated with anticancer drugs (Gupta *et al.,* 2001).Paclitaxel, administered with *W.somnifera*, may extend its chemotherapeutic effect through modulating protein-bound carbohydrate levels and marker enzymes, as they are indicators of cancer. The combination of paclitaxel with *W. somnifera* could effectively treat the benzo(a) pyrene-induced lung cancer in mice by offering protection from reactive oxygen species damage and also by suppressing cell proliferation (Senthilnathan *et al.,* 2006a). Studies on rabbits demonstrated that the tumor proteasome 5 subunit is the primary target of Withania and inhibition of the proteasomal chymotrypsin-like activity by withania *in-vivo* is responsible for, or contributes to, the antitumor effect of this ancient medicinal compound. The leaf extract kill cancer cells by at least five different pathways, viz. p53 signaling, GM-CFS signaling, death receptor signaling, apoptosis signaling and G2-M DNA damage regulation pathway (Widodo *et al.,* 2007; Widodo *et al.,* 2008). Along-term tumorigenesis study, with aniainhibited benzo (a) pyrene-induced fore stomach papillomagenesis, showing up to 60 and 92% inhibition in tumor incidence and multiplicity, respectively. Similarly, Withania inhibited 7, 12-dimethylbenzanthracene-

induced skin papillomagenesis, showing up to 45 and 71% inhibition in tumor incidence and multiplicity. The administration of Asgand rasayana (an ayurvedic polyherbal formulation containing Asgand) significantly reduced the lung tumor nodule formation by 55.6 % in experimental animal (Menon *et al.,* 1997). Simultaneous administration of withania extract and withanolide could significantly ($p < 0.001$) inhibit the metastatic colony formation of the melanoma in lungs of mice. Administration of Asgand extract was found to significantly reduce leucopenia (low white cell count) induced by cyclophosphamide treatment. Treatment of Asgand along with cyclophosphamide was found to significantly ($P < 0.001$) increase the bone marrow cellularity compared to cyclophosphamide alone treated group (Davis and Kuttan, 1998). Administration of an extract from the powdered root of the plant Asgand enhanced the levels of Interferon gamma (IFN-gamma), Interleukin-2 (IL-2) and Granulocyte macrophage colony stimulating factor (GM-CSF) in normal Balb/c mice (Davis and Kuttan, 1999). Treatment with Asgand had normalised the ratio of normochromatic erythrocytes and polychromatic erythrocytes in mice after the radiation exposure. Major activity of Asgand seemed to be in the stimulation of stem cell proliferation. Administration of Asgand (20 mg/dose/animal) for five days in conjunction with cyclophosphamide was associated with a reduction in urotoxicity. In a further study at the same dose it was found to inhibit the 20-methylcholanthrene induced sarcoma development in mice and increased the survival rate to 100% of tumor bearing animals (Davis and Kuttan 2000a; Davis and Kuttan, 2002a; Davis and Kuttan, 2002b).Oral administration of *W.somnifera* root extract reduced the tumor incidence, tumor volume and enhanced the survival of the mice compared with 20-methylcholanthrene injected mice (Prakash *et al.,* 2002).Pretreatment of rats with 1-oxo-5[beta], 6[beta]-epoxy-witha-2-enolide (20 mg/kg bwt.) isolated from the roots of *W. somnifera*, prevents the incidence of UV B radiation induced skin carcinoma and also prevents malignancy in the cutaneous tissue (Mathur *et al.,* 2006). An in vitro study showed withanolides from *W. somnifiera* inhibited growth in human breast, central nervous system, lung and colon cancer cell lines comparable to doxorubicin. Withaferin A more effectively inhibited growth of breast and colon cancer cell lines than did doxorubicin. These results suggest it may prevent or inhibit tumor growth in cancer patients and suggest a potential for development of new chemotherapeutic agents (Jayaprakasam *et al.,* 2003). Further withanolides inhibit the activation of NF-kappa B and NFkappaB-regulated gene expression, which may explain the ability of withanolides to enhance apoptosis and inhibit invasion and osteoclastogenesis (Ichikawa *et al.,* 2006). Treatment with *W. somnifiera* inhibited ochratoxin A (OTA) induced suppression of chemotactic activity and

production of interleukin-1 (IL-1) and tumour necrosis factor by macrophases (Dhuley, 1998).

Antibacterial: Both aqueous as well as alcoholic extract of *W. somnifiera* (roots as well as leaves) were found to possess strong antibacterial activity against a range of bacteria, as revealed by *in vitro* Agar Well Diffusion Method. Moreover, in contrast to the synthetic antibiotic (viz. chloramphenicol), the extracts did not induce lysis on incubation with human erythrocytes, advocating their safety to the living cells (Owais *et al.,* 2005). Methanol and hexane extract of both leaves and roots of *W. somnifiera* (WS) exhibited potent antibacterial activity against *Salmonella typhimurium* and *Escherichia coli* by agar plate disc-diffusion assay. A synergistic increase in the antibacterial effect of Tibrim (combination of rifampicin and isoniazid) was noticed when MIC of Tibrim was supplemented with the WS extract (Arora *et al.,* 2004).

Spermatogenic: Lyophilized aqueous extract of *W. somnifiera* produced increase testicular weight and found to have a direct spermatogenic influence on the seminiferous tubules of immature rats presumably by exerting a testosterone-like effect (Abdel-Magied *et al.,* 2001).

Cardiovascular: *W. somnifiera* (50 mg/kg) exerts a strong cardioprotective effect in the experimental model of isoprenaline-induced myonecrosis in rats. Augmentation of endogenous antioxidants, maintenance of the myocardial antioxidant status and significant restoration of most of the altered haemodynamic parameters may contribute to its cardioprotective effect. *W.somnifera* had a prolonged hypotensive, bradycardia, and respiratory-stimulant action in dogs (Malhotra *et al.,* 1965). Significant increase in relative heart weight and glycogen content in heart and liver was observed in the extract treated animals. It increased the duration of contractility of frog heart muscle and resulted in significant increase in coagulation time which attains normalcy seven days after cessation of treatment. The ethanolic and aqueous extract exhibited low angiotensin-converting enzyme (ACE) inhibitory activity (Nyman *et al.,* 1998).

Sexual Behaviour: Methanolic root extract of *W. somnifera* induced a marked impairment in libido, sexual performance, sexual vigour, and penile erectile dysfunction. These effects were partly reversible on cessation of treatment. This antimasculine effect was not due to changes in testosterone levels but attributed to hyperprolactinemic, GABAergic, serotonergic or sedative activities of the extract. *W. somnifera* roots may be detrimental to male sexual competence (Ilayperuma *et al.,* 2002).

Anti-Ulcer: *W. somnifiera* root extract given orally (100 mg/kg BW/day p.o.) for 15 days significantly reduced the ulcer index, volume of gastric secretion, free acidity and total acidity in indomethacin and restraint induced gastric ulcer rats (Bhatnagar *et al.,* 2005). Asgand kwatha (equivalent to 1000 mg/kg) exhibited protective effect against rifampicin and isoniazid induced liver damage in mice (Chhajed *et al.,* 1991). The root powder produced dose dependent significant antiulcerogenic effect on aspirin induced gastric ulcers in rats.The equimolor combination of sitoindoside VII, sitoindoside VIII and withaferin A and hydromethanolic extractives of the roots reduced the incidence and the severity of restraint stress induced gastric ulcers in rats (Bhattacharya *et al.,* 2000).

Hypolipidemic: When the root powder of *W. somnifiera* was added to the diet at 0.75 and 1.5 gm/rat/day, hypercholesteremic animals registered significant decreases in total lipids, cholesterol and triglycerides in plasma. On the other hand, significant increases in plasma HDL-cholesterol levels, HMG-CoA reductase activity and bile acid content of liver were noted in these animals. A similar trend was also noted in bile acid, cholesterol and neutral sterol excretion in the hypercholesteremic animals with *W. somnifera* administration. Further, a significant decrease in lipid-peroxidation occurred in *W.somnifera* administered hypercholesteremic animals when compared to their normal counterparts. However, it appeared that *W. somnifera* root powder is also effective in normal subjects for decreasing lipid profiles (Visavadiya *et al.,* 2007). The root powder given for 30 days in a dose of 3 g/day in a small clinical trial of six NIDDM and six hyper-cholesterolemic patients exhibited hypoglycaemic, diuretic and hypolipidaemic effects.

Hepatoprotective: Iron overload induced increase in hepatic lipid peroxidation and serum levels of the enzymes, were attenuated by *W. somnifera* glycowithanolides in a dose related manner which explains their hepatoprotective action against heavy metals and other environmental toxins in rats (Bhattacharya *et al.,* 2000). Withaferin a reduced CCl_4 induced hepatotoxicity in rats (Sudhir and Budhiraja, 1992). The liver and kidney of rat underwent severe histopathological lesions when treated with a single bolus dose of carbendazim, a fungicide, particularly affecting the hepatocytes and the renal corpuscles, respectively. The effects appear to be manifestations of the microtubule-disrupting activity of carbendazim. Treatment of carbendazim-treated rats with the powder of tuberous root of *W. somnifiera* for 48 days resulted in complete cure of these organs (Akbarsha *et al*., 2000).

Thyroid Stimulating: Daily administration of *W. somnifiera* root extract (1.4g/kg body wt) for 20 days on thyroid function in female mice showed

an increase in hepatic glucose-6-phosphatase(G-6-Pase) activity and antiperoxidative effects as indicated either by a decrease in hepatic lipid peroxidation (LPO) and by an increase in the activity of antioxidant enzymes. The results indicates its thyroid stimulating function. These results indicate Asgand may be a useful botanical in treating hypothyroidism (Panda *et al*., 1997; Pandaand Kar, 1997).

Anti-Inflammatory: *W. somnifiera* root extract (1g/kg, oral) reduced Freund's complete adjuvant induced inflammation in rats; phenylbutazone was given as a positive control. The α2- glycoprotein (an indicator useful for diagnostic and prognostic assessment of arthritic and inflammatory conditions) found only in inflamed rat serum was decreased to undetectable levels in the *W.somnifera* group. Phenylbutazone, on the other hand, caused a considerable increase in the α2-glycoprotein in both arthritic and healthy rats (Anabalagan and Sadique, 1985; Anabalaganand Sadiques, 1981).*W. somnifiera* root powder also decreased air pouch granuloma induced by carrageenan on the dorsum of rats. *W. somnifera* decreased the glycosaminoglycans content in the granuloma tissue more than hydrocortisone treatment. Italso uncoupled the oxidative phosphorylation by significantly reducing the ADP/O ratio in mitochondria of granuloma tissue (Begum and Sadique, 1987). In a different study, *W. somnifera* root extract (1000mg/ kg, oraly daily for 15 days) caused significant reduction in both paw swelling and bony degenerative changes in Freund's adjuvant-induced arthritis in rats as observed by radiological examination. The reductions were better than those produced by the reference drug, hydrocortisone (Begum and Sadique, 1988). It has inhibited the granuloma formation in cotton-pellet implantation in rats and the effect was comparable to hydrocortisone sodium succinate (5 mg/kg) treatment. In another study 80% ethanolic extract of *W.somnifera* possessed anti-inflammatory activity in carrageenan-inducedrat paw edema model.Few studies have been conducted on the mechanism of action for the anti-inflammatory properties of *W. somnifera.* In one study, rats injected with formaline in the hind leg footpad showed a decrease in absorption of ^{14}C-glucose in rat jejunum (Somasundaram *et al.,* 1983). Glucose absorption was maintained at the normal level by both *W. somnifera* and the cyclooxygenase inhibitor oxyphenbutazone. Both drugs produced anti-inflammatory effects. Similar results were obtained in parallel experiments using ^{14}C-leucine absorption from the jejunum (Somasundaram *et al.,* 1983). These studies suggest cyclooxygenase inhibition may be involved in the mechanism of action of *W. somnifera*.

Anti-Stress: Hydroalcoholic extract of *W. somnifiera* roots (50 mg/kg b.w orally once daily for 21 days) containing glycowithanolides [WSG] normalized chronic foot-shock stress induced increase in superoxide dismutase (SOD) and reversed the decrease in catalase (CAT) and glutathione peroxidase (GPX) values in both the brain areas (frontal cortex and striatum) of rats, indicating its anti-stress adaptogenic property (Bhattacharya *et al.,* 2001). In another study, root extract and equimolar combination of Sitoindosides VII, VIII and Withaferin-A were uniformly effective in attenuating restraint stress induced responses ranging from anxiety, depression, analgesia, thermic changes, gastric ulcers, convulsions, tribulin activity and adrenocortical activation in rats (Bhattacharya *et al.,* 1997). It reversed the cold swimming-induced increases in plasma corticosterone, phagocytic index and avidity index to control levels. *W. somnifera* root powder (100 mg/kg orally as an aqueous suspension daily for seven days) given before the swimming test in water at 10ºC also increased total swimming time, indicating better stress tolerance in rats (Archana and Namasivayam, 1999; Dhuley, 2000). The aqueous suspension of root extract of Asgand prevented the rise in lipid peroxidation in stress induced rabbits and mice (Dhuley, 1998). A new withanolide, 1-oxo-5 beta, 6 beta-epoxy-witha-2-ene-27-ethoxy-olide from aqueous extract of *W. somnifiera* exhibited adaptogenic activity on stress indices in the cold-hypoxia-restraint (C-H-R) model (Kaur *et al.,* 2003). The extract of Asgand (1:1 aqueous–methanolic extract; doses of 20, 50, 100 mg/kg ip.) and/or sitoindoside administered to mice and rats improved memory related performance in passive avoidance tasks and protected against stress induced response, ranging from anxiety, depression, thermic changes, gastric ulcers, convulsions and tribulin activity. This was accompanied by a preservation of adrenal ascorbic acid and corticosterone levels suggesting that a corticosterone sparing effect is one of the mechanisms of action of adaptogens (Singh *et al.,* 1982). Experimental rats were subjected to immobilization stress for 14 h and were treated with a root powder extract of *W. somnifera.* Control rats were maintained in completely, non stressed conditions. Thionin stained serial coronal sections (7 microm) of brain passing through the hippocampal region of stressed rats (E(1) group) demonstrated 85% degenerating cells (dark cells and pyknotic cells) in the CA(2) and CA(3) sub-areas. Treatment with *W.somnifera* rootpowder extract significantly reduced (80%) the number of degenerating cells in both the areas. The study thus demonstrates the antistress neuroprotective effects of *W. somnifera* (Jain *et al.,* 2001). Rat model of chronic stress (CS) induced significant hyperglycaemia, glucose intolerance, increase in plasma corticosterone levels, gastric ulcerations, male sexual dysfunction, cognitive deficits, immunosuppression and mental depression were attenuated by

W. somnifera (25 and 50 mg/kg po) administered 1 h before footshock for 21 days. The results indicate that *W. somnifera* has significant antistress adaptogenic activity, confirming the clinical use of the plant in Ayurveda (Bhattacharya *et al.,* 2002). In another study a new withanolide free hydro soluble fraction from roots of *W. somnifera* exhibited significant antistress activity in a dose dependent manner (Singh *et al.,* 2003; Singh *et al.,* 2001). An herbal formulation comprising of Asgand showed adaptogenic activity comparable to *Panax ginseng* against a variety of behavioral, biochemical and physiological perturbations induced by unpredictable stress in CF strain albino rats (Bhattacharya *et al.,* 2000). Sitoindosides VII and VIII from Asgand significantly suppressed immobilization stress induced increase in corpus striatum dopamine receptors in rats (Saksena, 1989).

Nootropic: Oral administration of Asgand attenuated the disruption of memory consolidation produced by chronic treatment with electroconvulsive shock and reversed the scopolamine induced delay in transfer latency in mice. On the basis of these findings, it has been suggested that Asgand exhibits a nootropic-like effect in naive and amnesic mice (Dhuley, 2001). Methanolic extract of Asgand showed potent inhibition of AChE activity, indicating its role in improvement of cognition (Vinutha *et al.,* 2007). Asgand extract showed cognition enhancing and memory-improving effects by increasing cortical muscarinic acetylcholine receptor activity (Schliebs *et al.,* 1997).Withanolide derivatives isolated from methanol extract of Asgand, showed neurite extension in normal and damaged cortical neurons and also showed neurite outgrowth in human neuroblastoma SH-SY5Y cells (Zhao *et al.,* 2002). In normal cortical neurons, the predominant dendritic out-growth was induced by treatment with withanoside IV or withanoside VI, whereas predominant axonal outgrowth was observed in treatment with withanolide A (Kuboyama *et al.,* 2005). Aß(25-35) or Amyloid beta is a major pathological cause of Alzheimers disease due to formation of a beta sheet structure and induces neuroal cell death, neurite atrophy, synaptic loss and memory impairment. Simultaneous treatment with Aß(25-35) and withanolides from Asgand significantly prevented both dendritic and axonal atrophy induced by Aß(25-35) in rat cortical neurons (Dadkar *et al.,* 1987). Extension of dendrites and axons in neurons may compensate for and repair damaged neuronal circuits in the dementia brain. Methanol extract of Asgand (roots of *W. somnifera*; 5 microg/ml) significantly increased the percentage of cells with neurites in human neuroblastoma SK-N-SH cells. These results suggest that the methanol extract of Asgand promotes the formation of dendrites (Kuboyama *et al.,*2002; Tohda *et al.,* 2000).

Nervous System: *W. somnifiera* significantly inhibited haloperidol or reserpine-induced catalepsy and provide hope for treatment of Parkinson's disease. 6-Hydroxydopamine (6-OHDA) is one of the most widely used rat models for Parkinson's disease. There is ample evidence in the literature that 6-OHDA elicits its toxic manifestations through oxidant stress. *W. somnifiera* reversed all the toxic manifestations induced by 6-OHDA in a dose dependent manner (Ahmad *et al.,* 2005). *W. somnifiera* glycowithanolides (WSG) administered concomitantly with haloperidol for 28 days, inhibited the induction of the neuroleptic tardive dyskinesia. Antioxidant effect of WSG, rather than its GABA-mimetic action reported for the prevention of haloperidol-induced tardive dyskinesia (Bhattacharya *et al.,* 2002). Chronic Asgand treatment was effective in preventing the behavioral deficit in depressive animal models, which was accompanied by an adaptive supersensitivity of postsynaptic 5HT2 receptors (Tripathi *et al.,* 1998).It also has got a significant anticonvulsive property (Rai *et al.,* 1983). Glycowithanolides (WSG) isolated from *W. somnifiera* roots exhibited potent anxiolytic and antidepressant actions in rats. The activity was comparable to those elicited by the benzodiazepine, lorazepam for anxiolytic studies and by the tricyclic anti-depressant, imipramine for the antidepressant investigations (Bhattacharya *et al.,* 2000).

Anti-Venom: Venom hyaluronidases help in rapid spreading of the toxins by destroying the integrity of the extra-cellular matrix of the tissues in the victims. A hyaluronidase inhibitor (WSG) is purified from *W. somnifera*. The glycoprotein inhibited the hyaluronidase activity of cobra (*Naja naja*) and viper (*Daboia russelii*) venoms, which was demonstrated by zymogram assay and staining of the skin tissues for differential activity. WSG completely inhibited the activity of the enzyme at a concentration of 1:1 w/w of venom to WSG. External application of the plant extract as an antidote in rural parts of India to snakebite victims appears to have a scientific basis (Machiah *et al.,* 2006). In another study antitoxin-PLA2 glycoprotein isolated from *W.somnifera* neutralized the PLA2 activity of the *Naja naja* venom (Lizano *et al.,* 2003).

Immunomodulatory: In a mouse study, *W. somnifiera* root extract enhanced total white blood cell count. In addition, this extract inhibited delayed-type hypersensitivity reactions and enhanced phagocytic activity of macrophages when compared to a control group (Davis and Kuttan, 2000a; Davis and Kuttan, 2002a). *W. somnifiera* extract indirectly modulates immune activity and probably disengages *Listeria monocytogenes* induced suppression of immune responses by inducing a higher reserve of myeloid progenitors in the bone marrow, proliferation of lymphocytes and increased INF-γ levels (Teixeira *et al*., 2006). Methanolic extract of *W. somnifera* root increased inducible nitric

oxide synthase protein expression in a concentration dependent fashion in mouse macrophages. The increased NO production by macrophages could account for the immunostimulant properties of *W. somnifera* (Iuvone*et al.,* 2003). In different study with the aqueous suspension of *W. somnifiera* root powder was investigated for their *in vivo* and *in vitro* immunomodulatory properties. *W. somnifera* showed potent inhibitory activity towards the complement system, mitogen induced lymphocyte proliferation and delayed-type hypersensitivity reaction. Administration of *W.somnifera* root powder did not have a significant effect on humoral immune response in rats (Rasool and Varalakshmi, 2006). Glycowithanolides and a mixture of sitoindosides IX and X isolated from *W.somnifera*, both produced statistically significant mobilization and activation of peritoneal macrophages, phagocytosis and increased activity of the lysosomal enzymes. Root extract of *W. somnifera* was tested for immunomodulatory effects in three myelosuppression models in mice: cyclophosphamide, azathioprine and prednisolone (Ziauddin *et al.,* 1996). *W. somnifiera* root extract was found to stimulate immunological activity in Babl/c mice. Treatment with Withania root extract (20 mg/dose/animal; i.p.) was found to increased significantly ($P<0.001$) the total WBC count, bone marrow cellularity as well as alpha-esterase positive cell number. When treated along with the antigen (SRBC) produced an enhancement in the circulating antibody titre and the number of plaque forming cells (PFC) in the spleen. It also inhibited delayed type hypersentivity reaction in mice (Mantoux test) and showed an enhancement in phagocytic activity of peritoneal macrophages when compared to control in mice (Davis and Kuttan, 2000). Treatment of immunized animals (DBT) with standardized aqueous extract of *W. somnifiera* (100 mg/kg/day) for 15 days resulted in significant increase of antibody titers to B. pertussis (Gautam *et al.,* 2004).On oral administration, Asgand churna showed a significant increase in neutrophil adhesion and delayed-type hypersensitivity (DTH) response. It is concluded that Asgand churna significantly potentiated the cellular immunity by facilitating the footpad thickness response to SRBCs in sensitized rats.Pretreatment with a polyherbal formulation contianing *W. somnifiera* extract increased proliferation of splenic leukocyte to B cell mitogen, lipopolysaccharidic and cytotoxic activity against K 562 cells in mice (Nemmani*et al.,* 2002). Withaferin A and withanolide E, two sterioudal lactones of withania were demonstrated to have specific immunosuppresive effects on human B and T lymphocytes as well as on mice thymocytes (Shohat*et al.,* 1978). *W. somnifera* given orally once daily for 7 consecutive days in a dose of 100 mg/kg after intravenous infection of *Aspergillus fumigatus* prolonged the survival period of infected mice. This protective activity was probably related to the observed increases

in phagocytosis and intracellular killing of peritoneal macrophages induced by Ashwaganda treatment (Tohda *et al.,* 2000).Cyclophosphamide-induced immunosuppression was counteracted by treatment with *W. somnifera* extract, revealing significant increase in hemagglutinating antibody responses and hemolytic antibody responses towards sheep red blood cells (Gautam*et al.,* 2004; Agarwal *et al.,* 1999). The effects of graded doses of a chemically standardized aqueous alcoholic (1:1) root extract (AGB) of *W. somnifera* on the immune system of SRBC immunized BALB/c mice were investigated. Mice were administrated AGB orally for 15 days. AGB stimulated cell mediated immunity, IgM and IgG titers reaching peak value with 30 mg/kg b.wt. Flow cytometric analysis of lymphocyte surface markers of T cells ($CD3^+$, $CD4^+$ and $CD8^+$) and B cells ($CD19^+$) indicated prominent enhancement in proliferation and differentiation of lymphocytes. The extract selectively, induced type 1 immunity because it guided enhanced expression of T helper cells (Th)1 cytokines interferon (IFN)-γ and interleukin (IL)-2 while Th2 cytokine IL-4 observed a moderate decline. Confirmation of Th1 polarization was obtained from augmented levels of IgG2a over IgG1 in the blood sera of AGB treated groups. Withanolide-A, a major constituent of AGB appeared responsible for Th1 skewing effect of the extract as it significantly increased the levels of Th1 cytokines, decreased moderately IL-4 and significantly restored the selective dexamethasone inhibition of Th1 cytokines in mouse splenocytes cultures *in vitro*. In addition, AGB also strongly activated macrophage functions in*vivo* and *in vitro* indicated by enhanced secretion of nitrite, IL-12 and TNF-α. In contrast IL-10 remained unchanged again suggesting that AGB critically influenced Th1 profile of the cytokines. The studies suggested that AGB supports predominantly Th1 immunity with increase in macrophage function. Glycowithanolides and mixture of sitoindosides IX and X isolated from *W. somnifiera* produced statistically significant mobilization and activation of peritoneal macrophages, phagocytosis and increased activity of the lysosomal enzymes indicating its immunomodulatory potential (Ghosal *et al.,* 1989).

Antiviral: Hydroalcoholic extract showed poor *in vitro* anti-HIV activity. Methanolic extract did not show any *in vitro* and *in vivo* inhibitory effect on *Herpes simplex virus* (Hattori *et al.,* 1995).

Endocrinology: Ethanolic extract prevented *in vitro* glucose-mediated collagen glycation and cross-linking which is the process involved in end-organ damages in diabetes mellitus. The activity of the ethanolic extract was comparable to metformin, an antiglyeating agent and it showed more prominent effect than the root powder in rats (Babu *et al.,* 2007).

Ocular/Ophthalmic Effects: Withaferin A and withanolide D exhibited potential effect against choroidal neovascularization in eye (Bargagna *et al.,* 2006).

Antirheumatic: In a non-randomized trial in 118 patients, the root powder was found to provide relief in cases of acute rheumatoid arthritis and acute exacerbation of chronic arthritis.It also showed marked improvement in 22% of the 77 patients cases and moderate response is 53 % case of rheumatoid arthritis in a single blind clinical trial. Patients suffering from chronicity of diseases less than a year and 1-2 years and mild to moderately severe diseases showed better results (Bikshapathi and Kumari, 1999).

Antifungal: Withaferin A exhibited antifungal activity against *Aspergillus niger, Candida albicans* and *T. rubrum* (Dasgupta *et al.,* 1970).

Radiosensitivity: Withaferin A modified the effect of radiotherapy on bone marrow cell survival of the mouse, as studied using exogenous spleen colony unit (CFU-S) assay and the effect was compared with cyclophasphamide (CP). Withaferin A alone produced the lower number of CFU-S as compared with normal control but had a lower cytotoxicity compared with CP. But in combination with radiotherapy, the Withaferin A modified the effect of radiotherapy, significantly enhancing the cell lethality to the same extent as combination of CP + RT (Ganasoundari *et al.,* 1997).

Further Reported Activities

Ethanolic extract of *W. somnifiera* displayed cytotoxic effects on FL-cells using the neutral red assay (Ali *et al.,* 2001) and exhibited potent anti-osteoporotic activity in female rats (Nagareddy and Lakshmana, 2006). It also exhibited most significant in vitro enzyme inhibition activities against acetylcholinesterase (AChE), butyrylcholinesterase (BChE) and lipoxygenase enzymes (LO) (Khattak *et al.,* 2005). *W. somnifiera* exhibits cytoprotective property (Shukla *et al.,* 2000). A polyherbal formulation containing aqueous extract of *W. somnifiera* proved to have hypoglycemic activity in normal and streptozotocin induced diabetic mice.

(b) Clinical Pharmacology

Anxiolytic: In a study involving a total of 39 patients (20 receiving the drug and 19 received placebo) in a double-blind placebo-controlled trial in patients of anxiety disorders the ethanolic extract was found to exert significant anxiolytic effects (Andrade *et al.,* 2000).

Hypolipidemic: When six mild hypercholesterolemic subjects were treated with the powder of roots of *W.somnifera* for 30 days significant decrease in serum cholesterol, triglycerides, LDL (low density lipoproteins) and VLDL (very low density lipoproteins) cholesterol were observed indicating that root of *W. somnifera* is a potential source of hypocholesterolemic agent (Andallu and Radhika, 2000).

Anti-inflammatory: One clinical trial supports the possible use of *W.somnifera* for arthritis. In a double-blind, placebo-controlled cross-over study, 42 patients with osteoarthritis was randomized to receive a formula containing Asgand or placebo for three months. Patients were evaluated for one month pretreatment, during which time all previous drugs were withdrawn. During both the pretreatment and treatment phase, pain and disability scores were evaluated weekly while erythrocyte sedimentation (SED) rate and radiological studies were conducted monthly. The herbal formula significantly reduced the severity of pain ($p<0.001$) and disability ($p<0.05$) scores, although no significant changes in radiological appearance or SED rate were noted (Kulkarni*et al.,* 1991).

Anti-Aging: In a double-blind clinical trial, Asgand was tested in a group of 101 healthy males, 50-59 years old, at a dosage of 3 grams daily for one year. A significant improvement in hemoglobin, red blood cell count, hair melanin, and seated stature was observed. Serum cholesterol decreased and nail calcium was reserved. Erythrocyte sedimentation rate decreased significantly and 71.4 % reported improvement in sexual performance (Kuppurajan *et al.,* 1980). In a double-blind clinical trial on children (8-12 years of both sex), Asgand increased body weight, total proteins and mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration significantly. The combination of punarnava and Asgand increased significantly haemoglobin and mean corpuscular haemoglobin concentration levels. This study indicated Asgand usefulness as haematinic and growth promoters in the growing children (Venkataraghavan*et al.,* 1980).

Anti-Diabetic: The hypoglycemic, diuretic and hypocholesterolemic effects of roots of *W. somnifera* were assessed in six mild NIDDM subjects and six mild hypercholesterolemic subjects. The treatment consisted of the powder of roots over a 30 day period. At the end of the study, researchers noted a decrease in blood glucose comparable to that of oral hypoglycemic drug and a significant increase in urine sodium, urine volume, significant decrease in serum cholesterol, triglycerides, LDL (low density lipoproteins) and VLDL (very low density lipoproteins) cholesterol, with no adverse effects (Andallu and Radhika, 2000).

Nootropic: In a placebo-controlled study, men and women given an extract of Asgand root showed improved mental skills by performing better in reaction times, mental arithmetic and logical deductions (Karnick, 1991). In another placebo-controlled double blind study, Ayurvedic capsules containing one of the ingredients as Asgand, appears to be superior in improving psychomotor function compared to placebo (Karnick, 1992). The methanolic extract exhibited potent acetylcholinesterase inhibitory activity *in vitro* and it was found more active than the aqueous extract which suggests its potential in Alzheimer disease (Vinutha *et al.,* 2007).

Immunomodulatory: The polyherbal drug Immu-25 showed a favourable effect in patients (36: 10 female and 26 male) with HIV infection. The test drug decreased the mean viral load, which was associated with good symptomatic improvement and an increase in the mean CD4 cell count. On the basis of these data, it can be concluded that this herbal drug may have a good immunomodulatory effect and has potential as a co-therapeutic agent in the management of HIV infection (Usha *et al.,* 2003)**.**

Conclusion

From the above it is evident that Asgand is one of the most important herbal drugs having scientically proven therapeutic efficacy.

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Development of Pharmaco-poeial Standards and Microbial Studies on Jawarish-e-Qaiser*

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Abstract

Herbal medicines are called as natural products of traditional system of medicines such as Unani, Ayurveda and Siddha. In Unani system of medicine, these herbal products are being prepared using different parts of plants such as root, stem, bark, leaves, flowers and seeds etc. Jawarish-e-Qaiser is one such type of polyherbal Unani formulation prepared by using ten single drugs. The physicians of unani system of medicine have considered this drug as one of the important Unani formulation for the ailments of Qulang (Stomach and Bowel disorder) and Qabz-e-Muzmin (Chronic constipation). The present study was aimed to evaluate pharmacopoeial standards, quality control standards and antimicrobial activity of the drug Jawarish-e-Qaiser. The organisms used in the study were eight type bacterial cultures, namely, *Escherichia coli* (NCIM 2931), *Staphylococcus aureus* (NCIM 5021), *Enterobacter aerogens* (NCIM 5139), *Bacillus subtilis* (NCIM 2197), *Pseudomonas aeruginosa* (NCIM 2945), *Salmonella typhimurium* (NCIM 2501), *Bacillus cereus* (NCIM 2458), *Pseudomonas putida* (NCIM 2847) and one fungal (yeast) culture *Candida albicans* (NCIM 3471). The study revealed that the obtained data of quality control parameters were within the permissible limits of WHO and the drug shows potent antimicrobial activity against all the tested organisms at 100mg/ml concentration. The MIC was found to be within the range of 1.562µg/µl to 3.125µg/µl for majority of the organisms tested. Comparatively the drug was found to be least effective against both the tested *Pseudomonas* spp.

Keywords: Jawarish-e-Qaiser, Physico-chemical, Quality control, Antimicrobial activity.

Introduction

In modern era the phytomedicines have become potential medicines to cure variety of diseases. The usage of traditional medicines such as Unani, Ayurveda and Siddha have increased in both developing and developed countries due to their natural origin and lesser side effects (Mukerjee, 2008). As the world's population relies on herbal based medicines, search for novel antibacterial and antifungal agents' validation of scientific standards has becomes necessary issue to establish safe and efficacious drugs. In this context, quality standardization and biological activities of Unani medicine

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will open new frontiers for treatment of several ailments (Sharma and Arora, 2006). The drug Jawarish-e-Qaiser is one of the polyherbal Unani formulation listed in the National Formulary of Unani Medicine (NFUM, Part - IV). Literature studies revealed that some ingredients of the formulation have been reported to possess antimicrobial activity (Kaushik, 2011; Arora and Kaur, 2007)

Hence the present study was aimed to evaluate the pharmacopoeial and antimicrobial activity of Jawarish-e-Qaiser by using scientific methods.

Materials and Methods

Collection of raw drugs and preparation

To develop scientific method for the preparation of drug, raw drugs were procured from local raw drug dealers, Chennai. All the raw drugs were identified and authenticated using pharmacognostical methods (Kokate *et al*., 2000). Jawarish-e-Qaiser was prepared in three different batches using ten raw drugs namely, Tukhm-e-Karafs (*Apium graveolens* Linn. DSM - 81), Nankhwah (*Trachyspermum ammi* (L) Sprague ex. Turril. DSM - 83), Aaqarqarha (*Anacyclus pyrethrum* DC. DSM - 8), Namak Lahori (Rock salt), Filfil Daraz (*Piper longum* Linn. DSM - 45), Zanjabeel Khushk (*Zingiber officinale* Rosc. DSM - 86), Halela Zard (*Terminalia chebula* Retz. DSM - 64), Saqmonia (*Convolvulus scammonia* Linn. DSM - 148), Turbud Safaid (*Operculina turpethum* Linn. DSM - 151) and Qand Safaid (Sugar) as per the guidelines of NFUM Part-IV (Anonymous, 2006).

Collection of microorganism

To evaluate the microbial studies, the typed cultures were procured from National Chemical laboratory (NCL) Pune. The organisms used were *Escherichia coli* (NCIM 2931), *Staphylococcus aureus* (NCIM 5021), *Enterobacter aerogens* (NCIM 5139), *Bacillus subtilis* (NCIM 2197), *Pseudomonas aeruginosa* (NCIM 2945), *Salmonella typhimurium* (NCIM 2501), *Bacillus cereus* (NCIM 2458), *Pseudomonas putida* (NCIM 2847) and *Candida albicans* (NCIM 3471). All the organisms were confirmed using specific biochemical tests (Mackie & McCartney, 1996).

Physicochemical analysis

All the three batch samples of the drug were subjected to evaluate physico-chemical studies (Anonymous, 1987).

Thin Layer Chromatographic Studies

TLC studies of chloroform and alcohol extracts of the drug samples were performed using the standard methods (Wagner *et al*., 1984).

Quality Control parameters

To evaluate quality of the drug samples, parameters viz., microbial content, heavy metals, aflatoxin and pesticide residues were studied using WHO guidelines (Anonymous, 1998; 2000).

Microbial studies

Inoculum Preparation

A uniform suspension of the organisms listed above were prepared in 6ml of saline, and compared with the McFarland's standards (Mackie & McCartney, 1996). Each microbial suspension was diluted with the saline to a density visually equivalent to the Barium sulphate standard, 0.5 McFarland's unit. The plates were inoculated within 15 minutes of the preparation of the suspension to avoid changes in the density of the cultures.

Preparation of plates and Inoculation of microbial cultures

The required quantities of the Muller Hinton agar were prepared. The pH of medium was adjusted to 7.2. Each plate was poured with 20ml of the media and was allowed to solidify. The tubes containing 0.5 McFarland's unit equivalent microbial cultures were dipped with sterile cotton swabs, and excess of the fluid was removed by gently rotating the swabs against the sides of the test tube. The dipped swabs were swabbed over the Muller Hinton agar plates covering the entire surface of the plate by rotating the plates in all the directions. After solidification wells of 6 mm diameter were punched in agar plates. Plates were then allowed to set for few minutes.

Drug concentration

1gm of drug Jawarish-e-Qaiser was accurately weighed and dissolved in 10ml of DMSO solvent (Divakar and Nair, 2001) to make the stock solution containing 100mg/ml concentration. A series of dilutions were made from the stock solution to obtain 100µg/µl, 50µg/µl, 25µg/µl, 12.5µg/µl, 6.25µg/µl, 3.125µg/µl, 1.5625µg/µl, and 0.78µg/µl for determination of MIC.

Antibacterial assay and Determination of Minimum Inhibitory Concentration (MIC)

Antibacterial activity was assayed in duplicates by agar well diffusion method (Vasudha Rai, *et al*., 2011) using the above mentioned test organisms. The well was loaded with 50µl of the drug (100mg/ml conc.). The commercially available drug Norfloxacin (10mcg/disc) was used as control. The plain disc with 50µl loaded solvent DMSO was placed as the vehicle control. The plates were incubated at 37°C for 24 hours. The diameter of the clearing zones were measured in mm using the calipers.

The precise assessment of the effectiveness of the drug Jawarish-e-Qaiser against the susceptible bacteria was achieved by determining the MIC with varying concentration ranging from 0.78µg/µl to 100 µg/µl by agar well diffusion method. The plates were incubated at 37□C for 24hrs and were observed for the MIC, which was read as the lowest concentration of the drug required to completely inhibit the growth of the organism.

Results and Discussion

Physico-chemical analysis

The evaluated physico-chemical data of the drug are shown (Table – 1).

Thin Layer Chromatographic Studies

The TLC studies of the chloroform and alcohol extracts of all the three batch samples showed identical spots under UV - 254nm, 366nm and VS reagent. The Rf values of the chloroform and alcohol extracts are shown (Table 2 & 3, Fig. 1 & 2.)

Quality Control parameters

The study carried out on analysis of heavy metals, microbial load, aflatoxins and pesticide residues were shown (Table 4, 5 6 & 7) respectively.

Antimicrobial activity study and MIC

Antibacterial activity was studied against eight bacterial cultures viz., *Escherichia coli* (NCIM 2931), *Staphylococcus aureus* (NCIM 5021), *Enterobacter aerogens* (NCIM 5139), *Bacillus subtilis* (NCIM 2197),

Pseudomonas aeruginosa (NCIM 2945), *Salmonella typhimurium* (NCIM 2501), *Bacillus cereus* (NCIM 2458), *Pseudomonas putida* (NCIM 2847) and one yeast culture *Candida albicans* (NCIM 3471). A significant growth inhibition was shown by most of the organisms tested indicating the profound potency of the drug Jawarish-e-Qaiser. Among the tested organism *Salmonella typhimurium* was found to be the most sensitive organism followed by *Candida albicans, Escherichia coli, Bacillus spp., Staphylococcus aureus* and *Enterobacter aerogens* with zone of diameter ranging from 26mm to 7 mm (MIC Conc 100µg/µl to 12.5µg/µl). Both the species of *Pseudomonas* organism exhibited only minimum sensitivity to the drug with zone of diameter ranging from 11 mm to 7 mm (MIC Conc 100µg/µl to 12.5µg/µl). The results of the antibacterial activity and MIC of the drug Jawarish-e-Qaiser for all the organisms were observed and tabulated (Table 8, Fig. 3).

Table 1 : (Physico-chemical parameters)

Parameters Analyzed	Batch Number (n = 3)		
	I	II	III
Extractives Alcohol soluble matter Water soluble matter	48.84% 64.52%	49.04% 64.80%	48.52% 65.04%
Ash Total ash Acid insoluble ash	 2.13% 0.061%	 2.32% 0.055%	 2.46% 0.048%
pH values 1% Aqueous solution 10% Aqueous solution	 5.53 4.34	 5.79 4.52	 5.49 4.46
Sugar estimation Reducing sugar Non-reducing sugar	 38.39% 9.15%	 38.43% 9.24%	 38.41% 9.19%
Moisture	19.30%	19.84%	19.46%
Bulk Density	1.4099	1.4265	1.4205

Table 2 : (R_f values of Chloroform extract)

Solvent System (Toluene: Ethylacetate) (9:1) (Fig. 1)	Rf values		
	UV 254 nm	UV 366 nm	V.S. Reagent
	0.93 Grey 0.78 Blue 0.65 Pink 0.56 Pink 0.46 Pink 0.37 Light Pink 0.30 Light Pink 0.24 Pink 0.12 Pink	0.93 Yellowish Brown 0.78 Blue 0.72 Blue 0.56 Blue 0.46 Blue 0.41 Light Blue 0.34 Blue 0.29 Light Blue 0.21 Blue	0.93 Yellowish Green 0.80 Grey 0.72 Light Grey 0.56 Violet 0.46 Light Grey 0.26 Grey 0.12 Grey

Table 3 : (R_f values of alcohol extract)

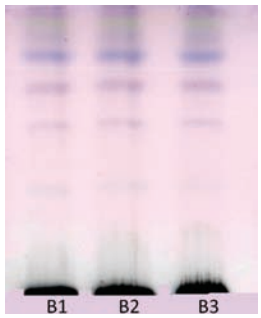
Solvent System (Toluene:Ethylacetate) (6:4) (Fig. 2)	Rf values		
	UV 254 nm	UV 366 nm	V.S. Reagent
	0.93 Pink 0.85 Light Pink 0.68 Pink 0.52 Pink 0.31 Light Pink	0.93 Yellow 0.85 Fluorescent Blue 0.80 Blue 0.73 Blue 0.65 Yellowish Green 0.56 Blue	0.93 Yellowish Green 0.86 Grey 0.81 Blue 0.71 Grey 0.58 Grey 0.36 Light Grey 0.20 Light Grey

Table 4 : Estimation of Heavy Metals

Parameters	Results	WHO/API Limits
Lead	0.0351ppm	10 ppm
Cadmium	Nil	0.3 ppm
Mercury	Nil	1 ppm
Arsenic	Nil	3 ppm

Table 5 : Estimation of Microbial load

Parameters	Results	WHO Limits for internal use
Total Bacterial Count (TBC)	$8x10^1$cfu/g	$1x10^5$cfu/g
Total Fungal Count (TFC)	$1x10^2$ cfu/g	$1x10^3$cfu/g
Enterobacteriaceae	Absent	$1x10^3$cfu/g
Escherichia coli	Absent	$1x10^1$cfu/g
Salmonella spp	Absent	Absent
Staphylococcus aureus	Absent	Absent

Table 6 : Estimation of Aflatoxin

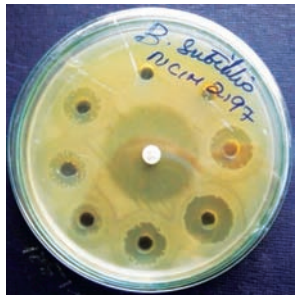
Aflatoxin	Results	Detection limit
B1	Nil	DL:1.0 ppb
B2	Nil	DL:0.5 ppb
G1	Nil	DL:1.0 ppb
G2	Nil	DL:0.5 ppb

Table 7 : Estimation of Pesticidal residue

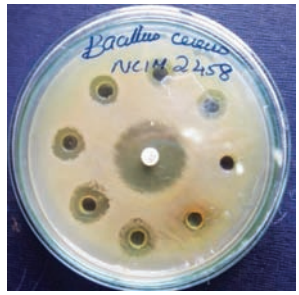
S. No.	Pesticide residues	Results
1	Organo Chlorine Group	ND
2	Organo Phosphorus Group	ND
3	Acephate	ND
4	Chlordane	ND
5	Dimethoate	ND
6	Endosulphan	ND
7	Endosulfan	ND
8	Endosulfon	ND
9	Ethion	ND
10	Endosufon sulphate	ND
11	Fenthion	ND
12	Heptachlor	ND
13	Lindane	ND
14	Methoxychlor	ND
15	Phorate sulfoxide	ND
16	Phorate sulfone	ND
ND – Not detected		

Table 8. Antimicrobial activity (MIC)

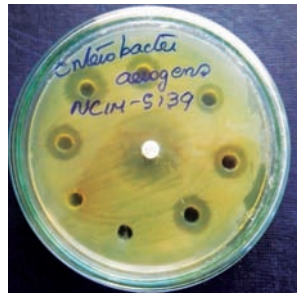
Sl. No.	Organisms	Zone diameter in mm								
		100 µg/µl	50 µg/ µl	25 µg/ µl	12.5 µg/ µl	6.25 µg/ µl	3.125 µg/ µl	1.562 µg/µ1	0.781 µg/µ1	Std (Nor)
1	*Escherichia coli* (NCIM 2931)	24	22	20	17	15	14	-	-	S
2	*Staphylococcus aureus* (NCIM 5021)	18	17	16	14	12	9	8	7	S
3	*Enterobacter aerogens* (NCIM 5139)	18	17	15	14	13	10	8	-	S
4	*Bacillus subtilis* (NCIM 2197)	22	19	18	13	12	10	9	-	S
5	*Pseudomonas aeruginosa* (NCIM 2945)	10	9	8	-	-	-	-	-	S
6	*Salmonella typhimurium* (NCIM 2501)	26	25	24	23	22	15	13	-	S
7	*Bacillus cereus* (NCIM 2458)	19	15	14	12	11	10	-	-	S
8	*Pseudomonas putida* (NCIM 2847)	11	10	8	7	-	-	-	-	S
9	*Candida albicans* (NCIM 3471)	25	24	23	22	19	16	13	-	S
Nor: Norfloxacin; S: Sensitive										



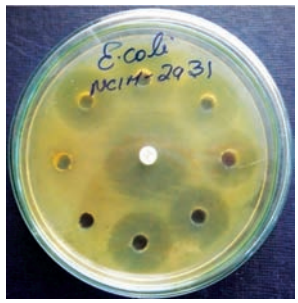
Bacillus subtilis
NCIM 2197



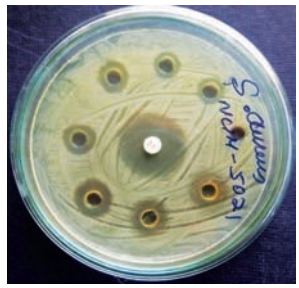
Bacillus cereus
NCIM 2458



Enterobacter aerogens
NCIM 5139

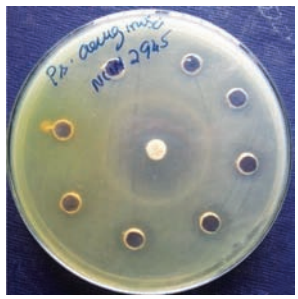


Escherichi coli
NCIM 2931

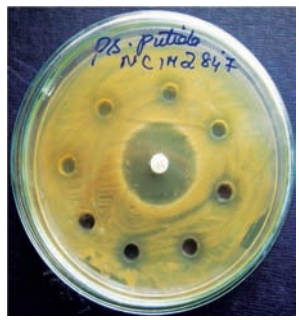


Staphylococcus aureus
NCIM 5021

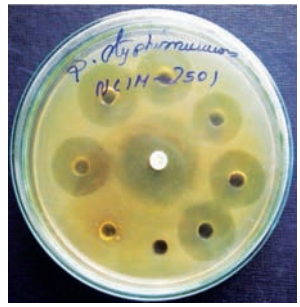
1. 100µg/µl
2. 50 µg/µl
3. 25 µg/µl
4. 12.5 µg/µl
5. 6.25 µg/µl
6. 3.125 µg/µl
7. 0.78 µg/µl
8. Vehicle control
9. Std (Norfloxacin)



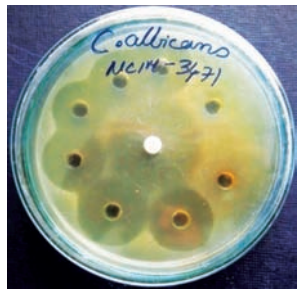
Pseudomonas aeruginosa
NCIM 2945



Pseudomonas putida
NCIM 2847



Salmonella typhimurium
NCIM 2501



Candida albicans NCIM 3471

Fig. 3: Plates showing antimicrobial activity of Jawarish-e-Qaiser

Conclusion

The results of the present investigation on physicochemical parameters and quality control parameters clearly emphasizes that the drug Jawarish-e-Qaiser is free from toxic substances indicating the safety and purity of the drug. Antimicrobial activity indicates that the drug possesses the antimicrobial property and it can be used as an alternative medicine.

Acknowledgement

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Ethnopharmacological Studies in Health Care Among the Tribals of Angul Forest Division, Odisha

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Abstract

Ethnobotanical leads are invaluable for the discovery of novel active compounds of therapeutic value from natural sources, particularly from plants. Based on this rational, an ethnopharmacological field investigation of medicinal plants was carried-out in Angul forest division, Odisha, between November-December 2013. Some 202 medicinal species have been collected and identified from the study area. Of these, 33 have been found to be used by local inhabitants for treating their diseases and conditions. The information on folk medicinal uses of plants viz. botanical name, family, Unani name (if any), mode of application etc. have been presented in this communication.

Keywords: Ethnopharmacological leads, Tribals, Angul forest division, Odisha.

Introduction

For many thousands of years, plants have been used to heal a broad range of illnesses, from minor ailments such as cuts and skin infections, to more serious diseases including typhoid fever, diabetes and cancer-like conditions. By targeting medicinal plants rather than surveying at random, there is a significantly increased chance of finding lead compounds (Mcrae *et al.*, 2005). The present investigations are based on this rationale and provide first-hand data on 33 medicinal species widely used in the folk treatment of various diseases and conditions by the tribals and ethnic groups of the study area.

Angul district is one of the centrally located district of the state of Odisha. It lies between 20°37′ to 21°10′ N latitude and 84°53′ to 85°28′ E longitude. Most of the area of this district is covered with dense forests which are of tropical dry deciduous type. The total forest cover of the district is 3509.59 km^2. From the point of view of area, it stands 11^{th} among the 30 districts of Odisha. Angul forest division is divided into six distinct ranges i.e., Raigoda, Durgapur, Chhendipada, Kaniha, Talcher, Purunagarh. The forests in the region are: Dry mixed deciduous forest, Tropical dry deciduous forest and moist deciduous forest. The areas visited include Khinda, Jamunda, Hinsida, Takursinga, Shankarpur, Pampasar, Jamunda, Balanga, Jamudibridge, Purunakote, Tikarpada, Nuakheta Banamira. Badakera, Tukuro, Jarpada, Antulia, Chhotkei, Tarava, Utunga, Kumuri, Lohiagargh, Tayansi. Chhendipada, Balipata. Dalaka, Talpada, Kaniha, Brahmandei, Rengali, Rengali Dam. Rutbhui, Bolangi, Samal Barrage, Baruan, Biru, Bulajhar, Kandhal, Bikisar. Angul & Adjoining Area forest areas were surveyed.

[1]* Author for correspondence

The study area is largely inhabited by rural population including tribes such as Kondh, Gond, Munda, Santal, Juang, Khaira and Bhuiyan. The detailed ethnopharmacological study of the district has been taken up with a view to enlist to plant resources and their utilization by the natives. Ethnobotanical plants are known for their therapeutically interest in both organized system of medicine such as Unani and Ayurveda as well as unorganized system of medicine such as Folk medicine. They exhibit great chemical diversity and several of them have been listed as source of valuable drugs (Kirtikar & Basu, 1935; Khare, 2007). Our study suggests that these people have accumulated a wide knowledge in the medicinal usage of plant wealth over the centuries. The present paper gives an account of 33 plant species belonging to 22 families used by the natives in the treatment of various diseases. Most of the uses were found reported when compared with published literature on Indian ethnobotany (Jain, 1991; Chopra *et al.*, 1956).

Materials and Methods

Ethnobotanical field trip was undertaken during November-December 2013 in order to explore the traditional knowledge of the inhabitants of Angul forest division and to make collections of native medicinal plants. Information regarding folk medicinal plants was obtained through field interviews with tribal people who practice indigenous medicine. In many cases, it was necessary to make a good rapport with these people in order to win over their confidence. Most of the information included in this study was gathered from elderly and experienced practitioners who were very knowledgeable about medicinal plants. The gathered data were cross-checked for reliability and accuracy by interacting with different groups of the tribals in other areas to confirm the use, mode of administration and dosage and differences of the herbal materials, if any. The medicinal plants were botanically identified by using the Flora of Orissa (Saxena & Brahmam, 1994-1996) and the Botany of Bihar & Orissa (Haines, 1921-25). After eliciting detailed information regarding the wild medicinal plants, the collected materials were carefully brought to the Survey of Medicinal Plants Unit, Regional Research Institute of Unani Medicine, Bhadrak, for identification and processing. Herbarium sheets for all the collected plant specimens were prepared and deposited in the Herbarium of Survey of Medicinal Plants Unit, Regional Research Institute of Unani Medicine, Bhadrak, India, for future reference and record.

Enumeration

The medicinal plants used as folk medicine in the study area are arranged in

alphabetical order. Their botanical name, family in bracket, local name, Unani name (if any), locality with collection number, part used, name of the disease(s) against which used, mode of preparation and administration, and informant who shared his valuable information are given for each recipe discussed.

1. *Acorus calamus* L. (Araceae); Hemokedar, Waj-e-Turki, Kumuri-9653, Root. Dysentery; Root paste is given orally to treat blood dysentery. (Bhuiyan).

2. *Andrographis paniculata* (Burm.f.) Wall. *ex* Nees (Acanthaceae); Bhuinimbo; Balanga-9590; Leaf; Malarial fever, Skin disease; Leaf decoction is used with honey to treat malarial fever. Leaf juice is taken orally to treat skin diseases. (Munda).

3. *Asparagus racemosus* Willd. (Liliaceae); Satabari; Satawar; Purunakote-9608; Root; Dyspepsia; Root juice is mixed with honey and used for dyspepsia. (Laku Bhuiyan)

4. *Azadirachta indica* A. Juss. (Meliaceae); Nimbo; Neem; Kandhal-9746; Leaf; Skin Diseases; Leaf juice 100 ml is taken for a month to treat skin diseases. (Kharia).

5. *Bauhinia racemosa* L. (Caesalpiniaceae); Barada; Kachnal; Antulia-9625; Stem bark, Leaf; Stem bark one teaspoon is used in dysentery. Two tea spoonful leaves decoction is used in malarial fever. (Naik).

6. *Biophytum sensitivum* (L.) DC (Oxalidaceae); Lajkoli; Tikarpada-9617; Leaf; Diabetes; One teaspoonful leaf juice is taken twice a day to treat diabetes. (Paresh)

7. *Bridelia retusa* (L.) Spreng. (Euphorbiaceae); Kassi; Tikarpada-9619; Stem Bark; rheumatism; Stem bark decoction is used to treat rheumatism. (Singlu).

8. *Butea superba* Roxb. (Fabaceae); Palasnoi; Antulia-9626; Shoot; piles; two teaspoonful shoot decoction is given to treat piles. (Munda).

9. *Chromolaena odorata* (L.) King & Robins (Asteraceae); Poksunga; Hinsida-9560 leaf; cuts; Leaf juice is applied locally on cuts to check bleeding. (Kapoor Gond)

10. *Costus speciosus* (Koenig) Sm. (Zingiberaceae); Andkhira; Talpada-9694; Root; anthelmintic; Two spoon root juice is taken thrice daily as anthelmintic. (Tunu).

11. *Crateva magna* (Lour.) DC (Capparaceae); Baruna; Kumuri-9651; Leaf/ Bark; Leaf/Bark paste is applied locally on boils to reduce pain & early healing. (Bhuiyan).

12. *Curculigo orchioides* Gaertn. (Hypoxydaceae); Talmuli; Musli Siyah; Purunakote-9613; Root; Wounds; Crushed roots are applied on cuts to check bleeding & healing wounds. (Bhuiyan).

13. *Dendrophthoe falcata* (L.f.) Etting. (Loranthaceae); Madang; Baruan-9735; Whole plant; Asthma; Whole plant is crushed and taken one tea spoonful twice daily to treat asthma. (Raghu Bhuiyan).

14. *Ficus benghalensis* L. (Moraceae); Baro; Baragad; Kandhal-9748; Latex; Spermatorrhoea; Latex along with Misri is used to treat spermatorrhoea. (Kharia).

15. *Gardenia latifolia* Ait. (Rubiaceae); Damagaruda; Purunakote-9611; Fruit; Joint pain; Fruit with Harida & Bahada is taken in equal quantity and boiled in mustard oil. This oil is applied locally on joints to treat joint pain. (Bhuiyan).

16. *Helicteres isora* L. (Sterculiaceae); Muda; Marorphali; Purunakote-9607; Fruit; Stomachache; Fruits boiled in mustard oil & filtered & filtered oil is applied locally on stomach to treat stomachache. (Laku Bhuiyan)

17. *Holarrhena pubescens* (Buch.-Ham.) Wall. *ex* G. Don (Apocynaceae); Kurmi; Inderjo Talkh; Balanga-9594; Follicles; Dysentery; Crushed follicle's juice is taken one teaspoon to treat dysentery. (Mahendra Bhuiyan)

18. *Kalanchoe pinnata* (L.) Pers. (Crassulaceae); Amarpoi; Zakhm-e-Hayat; Nuakheta-9679; Leaf; Skin diseases; Leaf juice is applied locally to treat skin diseases. (Naik)

19. *Lannea grandis* Engl. (Meliaceae); Moi; Talpada-9696; Bark; Wounds; Bark juice is applied locally to check burning & healing wounds. (Kharia).

20. *Leonotis naepetifolia* (L.) R. Br. (Lamiaceae); Bhutabhairavi; Shankarpur-9563; whole Plant; cuts; Plant juice is applied locally on cuts to check bleeding. (Ramu Bhuiyan).

21. *Mimusops elengi* L. (Sapotaceae); Baulo; Mulsari; Chakrasi Samal Barrage-9729; Leaf; Dental Care; Leaves are chewing raw to treat toothache. (Pukar).

22. *Ocimum canum* Sm. (Lamiaceae); Nandabagudi; Shankarpur-9562; Seed; Jaundice; Seeds soaked in one glass of water to overnight and filtered and water taken early morning to treat jaundice. (Kapil Munda)

23. *Phyllanthus fraternus* Webster (Euphorbiaceae); Badiamla; Jamunda-9575; Plant; Diabetes; One cup plant juice is taken twice a day for 30-60 days to treat diabetes. (Prakash Sahoo)

24. *Pongamia pinnata* (L.) Pierr. (Fabaceae); Karanja; Karanj; Chakrasi Samal Barrage-9730; Seed, Stem/Root; Wounds, Dental Care; Seed oil is used to treat wounds & itching. Young stem/root also used as tooth stick. (Kharia).

25. *Pterocarpus marsupium* Roxb. (Fabaceae); Piyasal; Bijasar; Purunakote-9614; Seed, Wood; Diarrhea & dysentery, Diabetes; Seed oil is used in diarrhea & dysentery and extraction of wood is used in diabetes. (Gopal Bhuiyan).

26. *Rauvolfia tetraphylla* L. (Apocynaceae); Patalgarudu; Chhendipada-9662; Root; snake-bite; Root paste is given with one glass water orally to treat snake-bite. (Munda).

27. *Solanum nigrum* L. (Solanaceae); Nununia; Mako; Balanga-9584; Whole Plant; Jaundice; One glass plant juice is taken twice a day for 7-15 days to treat jaundice. (Khira)

28. *Soymida febrifuga* (Roxb.) A. Juss. (Meliaceae); Rohini; Kandhal-9749; Stem bark; Fever, Diarrhoea & Dysentery; 3-4 teaspoon extract is given twice or thrice to treat intermittent fever, diarrhoea & dysentery. (Bhuiyan).

29. *Spermacoce hispida* L. (Rubiaceae); Jibakata; Bikisar-9750; Whole plant; Heamorrhoid; Plant Leaf juice is taken twice daily 3 teaspoon to treat heamorrhoid. (Kharia).

30. *Spilanthes calva* L. (Asteraceae); Poksunga; Pampasar-9650; Flower; Dental Care; Flowering heads are used in toothache. (Munda).

31. *Tephrosia purpurea* (L.) Pers. (Fabaceae); Kulthia; Sarphuka; Khinda Jamunda-9557; Root; Stomachache; Root juice is taken once a day to treat stomachache. (Tirtha Basi Naik)

32. *Vitex negundo* L. (Verbenaceae); Begunia; Sambhalu; Dalaka-9692; Leaf; Rheumatic disorders; Leaves boiled in oil and filtered. This oil is applied locally to treat rheumatic disorders. (Munda).

33. *Wrightia tinctoria* (Roxb.) R. Br. (Apocynaceae); Kuren; Inderjo Shreen; Balanga-9591; Follicles; Fever; 1-2 glass of tender tips decoction is given orally for treating common fever. (Prakash Sahoo)

Folk Medicinal Plants from the Study Area

Fig. 1: *Asparagus racemosus* Willd

Fig. 2: *Crateva magna* (Lour.) DC.

Fig. 3: *Curculigo orchioides* Gaertn

Fig. 4: Dendrophthoe falcata (L.f.) Etting

Fig. 5: *Helicteres isora* L.

Fig. 6: *Wrightia tinctoria* (Roxb.) R. Br.

Results and Discussion

In the present investigation 33 medicinal plants are used for the treatment of various diseases e.g., dental care, piles, stomach ache, fever, diarrhoea & dysentery, jaundice, snake-bite, cuts & wounds, asthma, spermatorrhoea, rheumatic disorders etc The utility lies through their roots, stem bark, latex, leaves, fruits and seeds. These are taken internally or applied externally in the form of infusion, decoction, paste or powder. Most of the plants used in medicines are either mixed with other ingredients or single. Some important medicinal plants needs immediate conservation and their cultivation should be encouraged through which their extinction can be prevented and local village people may also get low-cost cure their disease.

A detailed perusal of the ethnobotanical records reveals that a number of ethnobotanical studies have been conducted in different parts of Odisha (Ali *et al.*, 2010; Aminuddin and Girach, 1996; Aminuddin *et al.,* 2013; Dash *et al.,* 2003; Girach *et al*., 2011; Kandari *et al.,* 2012, Mohapatra and Sahoo, 2008; Mudgal and Pal, 1980; Mukesh *et al.,* 2012, 2013; Mukherjee and Namhata, 1990; Mund and Satapathy, 2011; Rout, 2007; Sahu, and Dhal, 2012; Sahu *et al.,* 2013a, 2013b; Singh, 2012; Singh *et al.,* 2010; Tripathy and Behera, 2008) and found that most of the folk medicinal plants are duly reported in the literature (Jain, 1991; Chopra *et al.*, 1956). However, their mode of application, ingredients and parts used are different. Therefore, the present study represents the contemporary folk uses of medicinal plants of the area investigated. It would be worthwhile to subject all these folk drugs to scientific testing in the context of claims reported herein.

It has been observed that un judicious exploitation of some species by the local tribes, medicinal plant collectors and exporters have created an alarming situation for the sustainable utilization of plant resources. Besides, the forest resources have been depleted at an alarming rate due to rapid industrialization and urbanization in the district. Further intensive study will be much useful to get more idea about the unexploited, underexploited and threatened plants of this region.

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Indian Herbal Drugs of Trade and Their Supply Chain Management: A Review

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Abstract

The use of herbal medicines is growing with approximately 40 per cent of population reporting use of herbs to treat diseases within the past year. India has 16 agro-climatic zones, 45000 different plant species out of which 15000 are medicinal plants. The Indian Systems of Medicine have identified 1500 medicinal plants, of which more than 500 species are mostly used in the preparation of drugs in direct or indirect ways and highly potential in the trade related practices in Indian and Global markets. Apart from requirement of medicinal plants for internal consumption, India exports crude drugs mainly to developed countries, viz. USA, Germany, France, Switzerland, UK and Japan. The supply base of 90% herbal raw drugs used in the manufacture of Ayurveda, Siddha, Unani & Homoeopathy (Ayush) systems of medicine is largely from the wild. Present communication reviews and highlights the supply chain management and trade practices of medicinal and aromatic plants (MAPs) in India.

Key words: Suply chain management, Herbal drugs, Medicinal and Aromatic plants (MAPs)

Introduction

It is estimated that 80 percent of the population in developing countries rely largely on plant based drugs for their health care needs, and the WHO has estimated that in coming decades a similar percentage of the world population may well rely on plant-based medicines. Thirty percent of the drugs sold worldwide contain compounds derived from plant material. As a result of the expanding interest in medicinal and aromatic plants, new income generating opportunities are opening up for rural populations. With many of the MAPs gathered from the wild, the collection and sale of MAPs is providing a complementary source of cash for many extremely poor rural households. However, despite the fact that the products collected can have very high value in the final products, the collectors typically receive only a small share of the final value, either because they are unaware of the real value, are unable to market it in the form wanted by buyers or are unable to market to these buyers.

Current trends all-over the world has shown that for one reason or the other, people are not only willing to try natural medicine especially those of plants based but are also actively seeking non-conventional remedies. As a result there is a global resurgence in the trade of herbal medicine. This indicates that

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production, consumption and domestic and international trade in medicinal plants based products is going to grow at a significant rate.

The international market of herbal products is estimated to be US $62 billion which is poised to grow to US $5 trillion by the year 2050, but India's share in the global export market of medicinal plants related trade is just 0.5 per cent (Sharma, 2004). India has 16 Agro climatic zones, 45000 different plant species out of which 15000 are medicinal plants. The Indian Systems of Medicine have identified 1500 medicinal plants, of which 500 species are mostly used in the preparation of drugs.

The Indian Systems of Medicine, particularly Ayurveda, Siddha, Unani, & Homoeopathy medicine largely use plant base materials, minerals, metals, marine and products of animal origin. Our ancient texts had documented medicinal uses of a large number of plants. These plants are being used for preparation of medicines for centuries.

The increased demand of herbal medicines has led to a sudden increase in herbal manufacturing units. There is a complex of large number of manufacturing units using herbal material for various purposes. Whereas the largest number of such manufacturing units are registered as 'pharmaceuticals', there are others that are engaged in making plant based cosmetics and food supplements. Even within the pharmaceutical units, there are manufacturers of Ayurveda, Siddha, Unani and Homeopathic formulations with a few even making western medicines. Another group of manufacturing units is engaged in making extracts and distilling oils for use by other industries and for exports. Raw materials for all these diverse industries are largely derived from wild sources.

The trade practices of MAPs and herbal products in India are extremely complex, secretive, traditional, confusing, badly organised, highly under-estimated and unregulated. This requires a grand strategic plan to augment the availability of quality raw materials, standardised finished products and proper marketing infrastructure.

Keeping in view, the present review article is designed to find out the current situation and trends of herbal drug sector, supply and demand equilibrium and supply chain management of MAPs and herbal products.

Material and Methods

A field survey of herbal drug dealers was done during the period of 2010 to 2012 and primary as well as secondary data were obtained. Other than the

secondary sources available to provide the relevant information from different companies, government agencies and the libraries, the focus in this study was on the primary source of information which was, collected through survey of the following groups of respondents viz. Dealers/retailers of the MAPs or herbal products, Procurement force of herbal manufacturing unit and Consumers of the MAPs and herbal products. Covering the whole population of India was beyond the time and cost resources. Therefore, the scope of the study was kept limited. It was decided to cover three major herbal markets of Delhi, Uttar Pradesh and Uttarakhand. Respondents were preselected according to the nature of study by using the judgement sampling method. Respondents are mainly far from each other that's why the internet, telephonic and post survey method was applied. Open ended questionnaire were sent to the respondents through email or by post and there answer were recorded. Somewhere, if possible, telephonic interviews were also carried out. After getting the primary data from the questionnaire. These were sorted and analysed.

Results and Discussion

Asia has abundant species of medicinal and aromatic plants (MAPs) and traditional medicine has been practiced in Asia since ancient times. The Chinese and the Indians have made use of medicinal plants to cure ailments for thousands of years. According to the World Health Organisation (WHO), the goal of 'Health for All' cannot be achieved without herbal medicines. While the demand for herbal medicines is growing in developing countries, there are indications that consumers in developed countries are becoming disillusioned with modern healthcare and are seeking alternatives in traditional medicines. There is, therefore, an increasing consumer demand for herbal medicines in developed countries.

During recent years, the global attention of the pharmaceutical industry has switched once more to the natural world and this may be illustrated by reference to three clinical drugs, taxol, etoposide and artemisinin (Phillipson, 1999). Taxol is obtained from the bark of the *Taxus brevifolia* and Artemisinin is an unusual sesquiterpene endoperoxide that has been isolated as the active principle of the antimalarial herb *Artemisia annua* both plants are grown in India.

In the recent years, there has been a boom in the herbal industry globally. According to WHO, demand for medicinal plants by the year 2050 is estimated at US$ 5 trillion. Demand for nutraceuticals and functional food has been rising in developed markets, particularly in USA, Europe and Japan. Nutraceutical

market in USA is estimated at about US$ 80 billion to US$ 250 billion, with a similar market size in Europe, and Japanese nutraceutical market is estimated at US$ 1.5 billion. Global market for Functional Food is pegged at US$ 60 billion to US$ 80 billion, growing by around 10% per year. Indian nutraceutical market is estimated to be around US$ 270 million growing at a CAGR of 18%, against the CAGR of 7% witnessed in global market (Anonymous, 2010).

India, with approximately 8% of world's biodiversity including plant genetic diversity with medicinal properties, has the potential of becoming a major global player in market for medicinal plants based herbal formulations, medicines and products (Singh, 2006).

Indian herbal medicine market has been growing at a steady pace of between 15% and 20% every year. The market size of domestic herbal industry is currently estimated at over rupees 5000 crore. According to a study the industry is envisaged to grow at a level of repees 5,500 crore after 2010 Commonwealth Games (CWG), and Ayurvedic industry alone is envisaged to earn a business of rupees 500 crore during the Games. The study also envisages that Indian Spa industry to receive an investment of US$ 35 billion over the next 3 to 4 years (Anonymous, 2010).

The FRLHT researchers also noted that while amla fruit (*Phyllanthus emblica*) is the highest consumed botanical raw drug by the domestic herbal industry, 70% of total botanical raw material exports (by volume) are made up just a few species, namely psyllium husk (*Plantago ovata*), senna leaf and pod (*Cassia angustifolia*), henna leaf & powder (*Lawsonia inermis*), and the three myrobalans: amla fruit (*Phyllanthus emblica*), belleric myrobalan fruit (*Terminalia bellerica*), and chebulic myrobalan fruit (*Terminalia chebula*) (Ved and Goraya, 2008).

Indian Herbal Drugs in Trade

Although a large number of medicinal plants are described in literature for medicinal use but their commercial exploitation is in limited extent. The species noticed in trade are tabutaled a below:

Table 1: Inventory of Indian Herbal Drugs in trade

Trade Name	English Name	Botanical Name	Morphological Part used
Afastatin	Artemisia	*Artemisia vulgaris*	Whole plant
Agaru	Eagle wood	*Aquilaria agallocha*	Wood

Trade Name	English Name	Botanical Name	Morphological Part used
Ajalu	Mimosa	*Mimosa pudica*	Leaves, seeds
Akarkara	Pellitory	*Anacyclus pyrethrum*	Roots
Alsi	Flax seed/lin seed	*Linum usitatissimum*	Seeds
Ambahaldi	Turmeric	*Curcuma amada*	Rhizome
Amla	Indian gooseberry	*Emblica officinalis*	Fruits
Anantmool	Indian sarsaparilla	*Hemidesmus indicus*	Roots
Anar	Pomegranate	*Punica granatum*	Seeds, rind
Anjbar	—	*Polygonum viviparum*	Roots
Annato	Bixa	*Bixa orellana*	Seeds
Arjun	Arjuna	*Terminalia arjuna*	Bark/heartwood
Arlu, shyonaka	Oroxylin	*Oroxylum indicum*	Root bark
Arni	Premine	*Premna integrifolia*	Whole plant
Ashoka	Saraca bark	*Saraca indica*	Bark
Ashwagandha	Winter cherry	*Withania somnifera*	Roots/leaves
Attis	Aconitum	*Aconitum heterophyllum*	Roots
Attis mitha	Aconitum	*Aconitum napellus*	Roots
Babchi	--	*Psoralea corylifolia*	Seeds
Babuna	Chamomilla	*Matricaria chamomilla*	Flowers
Bach	Sweet flag	*Acorus calamus*	Roots
Bach nag	Aconitum	*Aconitum ferox*	Roots
Baheda	--	*Terminalia belerica*	Fruit
Bakul	Indian medler	*Mimusops elengi*	Bark
Balchar	Cat's claw	*Nardostachys jayamansi*	Rooys
Bankakri	Podophyllum	*Podophyllum emodi*	Roots
Banmethi	Melilotus	*Melilotus indica*	Seeds
Basant	St.john wart	*Hypericum perforatum*	Leaves
Belladona	Belladona	*Atropa belladonna*	Roots/leaves
Bhangra	Calendulacea	*Wedelia calendulacea*	Leaves
Bharangi	Clerodendrum	*Clerodendrum indicum*	Root
Bhringaraj	Eclipta	*Eclipta alba*	Leaves

Trade Name	English Name	Botanical Name	Morphological Part used
Bijaysar	Pterocarpus	*Pterocarpus marsipium*	Bark
Bilva	Stone apple	*Aegle marmelos*	Pulp
Biranjasaf`	—	*Achillea millefolium*	Whole plant
Bisfaij	Drynaria	*Polypodium vulgare*	Roots
Boswellia	Olibanum	*Boswellia serrata*	Gum
Brahmi	Gotu kala	*Centella asiatica*	Whole plant
Chaksu	—	*Cassia absus*	Seeds
Chakunda	Foetid cassia	*Cassia tora*	Seeds
Champa	Champa	*Michelia champaca*	Root
Chandan	Red sandal	*Pterocarpus santalinus*	Wood
Chaulai	—	*Amaranthus Spinosus*	Seeds
Chaulmogra	—	*Gynocardia odorota*	Seeds
Chiraita	Swertia bitter	*Swertia chirata*	Whole plant
Chirchita	Barbarum	*Lycium barbarum*	Berries
Chobchini	Smilax	*Smilax glabra*	Roots/leaves
Chora	Angelica	*Angelica galuca*	Roots
Cinchona	Cinchona	*Cinchona officinalis*	Bark
Coleus	Coleus	*Coleus forskohli*	Roots
Dalchini	Cassia	*Cinnamomum cassia*	Bark
Daru haridra	Berberis	*Berberis aristata*	Roots/stem/ prep.
Daryakanaryal	Maldivica	*Lodoicea seychellarum*	Fruit
Datura	Thorn apple	*Datura metel*	Seeds
Devdaru	Cedrus	*Cedrus deodara*	Wood
Digitalis	Grecian foxglove	*Digitalis purpurea*	Leaves
Dikamali	Gummifera	*Gardenia gummifera*	Gum
Ergot	Ergot	*Claviceps purpurea*	Fungal grass
Gajar	Carot	*Daucus carota*	Seeds
Gajpipal	Scindapsus	*Scindapsus officinalis*	Fruits
Gazaban	Bracteatum	*Onosma bracteatum*	Leaves
Ginseng	Ginseng	*Panax ginseng*	Roots

Trade Name	English Name	Botanical Name	Morphological Part used
Gloriosa	Glory lily	*Gloriosa superba*	Seeds
Gokhroo	Caltrops	*Tribulus terrestris*	Fruits/plant
Guduchi	Tinospora	*Tinospora cordifolia*	Stems
Guggal	Myrrha	*Comiphora mukul*	Gum
Gul banafsha	Viola	*Viola odorata*	Flowers/leaves
Gul khair	—	*Malus sylvestris*	Leaves
Gulab	Rose	*Rosa damascena*	Petals
Gurmar	Gymnema	*Gymnema sylvestre*	Leaves
Hansraj	—	*Adiantum capillus*	Whole plant
Haridra	Turmeric	*Curcuma longa*	Rhizome
Haritaki	Myrobalan	*Terminalia chebula*	Fruit
Harmal	Harmalol	*Peganum harmala*	Seeds
Harsinghar	Nyctanthin	*Nyctanthes arbortristis*	Flowers
Hauber	Juniper	*Juniperus communis*	Berries
Hawthorn	Hawthorn	*Crataegus oxyacantha*	Fruit
Hing	Asafetida	*Ferula foetida*	Gum resin
Horjora	Quadrangularis	*Cissus quadrangularis*	Whole plant
Imli	Tamarind	*Tamarindus indica*	Fruit
Isafgol	Psyllium	*Plantago ovata*	Husk/seeds
Jal-brahmi	Indian pennywort	*Baccopa monnieri*	Whole plant
Jamalghota	Croton	*Croton tiglium*	Seeds
Jangli haldi	Wild turmeric	*Curcuma aromatica*	Rhizome
Jiwanti	Leptadenia	*Leptadenia reticulata*	Leaves
Jiyaputra	Putrajiva	*Putrajiva roxburghii*	Fruit
Kachura	Wild turmeric	*Curcuma zedoria*	Rhizome
Kaiphul	Myrica	*Myrica nagi*	Bark
Kakmachi	Makoh	*Solanum nigrum*	Berries
Kakrashringi	Pistacia	*Pistacia integerrima*	Fruits
Kalimusli	Curculigo	*Curculigo orchioides*	Rhizome
Kalmegh	Andrographis	*Andrographis paniculata*	Whole plant

Trade Name	English Name	Botanical Name	Morphological Part used
Kalonji	Black cumin seed	*Nigella sativa*	Seeds
Kamila	—	*Mallotus philipinensis*	Powder
Kanchana	Toddaline	*Toddalia asiatica*	Seeds
Kapur kachri	Hedychium	*Hedychium spicatum*	Rhizome
Karanja	Pongamia	*Pongamia pinnata*	Seeds
Kasni	Cichorin	*Cichorium intybus*	Seeds
Kavanch	Cowhage	*Mucuna pruriens*	Seeds
Kesar	Saffron	*Crocus sativus*	Flower
Khair	Catechu	*Acacia catechu*	Bark
Khas	Vettiver	*Vetiveria zizanioides*	Roots
Kikar	Gum tree	*Acacia arabica*	Gum/bark
Kokam	Garcinia	*Garcinia cambozia*	Fruit
Kuchla	Nux vomica	*Strychnos nux vomica*	Seeds/bark
Kulanjan	Galangal	*Alpinia galanga*	Rhizomes
Kushtha	Sassurea	*Saussurea lappa*	Roots
Kusum	Safflower	*Carthamus tinctorius*	Flower
Kutaja	Conessi bark	*Holarrhena antidysenterica*	Bark
Kutki	Kurroo	*Gentiana kurroa*	Root
Kutki	Picrorhiza	*Picrorhiza kurroa*	Roots
Lasora	Dichotama	*Cordia dichotama*	Fruit
Lobiya	Beans	*Phaseolus lunatus*	Seeds
Lodhra	Symplocos	*Symplocos racemosa*	Bark
Luban	Luban	*Styraz benzoin*	Gum resin
Mahwa	—	*Madhuca indica*	Flowers/bark
Majuphul	Gallnuts	*Quercus infectoria*	Fruit
Mal kanguni	—	*Celastrus paniculatus*	Seeds
Mamira	Copteeta	*Coptis teeta*	Rhizome
Mamira	Gold seal	*Thalictrum foliosum*	Root
Manjistha	Rubia	*Rubia tinctorum*	Roots
Marjal	Iris	*Iris ensata*	Roots

Trade Name	English Name	Botanical Name	Morphological Part used
Mehndi	Henna	*Lawsonia alba*	Leaves
Morinda	Morinda	*Morinda citrifolia*	Fruits
Mulethi	Licorice	*Glycyrrhiza glabra*	Roots
Murva	Sanservierine	*Sansevieria zeylanica*	Rhizome
Muskdana	Hibiscus abelmoschus	*Abelmoschus moschatus*	Seeds
Musta	Nutgrass	*Cyperus rotundus*	Tubers
Nagkesar	Cobras saffron	*Mesua ferrea*	Flowers
Nagkesar	—	*Ochrocarpus longifolius*	Flower buds
Narkachura	Black turmeric	*Curcuma caesia*	Rhizome
Neeli	Indigo	*Indigofera tinctoria*	Leaves
Nirmasi	Kyllinga triceps	*Delphinium denudatum*	Roots
Nisoth	Ipomoea	*Operculina turpethum*	Roots
Pakhanbed	Bergenia	*Bergenia ligulata*	Roots
Palas	Flame of forest	*Butea monosperma*	Seeds
Patha	Cissampelos	*Cissampelos pareira*	Roots
Pindalu	Dioscorea	*Dioscorea deltoidea*	Tubers
Pitpapada	Fumaria	*Fumaria officinalis*	Whole plant
Posta	Poppy	*Papaver somniferum*	Seeds
Prasarni	Paederia	*Paederia foetida*	Leaves
Prishnparni	Lagopoides	*Uraria picta*	Whole plant
Pudina	Mint	*Mentha piperita*	Leaves
Punarnava mool	Hogweed	*Boerhaavia diffusa*	Root
Pushkar	—	*Inula racemosa*	Roots
Rajma	Kidney beans	*Phaseolus vulgaris*	Seeds
Revandchini	Rhubarb	*Rheum emodi*	Rhizome
Ritha	Soap nut	*Sapindus mukorossi*	Fruit/shell
Rudanthi	Cretica	*Cressa cretica*	Fruit
Rumi mastungi	Lentiscus	*Pistacia lentiscus*	Gum resin
Rusemari	Rosemary	*Rosmarinus officinalis*	Leaves
Sadabahaar	—	*Vinca rosea*	Leaves

Trade Name	English Name	Botanical Name	Morphological Part used
Safed chandan	Sandalwood	*Santalum album*	Wood
Salacia	Salacia	*Salacia reticulata*	Roots
Salapmishri	Laxiflora	*Orchis laxiflora*	Tuber
Salibmisri	Salibmisrie	*Eulophia campestris*	Rhizome
Samallu	Agnus castus	*Vitex agnus castus*	Seeds
Sarapgandha	Reserpine	*Rauwolfia serpentina*	Roots
Satawar	Asparagus	*Asparagus racemosus*	Tubers
Sathra	Origanum	*Origanum vulgaris*	Whole plant
Saunth	Ginger	*Zingiber officinale*	Rhizome
Senna	Senna	*Cassia angustifolia*	Leaves
Shalaparni	Desmodium	*Desmodium gangeticum*	Whole plant
Shikakai	Soap pods	*Acacia consinna*	Pods
Shila pushpa	Stone flower	*Didymocarpus pedicellata*	Fungul leaves
Shilajit	Mineral pitch	*Styrax officinalis*	Stone
Shirisha	—	*Albizzia lebbeck*	Bark
Siymarin	Milk thistle	*Silybum marianum*	Seeds
Soanjna	Moringa	*Moringa oleifera*	Seeds
Somlata	Ephedra	*Ruta graveolens*	Whole plant
Surya mukhi	Sunflower	*Helianthus annus*	Seeds
Tabashir	—	*Bambusa arundinacea*	Crystal
Tagara	Valerian	*Valeriana wallichii*	Roots
Talispatra	Taxus	*Taxus baccata*	Leaves
Talmakhana	—	*Astercantha longifolia*	Seeds
Tikhur	Wild turmeric	*Curcuma angustifolia*	Rhizome
Til	Seasame	*Sesamum indicum*	Seeds
Tulsi	Basil	*Ocimum sanctum*	Leaves, whole plants
Tutmalanga	Nepeta	*Nepeta elliptica*	Seeds
Udsalap	—	*Paeonia officinalis*	Tubers
Ustakhadus	Lavendor	*Lavandula stoechas*	Leaves
Uttanjan	Blepharin	*Blepharis edulis*	Seeds

Trade Name	English Name	Botanical Name	Morphological Part used
Varuna	Nurvala	*Crataeva nurvala*	Bark
Vasaka	Vasaka	*Adhatoda vasica*	Leaves
Vidanga	Embelia	*Emblia ribes*	Fruits
Vidhara	Aggregata	*Argyreia nervosa*	Seeds
Vidhara	Santaloides	*Santaloides minus*	Roots
Zarul	Banaba leaves	*Lagestroemia speciosa*	Leaves
Zuffa	Hyssopus	*Hyssopus officinalis*	Flowers

Supply of MAPs

The bulk trade in medicinal plant products takes place at informal markets, and involves the sale of relatively large quantities of unprocessed or semi-processed products. MAPs are sold in various markets: rural, urban, regional, state, national and international. There are two primary sources of MAPs, first wild collection and second cultivated collection.

1. Wild collection

Wild collection is the harvesting of plant material from wild sources. This material can take many forms, such as the bark, leaves, fruits, herbs, flowers, wood or roots. It may be collected from many locations, including open pasture, waste agricultural land, gardens, the roadside or forest land. In some cases the plants may be “weeds” found in agricultural or waste land; in others they may be plants or parts of plants found in horticultural areas or in forest land. The bulk of the material traded (both domestically and internationally) is still wild harvested and only a very small number of species are cultivated.

According to the Planning Commission Report (2000), a critical factor in wild harvesting is the availability of cheap labour to undertake the very labour intensive work of gathering. Because in many cases income from such sources represents the only form of paid employment for inhabitants of remote rural areas, there is a ready availability of workers. Further, contractors who employ the collectors often act as middlemen and traders as well. Collectors are often dependent on contractors as they are poor and often owe money to the contractors. Most countries have few or no regulations and policies which control the wild collection of MAPs. India has banned the export of several wild species in their raw material form, although the export of finished products containing the material is allowed (Anonymous, 2000).

2. Cultivated collection

Cultivated collection is more suitable for large scale uses, such as the production of drugs by pharmaceutical companies, which require standardized products of guaranteed or known content and quality. These quality requirements are becoming increasingly important as drug regulations become more stringent in many countries. Given the higher cost of cultivated material, cultivation is often done under contract. In the majority of cases, companies tend to cultivate only those plant species which they use in large quantities or in the production of derivatives and isolates, for which standardization is essential and quality is critical.

Demand and supply at present is mis-matching. At present 90 per cent of the supply is from forest and only 10% by way of cultivation. Traditionally, the tribes and local communities living in and around forest were allowed to collect minor forest products and there are only 80 medicinal plants in the list of minor forest products. Due to non-identification of entire medicinal herbs from forest, a lot of herbal items are uncollected and lost. Similarly due to unscientific, unsustainable and discriminative collection practices followed, availability of medicinal plants in its natural home has been depleted over the years. Some of the spices even became scarce due to over exploitation. Rapid expansion of area under food crops and commercial crops, conversions of non-forest areas for other alternate land use, degradation of forest through fire, grazing etc. have reduced availability of valuable medicinal plants.

Supply Chain Management

The supply chain of MAPs is often very long with as many as six or seven marketing stages involving primary collectors and producers, local contractors, regional wholesale markets, large wholesale markets and specialized suppliers. The long supply chain contributes to the low prices primary collectors and farmers receive for their products. As wild collection is still more common than cultivation, huge differences in the quality of raw materials occur. The differences concern the amount of active ingredients based on where the plants were grown, what parts of the plants are being used, how the plants were harvested and how they were stored. Raw material is often also adulterated as collection from the wild cannot guarantee the uniformity of raw material. Industry buys from suppliers and wholesalers rather than direct from smallholders because of the substantial quantities and broad range of raw material that is needed. This makes product traceability nearly impossible.

Medicinal herbs, and the products derived from them, also seem to have very varied value chains. However, despite the size of trade in medicinal herbs and herbal products, surprisingly, very few studies have looked at the value chain. The WHO has estimated the demand for medicinal plants is approximately $14 billion per annum (2006) and the demand is growing at the rate of 15–25% annually. The WHO estimates that by 2050 the trade will be up to US$ 5 trillion (Sharma, 2004).

The collection and marketing of medicinal plants from the wild is an important source of livelihood for many of the poor in India.

Supply chain of MAPs is start from the forest, because the wild sources are the major producer source of MAPs. Herbs are collected, dried and chopped by the local village person and supplied to the primary middle man, followed secondary middle man, who supplied the material to the local market or national MAPs mandies or direct to herbal vendors. The domestic end user of MAPs is the manufacturing units of herbal products which procure raw material from herbal vendors, MAPs mandies or directly from the farmers if they have contract farming deal with them (Fig. 1 & 2).

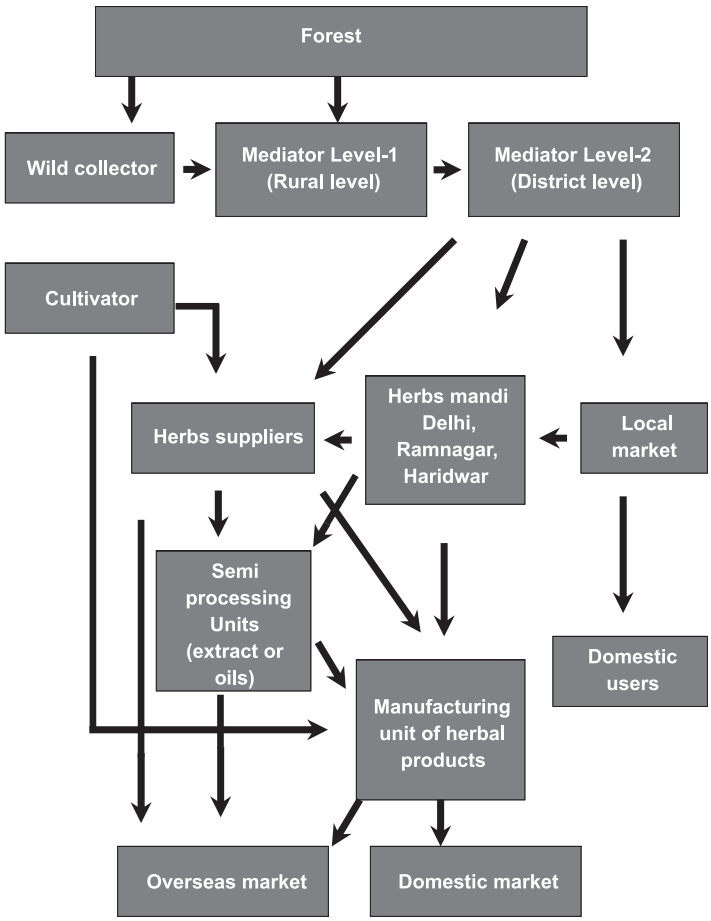
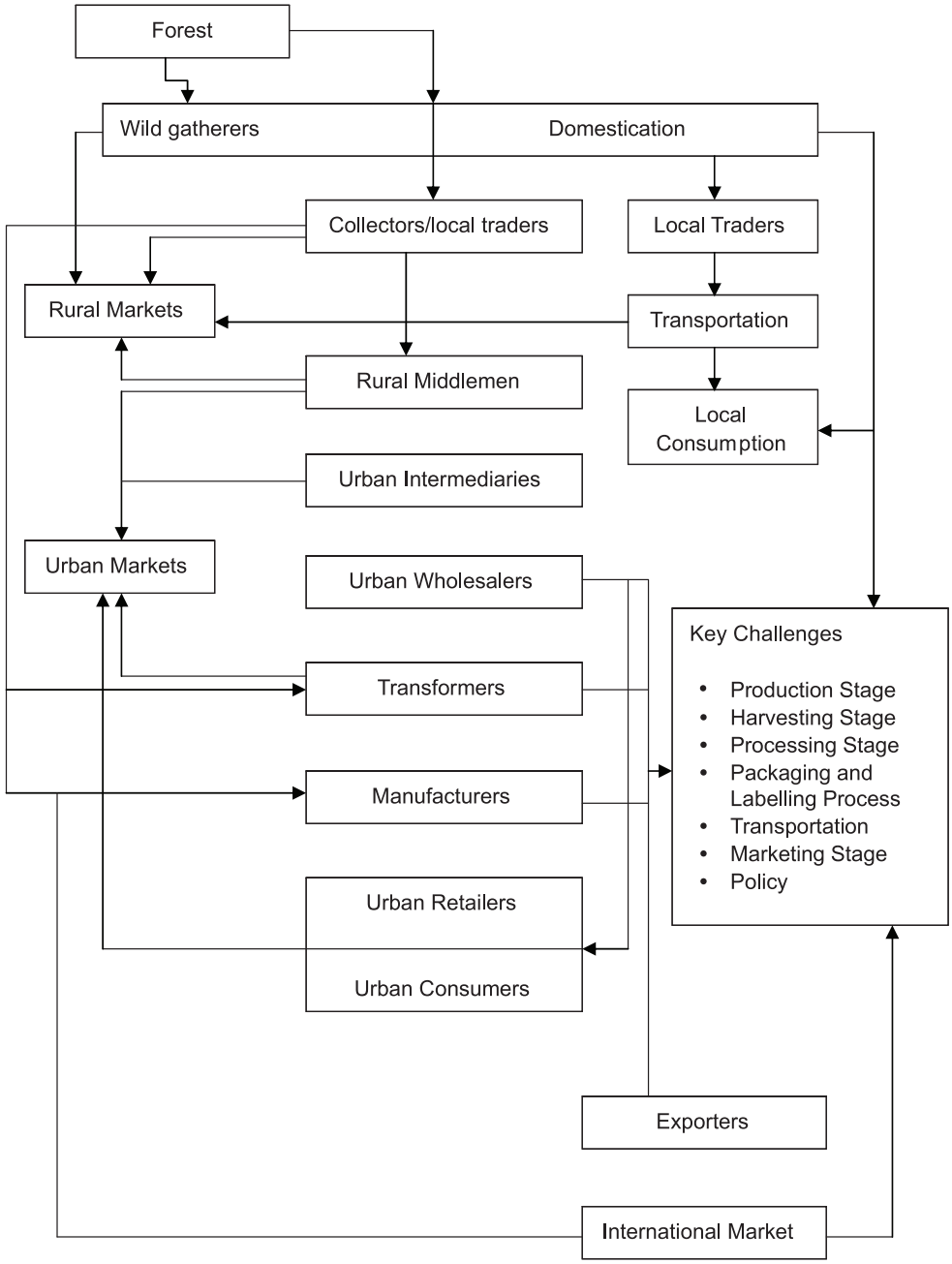


Fig. 1: Supply Chain of MAPs in India



(Source : Adopted from Ahenkan and Boon, 2010)

Fig. 2: The Supply Chain of MAPs

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A Contribution to the Ethnomedicinal Flora of Haldwani Forest Division, Nainital (Uttarakhand)

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Abstract

The results of an ethnobotanical survey conducted during March 2003 in the Haldwani Forest Division, Nainital of Kumaon region, Uttarakhand are presented in this report. Ethno-medicinal uses of 25 plant species belonging to 21 different families of angiosperms have been described. For each plant species are given the correct botanical and prevalent local names, part used, claimed medicinal use(s) and mode of administration. Majority of these uses have not been, hitherto, described. Investigations to their pharmacological action and chemical constituents are re-stressed in an effort to discover new drugs of plant origin to treat specific diseases and conditions so far incurable in modern medicine.

Keywords: Ethnobotanical survey, Folk medicine, Haldwani, Nainital, Kumaon.

Introduction

The Kumaon region of Uttarakhand has rich cultural heritage and floristic diversity. In spite of increasing healthcare facilities, tribal and other rural populations of the area have retained their reliance on herbal healing. From different parts of Nainital district of this region, a wealth of information on folk medicines of many cultural and ethnic groups has been documented (Ali et al., 2008, 2013a, 2013b, 2013c; Anonymous, 2001, 2008, Bisht et al., 1993; Gupta, 1960; Pant and Pandey, 1998; Singh, 1993, 2003; Singh et al., 1987; Singh and Maheshwari, 1990, 1993, 1994). A review of literature revealed that except the work of Agnihotri et al. (2003, 2012) no comprehensive scientific record of folk medicines from the Haldwani Forest Division of Nainital had previously been reported. Hence, this communication presents some useful ethnomedicinal information obtained during an ethnobotanical survey conducted in this forest tract.

Haldwani forest division is extended up to 64 Km in the form of a long strip in southern part of Nainital district and lying between 29° 01′ 05″ - 29° 17′ 00″ N latitude and 79° 32′ 40″ - 80° 10′ 00″ E longitude in the foothills hills of Himalayas. It is surrounded by Nainital and Pithoragarh Forest Divisions in the north, Tarai East Forest Division in the south, town of Tanakpur in the east, Ramnagar Forest Division and town of Haldwani in the west. There are five forest ranges viz. Chakata, Nandhour, Danda, Jaulasal (N) and Sarda. The forest here at many places is still in its natural form and has rich economically important species including medicinal plants. The division is inhabited by

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various indigenous communities (namely: Boxas, Raisikh, Tharus, Vangujjars, etc.). Traditional knowledge on phyto remedies is still intact with these people.

Methodology

Information on folk medicinal uses of plants was gathered through interviews with reliable medicine men and other knowledgeable village elders during the fieldwork carried out in March 2003. Data on the common name of the plant or the crude drug, medicinal use(s), the part used, other ingredients added (if any), method of drug preparation, mode of administration, dosage and duration of treatment were recorded for each claim. Botanical specimens of all the plants along with relevant field information were collected. These were later identified with the help of pertinent floras (Gupta, 1968; Hooker, 1872-1897; Osmaston, 1927) and nomenclature was updated according to a recent work on flowering plants of Uttarakhand (Uniyal et al., 2007). Voucher specimens were prepared and deposited in the Herbarium of Survey of Medicinal Plants Unit, Regional Research Institute of Unani Medicine, Aligarh (U.P.), India.

Observations

In the following enumeration plants are listed in an alphabetic order by their botanical names. Each entry provides the following information: plant scientific name together with respective family (in parentheses), local name of the plant, locality, voucher specimen number, claimed medicinal use(s) and mode of administration. As far as possible, the probable dosage and duration of these crude drugs are also given.

Achyranthes aspera L. (Amaranthaceae), 'Ultashaji', Chorgalian (*SMPA6895*). In cases of scorpion sting, leaf juice is given orally and also applied locally for instant relief from the painful and burning sensation. Root decoction is given for cough and fever.

Ageratum conyzoides L. (Asteraceae), 'Bhupania', Chorgalian (*SMPA6813*). Fresh leaves are crushed and squeezed to obtain the juice. It is applied on cut and wounds to check the bleeding.

Alangium salviifolium (L.f.) Wang. (Cornaceae), 'Barna', Tanakpur (*SMPA6930*). Stem bark powder in the dose of 10g is given with milk once at bedtime for 21 days to treat spermatorrhoea.

Artemisia nilagirica (C.B. Clarke) Pamp. (Asteraceae), 'Pati', Chorgalian (*SMPA6814*). Root paste is mixed with fodder and given to cattle for treating turgid stomach due to gastric troubles.

Bombax ceiba L. (Bombacaceae), 'Semal', Tanakpur (*SMPAA6846*). The tap root of the young plant is cut into small pieces, dried and ground to make a fine powder. About 20g of this powder are given with milk two times a day for one month in general weakness.

Butea monosperma (Lam.) Taub. (Fabaceae), 'Dhak', Nandhour (*SMPA6819*). Flowers are boiled in water. The liquid is strained and administered orally for anuria in cases of cattle.

Cassia fistula L. (Caesalpiniaceae), 'Amaltas'/'Karangal', Chorgalian (*SMPA6899*). Fruit pulp mixed with fodder is given to cattle in chronic constipation (locally known as 'band').

Cissampelos pariera L. (Menispermaceae), 'Butlanti', Jaulasal (*SMPA6920*). Aqueous decoction of the root is given twice daily for jaundice while root paste is used for burning micturition.

Cuscuta reflexa Roxb. (Cuscutaceae), 'Agasbel', Dugari (*SMPA6917*). Paste of the plant is applied locally for abdominal swelling.

Dendrobium crepidatum Lindl. (Orchidaceae), 'Hadjoran', Chorgalian (*SMPA6901*). For treating bone fracture, plant paste is plastered around the limb after setting the bones right.

Ehretia laevis Roxb. (Boraginaceae), 'Chamror', Nandhour (*SMPA6817*). Fresh stem bark is chewed for relieving cough.

Ficus benghalensis L. (Moraceae), 'Burai', Jaulasal (*SMPA6928*). The latex obtained from the leaf is applied on cut. Dried receptacles are ground to make a fine powder and given to induce conception.

Helicteres isora L. (Sterculiaceae), 'Pata', Jaulasal (*SMPA6855*). Powder of the fruit is given to children for worm infestation.

Holarrhena pubescens (Buch.-Ham.) Wall. ex G. Don (Apocynaceae), 'Kokar', Chhini (*SMPA6844*). Stem bark decoction is administered orally for mastitis in cases of cows and buffaloes.

Litsea glutinosa (Lour.) Robins. (Lauraceae), 'Meda', Durga Pipal (*SMPA6837*). Inner stem bark is ground to make a fine paste and applied locally as an anti inflammatory agent.

Mallotus philippensis (Lam.) Muell.-Arg. (Euphorbiaceae), 'Rohini', Nandhour (*SMPA6812*). An ointment is prepared by mixing the red powder, obtained from the dried fruits, in mustard oil and applied externally to treat ulcer. This powder is also given orally to cattle for worm infestation.

Melia azedarach L. (Meliaceae), 'Bakain', Chakata (*SMPA6848*). Kernel paste (10g) is given two times a day to relive piles.

Mimosa pudica L. (Mimosaceae), 'Chhuimui', Chorgalian (*SMPA6915*). In cases of cows and buffaloes, leaf paste is applied on prolapsed uterus and inserted inside.

Piper longum L. (Piperaceae), 'Pipli', Jaulasal (*SMPA6870*). About 2g of the powder of fruit are given with honey twice a day for 5 days for cough.

Pterocarpus marsupium Roxb. (Fabaceae), 'Bijasal', Jaulasal (*SMPA6865*). Stem bark decoction is given for body ache. The powder of gum-resin (gram size) mixed with mother's milk is given to infants suffering from pneumonia. The gum-resin is also applied to fresh cuts.

Pueraria tuberosa (Roxb. ex Willd.) DC. (Fabaceae), 'Hathibel', Jaulasal (*SMPA6929*). Root powder is used as galactagogue.

Saccharum spontanium L. (Poaceae), 'Kans', Chorgalian (*SMPA6920*). Root of the plant, 'hadjoran' (whole plant of *Dendrobium crepidatum*), stem bark of 'khair' (*Acacia catechu* (L. f.) Willd.), root of 'ultashaji' (*Achyranthes aspera*) are taken in equal quantities and crushed. About 20g of this preparation mixed with 'gur' (solidified sugarcane juice) are given two times a day for 5 days for treating diarrhoea.

Semecarpus anacardium L.f. (Anacardiaceae), 'Bhilwa', Nandhour (*SMPA6823*). A mucilaginous matter, oozing out on burning of dried fruits, is applied locally for cracks of heal and soles.

Solanum nigrum L. (Solanaceae), 'Geewian', Jaulasal (*SMPA6852*). About 25 ml of the fresh leaf juice are given twice daily for 21 days to treat jaundice.

Tinospora glabra (Burm. f.) Merr. (Menispermaceae), 'Gurja', Jaulasal (*SMPA6851*). Juice of stem-bits is given as refrigerant.

Results and Discussion

This paper provides a report on ethnomedicinal uses of some important local plants employed by the inhabitants of Haldwani forest division. Altogether, 25 species, represented by 21 families of angiosperms have been documented to treat about 26 different diseases and conditions of humans and cattle. The reported medicinal plants frequently used by the natives are mostly forest species and readily available. This ethnobotanical knowledge exists as oral among the indigenous societies. The data were collected from highly

reputed traditional healers who have long been using these plants in health care. A comparison with the available literature (Anonymous, 1948-1976, 2001; Chopra et al., 1956; Jain, 1991; Kirtikar and Basu, 1935; Nadkarni, 1954; Watt, 1889-1892) revealed that majority of these claims are new or imperfectly known. However, many phytotherapeutic applications coincide with those of other parts of Nainital district (Ali et al., 2008; 2013a, 2013b, 2013c; Anonymous, 2008, Bisht et al., 1993; Gupta, 1960; Pant and Pandey, 1998; Singh, 1993, 2003; Singh et al., 1987; Singh and Maheshwari, 1990, 1993, 1994). All such medicinal uses suggested by these informants seem to be reliable and deserve further scientific investigations.

It was emphatically noted during the current survey that knowledge of the medicinal plants is usually limited only to a few traditional healers who repose deep faith in the healing properties of herbal drugs while the younger generation has a poor phytotherapeutic knowledge. These traditional medicine men now represent a disappearing tradition which is not being passed on to the next generation. In this situation this traditional knowledge is in danger of being lost. It is, therefore, desirable to intensify ethnobotanical research work in other unexplored and under explored areas of the region before this traditional knowledge is lost permanently with the ever dwindling number of folk medicine men and cultural changes among the tribal communities as a result of modernization. Through such observations, based on properly designed field surveys, many more reliable folk medicinal uses of plants may be revealed which may yield useful leads needed in search of new plant-based pharmaceuticals.

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Pharmaco-Botanical Studies on *Capsicum frutescens* L.

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Abstract

Capsicum frutescens L. is used as drug and spice in Indian traditions. The drug (dried fruit), which is stimulant, antispasmodic, carminative, diaphoretic, counterirritant, antiseptic and rubeacient. The plants have also been used as folk remedies for dropsy, colic, diarrhea, asthma, arthritis, muscle cramps, and toothache. Consumption of red pepper may aggravate symptoms of duodenal ulcers. The present studies deal with detailed pharmacognostic studies and review related medicinal aspects of drug.

Key Words: *Capsicum frutescens* L., Drug standardization, Quality specifications.

Introduction

Capsicum frutescens L. (Family – Solanaceae) is commonly known as 'Chilly' or 'Paprika'; it is widely used as a pungent spice. The fruit of the capsicum plant is a common ingredient in many recipes. *C. frutescens* L. is an annual herb up to 1 m high, while other species are usually perennial woody shrub, the plant is indigenous to tropical America, Africa and widely cultivated. The plant derives its names from the Latin *capsa*, meaning box, referring to the partially hollow, box-like fruit. Capsicum was first mentioned in 1494 by Chauca, a physician who accompanied Columbus on his second voyage to West Indies plants were introduced into India by the Portuguese at an early date and later into Africa (Robbers *et al.*, 1996).

The medicinal values of Capsicum as a counterirritant depend on its pungency. This spice is also used as a homeopathic treatment for a variety of conditions. Capsicum is credited with a number of medicinal properties in different systems of medicines. As a medicinal plant, the Capsicum has been used as a carminative, digestive irritant, stomachic, stimulant, rubefacient, and tonic, it used in native practice in typhus, intermittent fevers, and dropsy also in gaunt, dyspepsia, and cholera. Externally it used as rubefacient, neuralgia and internally for colic, flatulent dyspepsia, chronic laryngitis, insufficiency of peripheral circulation (Ebadi, 2002).

Methodology

Drug samples were collected from different places as well from commercial sources with a view to find out any significant difference present within the

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same species. For studying powder, Jackson and Snowdon (1992) was followed. To determine physico-chemical constants, Indian Pharmacopoeia (Anonymous, 1955 & 1966) was consulted and for fluorescence study schedules mentioned by Trease and Evans (1972) were followed. Colours were named by consulting Rayner (1970). Standard prescribed procedures for histochemical studies (Johanson, 1940; Youngken, 1951; Cromwell, 1955; Trease and Evans, 1978), organic group detection (Robinson, 1963); U.V. Spectrophotometry (Willard *et al*., 1965) and Chromatography (Shellard, 1968; Stahl, 1969; Smith and Feinberg, 1972) were adopted. The informatics is complied by reviewing the available literature.

Informatics

Systematics

Family: Solanaceae

Genus: *Capsicum*

Capsicum frutescens L. is perennial erect herb or small sub herb 1-2 m high; branches angular. Leaves alternate, petiolate, simple, broadly ovate, and pointed with entire margins. Flowers born usually single in leaf and branch axils, white to violet, five-parted. Fruit a dry to fleshy red elongated, ovoid, obtuse or oblong berry with numerous flattened seeds (Fig. 1A).

Distribution: Capsicum native of the West Indies and tropical America is most probably of Brazil. Capsicum is cultivated in India since ancient times, commonly cultivated throughout the plains of India, and on the lower hills such as Kashmir and Chenab valley.

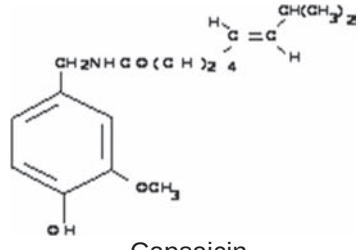
Drug Specification: The drug consist of dried ripe fruits.

Nomenclature:

The plant is known by different vernacular names e.g. Gachmarich, Lallankamurich and Lalmarich (Bengali), Mirchi (Gujarati), Gachmirich, Lalmirch and Lankamirchi (Hindi), Chabai, Chabelombok, Kappalmelaka, and Ladumira (Malayalam), Mirchi (Marathi), Mullagay (Tamil), Golakonda (Telugu) and Lalmarach (Urdu) etc.

Chemical Constituents:

Capsicum contains Capsaicinoids pungent principals, which are composed mainly major components capsaicin, dihydrocapsaicin,



Capsaicin

nordihydrocapsaicin, homodihydrocapsaicin and homocapsaicin. Capsicum also contain about 1.5 % of volatile oil, a fixed oil, carotenoids pigments (capsanthin, capsorubin, carotene, lutein).Other constituents proteins, fats, vitamins A and C,ascorbic acid, caffeic acid, caproic acid, cinnamic acid, para-coumaric acid, ferulic acid, mevalonic acid, pyrazine derivative, capsidiol, kaempferol derivative, quercetin derivative, lipids,pentosans, pectins.Acitic, butric and isobyteric acids.(Leug *et al.*, 1996; Roboers *et al.*, 1996; Barness *et al.*, 2002; Heurich *et al.*, 2004)

Pharmacology

Capsicum is a powerful local stimulant, its oleoresin or active principles capsaicin, it used as a neurochemical tool for studying sensory neurotransmission. Capsicum oleoresin and capsaicin are ingredients for relief of pain in muscle, tendon and joints. The protective effect of capsaicin acts on vanilloid receptors; it is used as a local analgesic in the treatment of post-herpetic neuralgia, shingles, diabetic, rhinopathy and osteoarthritis, neuropathy and other forms of intractable pain (Barness *et al.,* 2002). Digestive properties of capsaicin may be attributed to an enhancement of digestive enzyme activities or to indirect effects on vascular endothelia, smooth muscles and mast cell, increase of vascular permeability and mucosal blood flow. Body temperature, flow of saliva, and gastric juices may be stimulated by capsicum peppers Capsicum strongly irritant to eyes and tender skin, producing an intense burning sensation (Duke *et al.,* 2002).

Therapeutic and non-therapeutic uses

Capsicum is stated to possess stimulant, antispasmodic, carminative, diaphoretic, counterirritant, antiseptic and rubeacient.Traditionally, it used as remedy for diseases of skin, tuberculosis, mild conjunctivitis, it also has been used for colic, flatulent dyspepsia without inflammation, chronic laryngitis, insufficiency of peripheral circulation and externally for neuralgia including rheumatic pains and unbroken chilblains. Capsicum is useful for treating sore throats (Barness *et al.,* 2002).

Capsicum species are used fresh or dried, whole or alone and in combination with other flavoring agents. The extracts of Capsicum species have been reported to have antioxidant properties. Paprika is derived from *C. frutescens* L. and is used primarily in the flavoring of garnishes, pickles, meats, barbecue sauces, ketchup, cheese, snack food, dips, chili con came, salads, sausages and widely used as coloring agents. Chilies and chili pepper used

as a flavoring in many foods, such as curry powder and Tabasco sauce. Chili powder is a blend of spices that includes ground chilies.

The plants have also been used as folk remedies for dropsy, colic, diarrhea, asthma, arthritis, muscle cramps, and toothache. Consumption of red pepper may aggravate symptoms of duodenal ulcers. It is administered in the form of powder, tincture, liniment, plaster, ointment and used as a balm or cream, clinical trials have shown it effective in reducing pain and other neuropathy sensations. In some of these preparations, oleoresin Capsici B.P.C. syn. Capsaicin, the alcohol soluble fraction of the ether extract of capsicum is the active ingredient.

Adulterations and Substitutes

Adulterants in chilly powder are brick powder, soap stone and some artificial colors. Powdered fruits of 'Choti ber' (*Ziziphus nummularia*), red beet pulp, almond shell dust, extra amounts of bleached pericarp, seed, calyx and peduncle of chilly, starch of cheap origin, tomato waste and sweet bell peppers, paprika, pimento (Spanish paprika), and other red pepper products.

Regulatory Status: An official drug in Indian Pharmacopoeia, 1955 & 1966 and also covered under Food Safety and Standards Regulation 2011 (Anonymous, 1955, 1966 & 2011).

A. Flowering Plant

B. Seeds

C. Seeds (Magnified)

D. Seed Powdered

Fig. 1: *Capsicum frutescens* L.

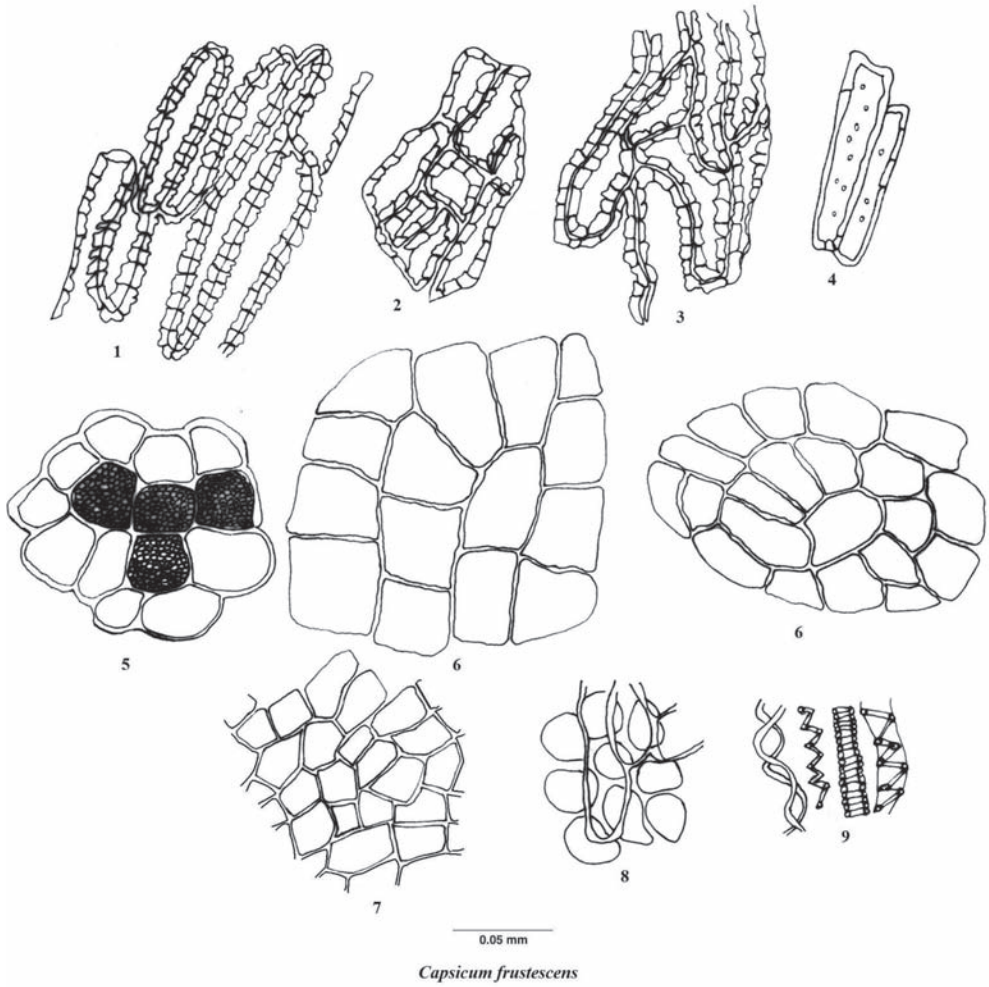


Fig. 2: 1. 2. 3. Elongated sclereids of endocarp in surface view; 4. Oblique longitudinal sclereids of endocarp; 5. Cells of endosperm of seed; 6. Epicarp cells; 7. Parenchymatous tissue; 8. Parenchyma of testa with underlying endosperm surface view; 9. Vessels.

Observations

I. Organoleptic Characteristics

Entire Drug—Fruit are 2.5 to 3.0 cm inches long and 1 cm wide; pod like berry, laterally compressed, conical, base blunt, apex sharp, pointed; calyx and peduncle usually attached to the larger fruits, and some times to the smaller; colour brownish-red to a rich deep-red, (Fig. 1 B,C)).

Powdered Drug – The powder is red in colour; odour characteristic, sternutatory, but not pleasant; taste is mild to slightly pungent (Fig. 1 D).

II. Micro-Morphological Characteristics

Powdered Drug- Pale yellow, single layer of polygonal to slightly elongated cells of epicarp in surface view. Epidermal cells are vary in shape, mostly rectangular-oblong or rectangular-square. Fragments of mesocarp are frequently attached to the epicarp or endocarp, usually containg red to orange oily globules. The sclereids of the endocarp occur in groups, in a single layer and may be found attached with parenchyma. The sclereids are polygonal to elongated in surface view, have sinuous walls and numerous distinct pits. The fragments of endosperm frequently found attached of the parenchyma of testa (Fig. 2).

III. Histochemistry

Micro – Chemical Tests and Behaviour of specific reagents towards Plant/Drug Tissues – Observations and results pertaining to micro-chemical tests and behavior of specific reagent towards plant tissues are presented in Table 1.

Table 1: Micro-chemical Tests and behaviour of specific reagents towards plant tissues and cells contents.

Sl. No.	Reagent	Test for	Inference	Histological zone/cell contents responded
1.	Dragendorff's reagent	Alkaloid	+	Mesocarp cells
2.	Marme's reagent	Alkaloid	+	Same as above
3.	Wagner's reagent	Alkaloid	+	Same as above
4.	Potassium hydroxide solution (5% w/v)	Anthocynin	+	Epicarp & Mesocarp cells
5.	Sulphuric acid (66% v/v)	Anthocynin	+	Same as above
6.	Acetic acid	Calcium oxalate	_	Not Responded
7.	Potassium hydroxide solution (5% v/v) + Hydrochloric acid	Calcium oxalate	_	Not Responded
8.	Sulphuric acid	Calcium oxalate	_	Not Responded
9.	Kedde reagent	Cardiac glycoside	_	Not Responded
10.	Iodine Solution followed by Sulphuric acid	Cellulose	+	Epicarp, mesocarp and other cellular region

Sl. No.	Reagent	Test for	Inference	Histological zone/cell contents responded
11.	Sudan III	Fixed oil and fats	_	Not Responded
12.	Chlor-zinc-Iodine Solution	Latex	_	Not Responded
13.	Aniline sulphate Solution followed by Sulphuric acid	Lignin	+	Vascular strands
14.	Phloroglucinol HCl	Lignin	+	Same as above
15.	Lugol's solution	Protein	+	Endosperm cells
16.	Millon's reagent	Protein	+	Same as above
17.	Picric acid	Protein	+	Same as above
18.	Heating with KOH (5% w/v) + H_2SO_4	Suberin	_	Not Responded
19.	Sudan III	Suberin	_	Not Responded
20.	Weak Iodine solution	Starch	+	All starch grains
21.	Potassium hydroxide solution (5% w/v)	Starch	+	Same as above
22.	Sulphuric acid	Starch	+	Same as above

Indications: '-' Absence and '+' presence of constituent.

Organic Groups of Chemical Constituents – The extracts of the drug were tested for presence of different organic groups and results are presented in Table 2.

Table 2: Major Group of Organic Chemical Constituents of Drug.

Sl. No.	Organic Groups of Chemical Constituents	Reagents/Tests	Inference
1.	Alkaloid	Dragendorff's and Mayer's reagents	+
2.	Anthraquinone	Borntrager reaction	+
3.	Coumarin	Alcoholic potassium hydroxide	+
4.	Flavonoid	Shinoda reaction	+
5.	Glycoside	Mollisch's test	+
6.	Protein	Xanthoprotein test	+
7.	Resin	Ferric chloride regent	_
8.	Saponin	Libermann-Burchard reaction	+
9.	Steroid	Salkowski reaction	+
10.	Tannin	Gelation test	_

IV. Identity, Purity & Strength

Physico-Chemical Constants – The analytical values in respect of physico-chemical constant of drug were established and results are reported in Table 3.

Table 3: Analytical Values of Physico-chemical Constants

Sl. No.	Physico-Chemical Contents	Analytical values
		Capsicum frutescens L.
1.	Moisture content, % w/w, Not more than	6.0
2.	pH	7.2
3.	Total Ash, % w/w	14.5
4.	Acid insoluble ash, % w/w, Not less than	2.5
5.	Alcohol soluble extractive % w/w, Not less than	15.6
6.	Water soluble extractive % w/w, Not less than	33.0
7.	Essential Oil, % v/w, Not less than	_

V. Fluorescence & Spectroscopy

Fluorescence Characteristic of Powdered drug under Ultra-Violet Light – Powdered drug was screened for fluorescence characteristic with or without chemical treatment. The observations pertaining to their colour in daylight and under ultra-violet light were noticed and are presented in Table 4.

Table 4: Fluorescence Characteristic of Powdered Drug under Ultra-Violet Light

Sl. No.	Treatments	*Capsicum frutescens* L.	
		Colour in day light	Nature of colour in fluorescence
1.	Powder as such	Brick red	Dark brown
2.	Powder with		
3.	Carbon tetra chloride	Reddish orange	Brown
4.	Ethyl acetate	Orange	Reddish brown
5.	Hydrochloric acid	Brown	Brown
6.	Nitric acid + water	Reddish orange	Brown
7.	Sodium hydroxide + methanol	Dark red	Brown
8.	Sodium hydroxide + water	Brownish red	Reddish brown
9.	Sulphuric acid + water	Dark brown	Dark brown
10.	Buffer - pH 5	Red	Reddish brown
11.	Buffer - pH 7	Red	Reddish brown
12.	Buffer - pH 9	Red	Reddish brown

Ultra-Violet Spectroscopy – The data related to Ultra-Violet Spectrophotometric characteristics as computed in Table 5.

Table 5: Ultra-Violet Spectrophotometer characteristic of drugs.

Sl. No.	Specifications	Data
1.	Tincture dilution ml/ml	1
2.	Maximum absorption peak	0.074 0.288
3.	λ Maxima at, nm	268.55 214.30

VI. Chromatographic Profile

Thin-Layer Chromatography – Best separation for TLC fingerprinting were obtained by using different layers and solvent systems. Inferences are shown in Table 6.

Table 6: TLC fingerprinting data

S. No.	Drug	Mobile Phase/ Solvent System	Derivatizing Reagents	Visualizations	No. of Spots	R_f Values of bands
1.	*Capsicum frutescens* L.	Toluene: Ethyl acetate (9:1) v/v	Anisaldehyde-Sulphuric Acid	Under UV 254nm	8	0.07 ,0.14 , 0.25, 0.34, 0.41, 0.48, 0.58 (all grey) and 0.86 (dark grey)
				Under UV 366 nm	5	0.07 (light green), 0.25 (dark grey), 0.41 (greenish yellow), 0.58 (dark grey) and 0.86 (dark grey)
				After derivatization	5	0.05 (violet), 0.34 (dark grey), 0.53, 0.58 (both grey) and 0.86 (dark grey)

Table 7 : Regulatory Specifications for fruits of *C. frutescens* L. in different regulatory compendium.

Sl. No.	Quality Specification	India Pharmacopoeia 55 & 66 Whole Drug	India Pharmacopoeia 55 & 66 Powdered Drug	Food Safety and Standards Regulation 2011 Whole Drug	Food Safety and Standards Regulation 2011 Powdered Drug
	Official Title	Capsicum	Capsicum Powder	Chillies and Capsicum (Lal Mirchi)	Chillies and Capsicum (Lal Mirchi powder)
	Botanical Species	*C. frutescens* L. & *C. annum* L. (Fam. Solanaceae)	*C. frutescens* L. & *C. annum* L. (Fam. Solanaceae)	*C. frutescens* L. & *C. annum* L. (Fam. Solanaceae)	*C. frutescens* L. & *C. annum* L. (Fam. Solanaceae)
	Morphological part/Official part	Dried ripe fruits	Dried ripe fruits	Dried ripe fruits or pods	Powder obtained by grinding, clean, ripe fruits or pods
	Description	I. Macroscopical II. Microscopical	I. Macroscopical	– –	
	Ash	Not more than 8.0 %		–	
	Calyces and pedicels	Not more than 3.0 %		–	
	Foreign organic matter	Not more than 1.0 %		–	
	Non-volatile ether extractive	Not less than 12.0 %		–	
	Mould, Living and dead insects, insect fragments, rodent contamination	–		Free from	Free from

Sl. No.	Quality Specification	India Pharmacopoeia 55 & 66 Whole Drug	India Pharmacopoeia 55 & 66 Powdered Drug	Food Safety and Standards Regulation 2011 Whole Drug	Food Safety and Standards Regulation 2011 Powdered Drug
	Extraneous coloring matter, coating of mineral oil and other harmful substances	--		Free from	Free from
	Extraneous matter	--		Not more than 1.0 % by weight	--
	Unripe and market fruits	--		Not more than 2.0 % by weight	--
	Broken fruits, seeds and fragments	--		Not more than 5.0 % by weight	--
	Moisture	--		Not more than 11.0 % by weight	Not more than 11.0 % by weight
	Total ash on dry basis	--		Not more than 8.0 % by weight	Not more than 8.0 % by weight
	Ash insoluble in dilute HCl on dry basis	--		Not more than 1.3 % by weight	Not more than 1.3 % by weight
	Insect damaged matter	--		Not more than 1.0 % by weight	Not more than 1.0 % by weight
	Crude fibre	--		--	Not more than 30.0 % by weight
	Non-volatile either extract on dry basis	--		--	Not more than 12.0 % by weight

Sl. No.	Quality Specification	India Pharmacopoeia 55 & 66 Whole Drug	India Pharmacopoeia 55 & 66 Powdered Drug	Food Safety and Standards Regulation 2011 Whole Drug	Food Safety and Standards Regulation 2011 Powdered Drug
	Any vegetable oil	--		--	Maximum limit of 2.0 % by weight under a label declaration for the amount and nature of oil used

Discussion

Present communication provides specification of *Capsicum frutescens L*. in respect of macro-morphology, micro-morphology, physico-chemical constants (total ash value, alcohol insoluble, water soluble extractive and alcohol soluble extractive), assay (essential oil limits) and Thin layer chromatography. Food Safety and Standards Regulation 2011 provides limited specification viz. e, insect damaged matter, moisture, extraneous matter, Insect damaged matter, Non-volatile either extract etc. (Table. 7) in respect of dried mature fruits and its powder. Indian Pharmacopoeia (1955 & 1966) also comprises specifications for dried ripe fruit and powder derived from the fruits (Table.8). In the present study pharmacognostic standardization of ripe fruit of *Capsicum frutescens* L. is carried out which can be employed in quality control of *Capsicum frutescens* L. used either as drug or spice or as other commodity in commerce. The monographic profile on *Capsicum frutescens* L. also reviews information on different aspects of drug.

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