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Hakim Mohammed Said

Did you have life easy?
No. But you made it your mission
To make it a little easier for others.

Orphaned at two,
You opened your heart to all children,
Giving them respect, education, care,
Making sure their little voices didn't go unheard.

As an adult, you had to start life twice:
Once in your birthplace, once in your land of choice.
You wore holes in your shoes,
But your spirit of service stayed intact.

Two rented rooms, pieces of rented furniture:
You started small, but your heart was big.
Your God-given gifts, you used in God's name,
And He blessed you hundredfold.

Many men's pride is swelled with success;
Yours increased your humility.
So you turned your institution over to Allah –
Its profits to profit the poor.

All men have dreams – a thing apart from life.
You said Why not? and worked to make them real.
Free clinics and dispensaries on wheels,
Hospitals, schools, colleges, even a university!

You married modern science to ancient medicine,
And bred respect for *hikmat* in doubting hearts.
Journals, books, societies, and conferences,
Assemblies, think-tank – all bear witness to your drive.

You spoke the truth, unwavering, unafraid.
One morning a gun spoke, to silence you forever.
O, vain attempt! Your words, your works live on.
The gun but gave you a martyr's immortality!

– A tribute from Khaula Yasmin Qureshi.

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Potential of Herbal Medicines in Modern Medical Therapy*

Shaheed Hakim Mohammed Said (1920-1998) *S.I.*

One of the important aspects of the Second Conference on Islamic Medicine is concerned with the beneficent nature of natural drugs in therapeutics. The importance of this aspect is hardly in the need of being underscored. When we say that treatment by natural drugs is closer to Nature, we actually do not state something vague or metaphysical but something that is concrete and observable. A balanced diet ensures wholesome corporal resistance and generation of antibodies. Secondly, treatment is effected through the administration of concentrated active principles in herbs which we eat or which are allied to them. They thus bring about cure without generating the side-effects which have become the bane of modern medicine, mostly based upon synthetics.

Plants and man are inseparable. On no other commodity has man lavished such tenderness and the way the wild plants have been genetically tamed is a separate story. Certain plants like ushr (*Calotropis gigantea* or gigantic swallowwort) and yebruj (*Mandragora officinarum* or mandrake) have certain superstitions attached to them. This is

no doubt because of the dual properties of many plants. Thus the root and leaves of *Raphanus sativus* Linn. or radish are likely to cause heaviness in the stomach, but the seeds and the decoction of the plant are likely to act as diuretic, laxative, and lithontriptic agents. And reports, through screening, upon even as familiar a plant as the carrot have established what untold good it is likely to do to man and to the smokers in particular. The very fact that plants like broccoli, spinach, and tomato, supply so much of vitamins to man should serve as an indemnity against disease and help bring about natural cure.

I should like to quote a few examples of how plants have led to the growth of synthetics. During the late thirties it was observed that the cattle fed upon spoilt sweet-clover died of haemorrhage. On further study it was found that this haemorrhagic effect was due to a chemical, dicoumarol, which in the *US Pharmacopoeia* is known as bishydroxycoumarin. The synthesis of this haemorrhagic agent was finally accomplished by Link, Stahmann, and Huebner in the laboratory in 1941. It was thought that the haemorrhagic property of this chemical

*Paper presented at The Second International Conference on Islamic Medicine, Kuwait, 29 March-2 April, 1982.

could be turned to advantage, and, in fact, Townsend and Mills in 1942 reported that in six patients repeated doses of 200 to 300 mg. every day prolonged prothrombin and clotting time. Vitamin K, about which we will speak later, counteracted this effect. If therefore man makes the sweet clover a part of his diet or takes an allied species like the fenugreek, some indemnity against thrombosis and embolism is expected. And from this particular mishap in the Prairies has cropped up a series of drugs allied in structure to dicoumarol, e.g. Cumopyran, Tromexan, Marcoumar, Dindevan, Warfarin (which was again synthesized by Link and co-workers in 1947), and so on.

Vitamin K, the antihaemorrhagic factor, was reported by the Danish scientist, Dam, for the first time in 1929. It was found that the haemorrhagic tendency in chicks was overcome by adding alfalfa, spinach, kale, or fish meal to the diet. Dam and his associates, as well as Doisy and his associates, isolated the pure vitamin from alfalfa, calling it K_1 to distinguish it from the vitamin called K_2 which Doisy, McCoquordale, and their co-workers isolated from putrefied sardine. Both K_1 and K_2 were shown to be naphthoquinones. And thus medicine was on way to having even more potent synthetic counterparts which apparently acted by counteracting the effects of dicoumarol by lessening, according to Martius and Nitz-Litzov (1953), the rate of aerobic phosphorylation. The structural resemblance of dicoumarol to Vitamin K has led to the view that dicoumarol competes with Vitamin K and displaces it from an enzyme system which is required in the synthesis of factor VII and prothrombin.

We thus find how an isolated case of the incidence of haemorrhage in cattle in the Prairies led to a series of drugs having reverse effects.

Griffith and co-workers (1944) also have a ketone group, although it is a flavone

compound, and is, in fact, the rhamnoglycoside of quercetin. It is of particular use against recurrent haemorrhages caused by or related to capillary fragility. It occurs in several plants; the stem of the tomato has sizeable amounts of this antihaemorrhagic agent and was first tried clinically in 1944.

It is certainly true that synthetic chemistry has come out with more potent antihistamines than are to be found in Nature. But we should not forget that for a long, long time ephedrine served as the drug of choice against asthma and hay-fever and that its preparations, the base, hydrochloride, and sulphate are still official.

It has been observed that patients with asthma are more sensitive to histamine than normal subjects and these attacks may be prevented by means of ephedrine, a plant drug (although now also synthetically prepared) and adrenaline, a body-product.

Work on chemotaxonomy has not yet started properly. Erdtmann and Darnley Gibbs have already shown that startling discoveries of both fundamental and applied nature could be expected if the work is pursued methodically. It is quite tricky also. An example of this trickiness was cited by Dr. S. Siddiqui 18 years ago when he reported that three crystalline solids had been isolated by himself and co-workers from the Bengal gram (*Cicer arietinum* Linn.) viz. biochanin A (5:7-dihydroxy, 4-methoxy isoflavone), biochanin B (identical with the isoflavone for menonatin occurring in soybean), and biochanin C (identical with asparagin which occurs in *Asparagus* spp. and in *Abutilon indicum* Linn., a plant belonging to Malvaceae). It was found that these solids could not be isolated when the gram sprouts were dried in the shade and extracted with solvents. Such observations bear out the Islamic concept of medicine which claims that drugs are liable to lose their potency if not given in their proper

form. Some drugs gain in potency on ageing; others lose. We have seen how even a harmless plant like the clover can become lethal to animals.

Nor is it true to hold that natural drugs, apart from antibiotics, do not counter microbial attacks. Garlic has been used for time immemorial as a carminative, expectorant, febrifuge, and in the treatment of intermittent fevers. Carallito and Bailey (1944) had already isolated allicin from it. Parry isolated two sulphur compounds from it in 1946, having antiseptic and hypotensive properties. Two more principles, having anti-bacterial properties, viz., allisatin I and allisatin II, were isolated from it in 1948.

Another interesting approach was opened with regard to *Peganum harmala* Linn. The isolation of the harmine series of alkaloids was reported as early as 1843, and studies on their constitution by Otto Fischer and Perkin, Robinson, and Manske form a classic in the annals of organic chemistry. As a result of studies by S. Siddiqui, *et al.*, following the mildest chemical procedures, an alkaloid melting 18°C higher than harmaline and yielding a phenolic base which melts about 50°C higher than harmalol, the corresponding phenolic base prepared from harmalin, a new base, harmadine, proved to be the principal alkaloid of the seed of *P. harmala* with an overall yield of 1.75% while no trace of phenolic base was found by S. Siddiqui and co-workers from three lots of the materials in the Punjab in Pakistan. This would suggest the possibility that harmalin and harmalol, according to Siddiqui *et al.*, reported in the literature are eutectic mixtures of bases, if it were not for the fact that the former were synthesized by Perkin, Robinson and Manske, and found to be identical with the natural product. Siddiqui further observes:

It may well be that harmidine is an isomer

of harmalin, the absence of which in the seeds may be due to varieties in soil and climatic conditions, but the study of *Peganuin harmala* seeds from Iraa seems to exclude this possibility.

The seeds of *P. harmala* in Islamic medicine are prescribed for the expulsion of the tapeworm. It has now been definitely established (*Biochemical Journal*, 264, 1934) that the alkaloids of the plant are toxic to helminths and protozoa. The highly vesicant principle, bhilawanol (a catamol derivative with a C₁₅ H₂₅ unsaturated straight-chain side in position 3), is effective in rheumatic pains.

Much work remains to be undertaken upon natural anti-diabetic drugs. Onion has been known to reduce the blood-sugar level. It is also likely that *Syzygium cumini* Linn. is effective against diabetes. Further studies are required upon the bitter gourd to establish whether the anti-diabetic principle in it acts independently of endogenous insulin. Some interesting development on hypoglycemic drugs is taking place in Central America.

One of the weaknesses of natural drugs from the higher plants, it is argued, is the poor microbial activity of such drugs. However, Lin Keng-Tao of the Institute of Materia Medica, Chinese Academy of Medical Sciences, has shown in a recent report that *Fructus schizandrae* which is commonly used as an astringent in traditional medicine, exercises therapeutic effect on certain types of viral or chemical hepatitis, particularly in lowering the elevated serum glutamic transaminase (SGPr) level and improving some of the symptoms in 68.2% cases. The accumulation of lipids in the liver is impeded, while the deposition of glycogen is increased.

The birth-control steroid, diosgenin, is dependent for its extraction upon *Dioscorea*

deltoidea Wall. Some important saponins like amelonin, digitonin, sarsaponin, tigorin, and trillium are also obtained from *Chlorogalum pomeridianum*, *Digitalis purpurea* and *D. lanata*, *Radix sarsaparilla*, and *Trillium erectum* respectively.

We now come to folklore and the present-day screening of drugs. G.A. Cordell makes the observation with regard to anti-cancer drugs of herbal origin: "... in almost every instance where a plant has a reputed folklore reputation in the treatment of cancer, a compound displaying either *in vivo* or *in vitro* activity has been obtained." Cordell *et al.*, have studied the following plants and have isolated their active principles as regards anti-cancer properties:

Quinoids	<i>Jacaranda caucana</i>
Sesquiterpenes	<i>Acanthospermum glabratum</i>
	<i>Michelia compressa</i>
	<i>Capsicodendron dinissi</i>
	<i>Centratherum punctatum</i>
Diterpenes	<i>Rondeletia panamensis</i>
	<i>Micrandra elata</i>
	<i>Baliospermum montanum</i>
	<i>Aquilaria malaccensis</i>
Simaroubolides	<i>Ailanthus excelsa</i>
	<i>Ailanthus integrifolia</i>
Steroids	<i>Asclepias albicans</i>
Miscellaneous compounds	<i>Amyris bipinnata</i>
	<i>Linum album</i>
	<i>Cassia quinquangulata</i>
Alkaloids	<i>Fagara zanthoxyloides</i>
	<i>Zanthoxylum rhetsa</i>
	<i>Ervatamia heyneana</i>

Two alkaloids isolated from *Catharanthus roseus* Linn., vincristine (VCR) and vinblastine (VLB), have yielded favourable results with regard to Hodgkin's disease and choriocarcinoma and acute leukemia in children

respectively. Partial synthesis of both has been achieved by Dr. Atta-ur-Rahman *et al.*

Another group of active principles against cancer has its origin in a plant growing in East Africa, *Maytenus oratus* Loes. This group is that of maytansinoids which includes some four maytanside esters attached to C₃ of the macrocycle as well as the free maytansides, maysine, normaysine and maysenine. Maysenine exhibits significant L 1210 and P 388 anti-leukaemic activity and powerful tumour-inhibitory properties against KB cells, mouse sarcoma 180, Lewis lung carcinoma, and Walker 256 intramuscular carcinoma.

The therapeutic aspects of herbal medicines have many facets. Hiroshi Saito, in his study of the pharmacological properties of *Panax ginseng* root, for example, has reported that the different fractions of its extracts exercise different actions, e.g., slight CNS stimulant action, CNS depressant action, histamine-like action, tranquillizing action, blood-pressure depression, blood-pressure elevation, etc. Once such a total study is extended to other plants, we may well check up why certain parts of a plant have been prescribed for certain ailments and which parts are rich in which active principles.

It has been estimated that roughly only 5% of the plant wealth has been studied. But perhaps this figure is on the larger side. The knowledge afforded by plants is almost infinite. The World Health Organization in 1977 realized this as is borne out by its report upon *The promotion and development of traditional medicine*. Among the reasons that it gave for the promotion of traditional medicine, one was that of the intrinsic qualities of medicine.

Since traditional medicine has been shown to have intrinsic utility, it should be promoted and its potential developed for the wider use and benefit of mankind. It

needs to be evaluated, given due recognition and developed so as to improve its efficacy, safety, availability, and wider application at low cost. It is already the people's own health care system and is well accepted by them. It has certain advantages over imported systems of medicine in any setting because, as an integral part of the people's culture, it is particularly effective in solving certain cultural health problems ... (p. 13).

This document's case-study of Egypt is rather interesting:

Ammi majus – a common plant in the fields and waste lands of Egypt - has been shown to contain ammoidin (xanthotoxin), ammidine (imperatorin), and majudin (bugaptene). The extracts of this plant have been shown to induce pigmentation in idiopathic leukoderma (vitiligo).

Ammi visnaga – another perennial plant, used in traditional medicine by the ancient Egyptians in the form of a decoction and as a diuretic to treat renal colic – was recently analyzed and found to contain the two principles, khellin and visnagin. Khellin is useful in the treatment of angina pectoris and whooping cough and in the relief of ureteric and gallbladder spasms. It has been found to contain anthelmintic, anti anaphylactic, anti atherosclerotic, antidiabetic, and anti ulcerogenic properties. (p, 11).

The report discusses herbs like *Nigella sativa* Linn. (*habbet el barakah*) and other plants which are under investigation in Egypt. Among these plants *Solanum laciniatum* is of special interest in that it contains alkamines which are steroidal in nature and which can be

converted into steroidal hormones. This plant is the main source of solasodine which is being isolated industrially for the preparation of pregnadienone and used for the synthesis of various hormones.

It ought to be appreciated that the same herb may be used for specific treatment in one country, while in other countries the emphasis may be different. In the Philippines, for example, onion is employed in high blood pressure. Similarly, in the Sub-continent, the rind of the pomegranate fruit is used, in conjunction with aromatics like cloves, as an antidiarrhoeic and antidyenteric agent, while in Sumatra it is employed as an abortifacient. In Cuba, the bitter gourd is used for the treatment of diabetes and chronic ulcers of the stomach, whereas in the Subcontinent the value of bitter gourd as a hypoglycemic agent has come up for appreciation recently. Expanded vision with regard to the therapy of herbal medicines is one of the likely contributions when the folklores of different countries are collected. It is also possible that an ingredient may be present in much higher quantities in the species in a specific region and hence emphasis is placed upon therapy deriving from that ingredient. Thus, of the different species of mint, the Japanese mint, *Mentha arvensis* var. *piperascens* contains the highest percentage of menthol (70-90%). This variety, known as Ryokubi, has begun to be cultivated in Thailand, where by 1977 the yield of crude oil from it had reached 60 tons/year. This variety has been successfully introduced by the PCSIR Laboratories, Lahore, into the Punjab.

In an illuminating paper presented at the 4th Asian Symposium on Medicinal Plants and Spices (Bangkok, 1980) Finn Sandberg discussed the results likely to be expected from an inventory of traditional medicines within a restricted area. He gives the illustration of *Oldenlandia affinis*

(family Rubiaceae) which is indigenous to Zaire and Central African Republic. The herb of course bears different native names and is known in the local folklores for facilitating child-birth. Work on the herb by Lorens Gran in Norway has established that the herb contains the so-called Kalata-peptide, comprising 31 amino acids. This peptide is effective orally, and has potent oxytocic activity; and thus in this case the folklore medicine has been scientifically verified. Sandberg has also noticed that some plants cannot be cultivated outside their local ecological zones. An example is that of *Strychnos lianas*. But a herb like *O. affinis* can be easily cultivated.

An interesting example in this context is that of *Acorus calamus* (family Araceae) which in the Subcontinent has not been prescribed for rheumatism. But in China the genera, *Acorus* and *Arisaema*, are reputed to be anti-rheumatic. Asaron and related compounds have been isolated from these species and have shown carminative, sedative, and analgesic effects. Triterpines from the corms of *Arisaema* have anti-convulsive, sedative, and analgesic properties. *Abutilon indicum* Linn. is put to different uses in the Subcontinent and Vietnam. Its leaves in the Subcontinent are considered demulcent, its bark astringent and diuretic, infusion of its roots febrifuge, and its seeds aphrodisiac, laxative, and demulcent. In Vietnam, on the other hand, the leaves are used as an emollient, stomachic, and anti-periodic. Decoction of its root is considered to be of use as febrifuge and also for the treatment of leukorrhoea. The leaves are also considered diuretic and the seeds are used against dysentery, carbuncles, and sore eyes. Work has been conducted upon *Rauwolfia serpentina* Benth. and other species of the genus in Vietnam, where, interestingly enough, rutin has been extracted from a leguminous plant indigenous to that country, *Sophora japonica*

Linn. Research is being undertaken in Vietnam on herbal drugs for affording relief against fatigue – a disorder inherent in the present civilization.

One of the most promising fields of natural drugs is that of anti-viral activity. Shoji Shibata reported in 1980 that the intravenous administration of a medical preparation of glycyrrhizin, a saponin of the liquorice root, in conjunction with cysteine and glycine, was proved by a double blind controlled trial to be effective against chronic hepatitis. Hemisuccinate of glycyrrhetic acid (*Carbenoxolone*) is orally administered in stomach ulcer. More recently, however, an antiviral activity of glycyrrhetic acid was reported and Interferon-inducing activity of a glycyrrhizin preparation was observed. Shibata believes that glycyrrhizin and glycyrrhetic acid are among the most promising natural products. Side-effects like oedema and hypertension have been overcome through chemical modifications. The results so far obtained show that olean-12-en-3 β , 30-diol chemically derived from glycyrrhetic acid by elimination of its 11-keto group and the replacement of 20-carboxyl with carbinol is one of the most promising compounds of this series showing separation of pseudo-aldosteronism from therapeutic such as anti-ulcer and anti-allergic effects.

Much of modern research on plant products has hinged upon folklore. Thus the *Mexican cactus*, *Opuntia streptacantha* Linn. and herbs like *Tecoma stans* Juss. are being subjected to clinical trials in Mexico for diabetes mellitus. In the field of cardiovascular research, studies are being made on the seeds of *Casimiroa edulis* La Llave, popularly known as a hypotensor, and flowers from *Talauma mexicana* Don and *Magnolia grandiflora* L. are considered to be cardiotonics.

Passing from the general to the specific,

on the occasion of this Conference, I thought that it might be worthwhile to write upon a theme of overriding importance in Islamic medicine, viz. upon the different sidelights of Islamic medicine from different aspects. I have also decided to present my personal experiences and impressions upon a drug which has gained considerable importance in the *materiae medicae* of the Subcontinent. This drug is based upon tamarisk. This drug has been specially selected as we have been able to prosecute the R & D effort required in its development on the basis of the knowledge bequeathed by the ancient and mediaeval masters of medicine and the conventional methods employed by the practitioners of Islamic medicine. This drug is being marketed under the trade name of *Icterene* and it is meant to minister to cases of jaundice.

Having briefly discussed the importance of herbal medicines in the treatment of diseases, I should now like to discuss my impressions about tamarisk. As I have said at the outset, I have chosen tamarisk because I have, by the Grace of Almighty, been able to manufacture a drug for the cure of jaundice from a self-growing and wild plant of the province of Sindh in Pakistan. I am giving as much information as I can without any reservations and without withholding any information.

1. TAMARISK: ITS NAMES IN ISLAMIC MATERIAE MEDICAE

The taxonomic name of tamarisk is *Tamarix gallica* Linn. syn. *T. troupii* syn. *T. gallica* Anct. Dyer. In Pakistan it is known as *ghazanjabin*, *gaz mazaj*, *ghadbar*, *gaz mazu*, *gazan-gaban*, *galaz*, *shur gaz*, *gaz* and *ma'in kalan*. Its Arabic synonyms are: *di manna*, *thamrat al-turfa*, *turfa* and *janz al-turfa*.

The greater and lesser tamarisk varieties

are denoted by the common designation of *gaz mazaj* or *gaz mazu*.

2. HISTORY OF THE USES OF THE DRUG

Tamarisk which occurs in the form of a shrub or small tree is indigenous to Asia, Africa, and Europe. Known as tamarisk in English, its French name is *tamarisc de France*. Dioscorides (I, 101) says that the plant which he designates as *murike* bears a seed like a gallnut. It is used as an astringent in Egypt and Syria, he states. Pliny calls the same tree *tamarika* (24, 41). It is the tamarix of Columella. Nicander named the tamarisk tree as *mantie* (prophetic). The Apollo of Lesbos has been represented with a branch of the tamarisk tree in his hand, and the Iranian Magi also prophesied with a spray of the tree in their hands. Herodotus and Pliny describe the plant in the light of similar use.

Coming to the synonyms of the tree in the Subcontinent, it was known as *jhauuka* in Sanskrit. In Hindi and Urdu it is known as *jhau* and *bari mayn*. It is known as *pilchi* in Punjabi, as *jhaunu-jhadu* in Gujerat as *jhauukam* in Malabar, as *siru sauukku* in Tamilnadu, and as *eirasaru* in Telegu.

It is probable that the galls of the tree have been in use in the Subcontinent since long, and the galls of the tamarisk tree were regarded as substitutes for oak-galls. The manna which drops from the tree is collected in the month of June in Arabia and Iran. It is known as *gazingabin* or *gazanjabin* in Persian. The manna is not produced in the Subcontinent.

In Iranian works on medicine, the galls of the tamarisk tree are called the fruit, and the manna is described as a dew which falls upon this and other trees, notably the willow and oak, and becomes solid. The practitioners of Islamic medicine consider *gazanjabin* or the tamarisk

manna to be detergent, aperient, and expectorant. According to Dymock *et al.* (*Pharmacographia Indica*, i, 160) it is the drosomeli of Galen. They further state:

In modern medicine manna is still used as a laxative; it slightly increases the action of the bowels, causing more frequent and softer stools without irritation. Its sweet taste makes it acceptable to children. The galls like those of the oak, contain tannic and gallic acids, and may be used as an astringent in the same manner as true galls.

The tamarisk tree has been included in the Islamic *maeriae medicae* of the Subcontinent, from Ayurveda, although it has been known since Classical Antiquity.

3. HABITAT AND IDENTIFICATION

Tamarisk belongs to the family, Tamaraceae. It grows throughout the Subcontinent as its names in different dialects should amply show. It occurs on riverine banks and near the sea-coast on sandy soils and in swampy areas. It is propagated by means of transplanting or sowing. Its tree, when small, grows rapidly and reaches maturity rapidly, and on maturity dies. It may attain a height of thirty feet. The diameter of its trunk is about three feet, and its boughs are curved. The bark of the fresh branches are slightly reddish and smooth, and bears small white marks. The bark of its foliage and the larger sprays is thin, greenish brown, and rough. Its flowers appear in the form of bunches and these are often white. The leaves are small. Its flowers do not appear separately as male and female. It is a hermaphrodite.

The taste of the tamarisk is bitter and astringent. One species of tamarisk is also prickly,

and is prolific in South India and Rajputana. Since it bears many spines, it is called *kanti jhau* and *kanti sharni* (i.e. the prickly tamarisk).

The tamarisk tree is of general occurrence in Iran and Afghanistan and is found in sandy areas in the Subcontinent, especially in the littoral areas and on the sea-coast.

Greek physicians have ascribed the occurrence of the tamarisk to river banks and have attributed four kinds to it.

1. The first kind is long, with its foliage like that of the cypress. It is called *athl* in Arabic. Its fruit is called '*adhba* in Arabic, and *nanhi ma'in* and *choti ma'in* in Urdu.
2. The second kind is similar to the first, but does not bear any flowers.
3. This kind has scanty foliage and bears white flowers with a slightly reddish tinge. Its flowers are in bunches and present an appearance of oak flowers. It is called *gaz mazaj* and *bari ma'in*. The taste of the flower is pungent and the blossoms possess a little scent. It is greatly favoured by the honey-bee.
4. This variety bears blossoms the size of *Buchanania latifolia* Roxb. and black pepper. The colour is greenish. No flowers appear upon it. It is used for dyeing purposes. This kind is not to be found in Iraq and Iran.

Some writers, on the other hand, say that it comprises only two kinds:

- i) This kind is large and cultivated. Known as *athl* in Arabic, it is known in the Subcontinent as {rash. Its fruit is called '*adhba*. The people of the Sub-continent designate it as *choti ma'in*. In Urdu and Hindi it is *lal jhau* (red tamarisk).

- ii) This variety is smaller and wild. Its flower is reddish-white. It is known as *turfa'* in Arabic, *gaz* in Persian and *jhau* in Hindi.

4. TAMARISK CONSTITUENTS

The galls of *Tamarix gallica* contain as much as 40% tannic acid (Kirtikar and Basu, 1933). *Tamarix aphylla* Karst. syn. *T. articulata* Vahl galls contain 36.8-43.9% tannin; its bark contains 10% tannin and the wood of the tree 1% tannin. The galls contain levulose and glucose, dextrin, and moisture.

As should be evident from the foregoing, the Subcontinent tamarisk galls are very rich in tannin. *British Pharmacopoeia* recommends the use of the galls in a powdery form. They are equally rich in tannic acid. *Gazangabin* or tamarisk manna contains sucrose, invert sugar, levulose, glucose, dextrin, and water.

5. DESCRIPTION

Gaz mazu, i.e. the tamarisk galls, is much smaller than the true gall; it is three-angled, knotted, and ugly in shape. It has a cavity in the centre which is sometimes filled by mosquitoes or flies, but generally the cavity contains excrementitious matter only. The manna occurs in the form of small grains. When fresh, it is white, but it has the tendency to become viscous and form a thick liquid-like honey. Material like this is produced upon willow and oak in consequence of the puncture by an insect. According to Ehrenberg, the insect which attacks the tamarisk is *Coccus manniparus*. The Persian word, *Gazangabin*, means tamarisk-honey. According to Haussknecht, in the nineteenth century it was applied to the manna which was collected in the mountainous districts of Chahar Mahal and Faridan from two species of *Astragalus* which is a leguminous plant.

Tamarisk manna is collected towards the end of June. According to Aitchison, it is

cultivated in Khurasan, where it is designated as *siah chub*. Manna-bearing tamarisk trees are abundantly found in Siah Kuh and Sufayd Kuh, and in the Ardiwan Pass they form thickets. Elsewhere the tree is found to grow in saline soils and by the banks of rivers. It is cultivated occasionally as an ornamental in gardens (Nadkarni, 1976). Tamarix galls are moderately emollient, expectorant, and deterrent with regard to blood. It is therefore incorporated into anti-tussive and cough medicines as well as in drugs promoting aperience. Its chief advantage is that it promotes the passage of stools without any attendant irritation or burning sensation. Not being repulsive in taste, it is regarded particularly useful for administration to children, and can be administered in conjunction with milk. It is also employed as a substitute for oak-galls (*Idem., ibid.*). Being revulsive, the leaves of the tree which are soft, resolve inflammations and in dyspepsia they promote the expulsion of stools from the mesentery and the liver. It abates the hardness of the spleen. It is a stomachic and liver tonic (*Khaza'in al-Adwiyah*, Vol. III, pp. 313-315). All of its constituents are tranquillizing. Drinking of water in a tamarisk bowl has been held to be useful in the inflammation of the spleen. But it is also suggested that this practice should be continued till the termination of the convalescent period.

Ibn Sina believes that tamarisk acts as a deterrent, astringent, and resolvent without exhibiting any intense desiccation. Its aqua, according to him, acts as detergent and desiccative, and it is this desiccative property which promotes constipation which, however, is slight, because it is cold. Its power to resolve is not excessive. Insofar as its desiccative power is concerned, it is not possible for desiccation to be promoted without any capacity being possessed to act as a resolvent. It is only after

the removal of humidity that resolution helps promote desiccation.

Tamarisk is also used in the cure of jaundice. When bile is retained in the gall-bladder and acts as an obstruction, a decoction of tamarisk-root with vinegar is useful. The juice of its leaves and flowers is also advantageous in jaundice.

6. TEMPERAMENT

Tamarisk is cold and dry in the first degree. Some physicians hold it to be dry in the second degree. Shaykh al-Rais Ibn Sina has said that it is cold and dry in the second degree. Being bitter, it should be hot and this hotness is due to its bitterness. Some investigators have openly said that it is hot and dry.

7. USE AND THERAPEUTIC ACTION

Tamarix has been in use in the Sub-continent since ancient times. Physicians have employed it in the treatment of pseudodysentery in which case a decoction of its leaves and soft branches is useful (*Khaza'in al-Adwiyah*, Vol. III, pp. 314-15).

Dioscorides regards its fruit to be useful in the ailments of the eye and the mouth. Ibn Ishaq al-Isra'ili believes that it is useful as a corrective for irregular periods. (Ibn al-Baytar, *Jami'li Mufradat al-Adwiyah ur-al Aghdhiyah*). All these aspects pertain to the use of its leaves, root, branches, fruits, and flowers.

It has been recommended for external use also, e.g. in the cure of the ailments of the spleen, oedema, and hot inflammations. Some of its other uses are:

- i) Cicatrization of wounds due to small pox by sprinkling a powder of its dried leaves upon the wounds.
- ii) Its fumigation brings about the drying of wounds. It also dries haemorrhoids in piles.
- iii) An infusion of its root and leaves is of utility in prolapsus ani and leukorrhoea.
- iv) Being astringent, a decoction of the herb is used as a gargle in the irritation of the throat, boils and itch in the mouth.
- v) It has been recommended in the cure of decomposed and putrefied flesh and as a gargle in pyorrhoea and toothache. The ash of the gall removes the yellowness of the teeth.
- vi) It acts as a styptic if the flow of blood from an organ cannot be controlled. It staunches the flow, if sprinkled upon the organ.
- vii) It destroys the lice, if the head is bathed with a decoction of its leaves.
- viii) Fumigation with its smoke dries the humid pox and other humid wounds. Tamarisk leaves, after drying and powdering, will expel malflesh. In this case they are applied externally.
- ix) A powder of tamarisk leaves soothes wounds due to burns.
- x) Physicians have recommended the chewing of its leaves for curing spongy gums.
- xi) For external use a poultice is made from its resin and applied to boils which have become chronic, according to the practitioners of Islamic medicine.
- xii) It is used as a tonic for the hair. The preparation used as hair tonic is prepared as follows: Fresh tamarisk root is heated with an equivalent weight of sesame oil and twice its weight of water. When all the water has evaporated, the remaining liquid is strained.
- xiii) Decoction of tamarisk root is recommended in colds.
- xiv) Poultice prepared from the tamarisk bark and pomegranate peel, if ground finely, is effective in abating the flaccidity of breasts.

in women. It should be applied twice in 24 hours.

- xv) Women suffering from leukorrhoea are advised to sit in a bath containing its decoction (*Khaza'in al-Adwiyah*, Vol. III, pp. 314-315).

8. CHEMICAL COMPOSITION

Berthelot submitted to chemical examination the manna obtained from Sina'i. It was a thick syrup and was found to comprise cane-sugar, inverted sugar (levulose and glucose), dextrin, and water. The *gazangabin* sample obtained from Iran and chemically analyzed by Ludwig was found to contain dextrin, uncrystallizable sugar.

The galls of tamarisk have as much tannic acid as those of oak.

9. PRESCRIPTION AND ADMINISTRATION

The drug has an adverse action upon the stomach, but this action is made wholesome and corrected by honey and oil. Its substitute is *athl* which is also known as *frash*. The physicians of Lucknow recommend a weight of 4 mashas in decoctions of the herb. Some have recommended a dose of 5 to 7 mashas.

10. DRUG PREPARATION

I am not in a position to discuss the Muslim contribution to the art of drug-making except to state here that they continually searched for new sources which could be brought to bear upon therapy, making the drugs progressively more efficacious, and providing all kinds of facilities to patients. They not only used their imagination but also at every step took full advantage of the treasure-house of experience which was left to them by their predecessors.

Among the achievements of Muslim

physicians is their discovery of salts in herbs. They obtained salts by heating the plant or its particular part and scouring them from the ash. Such salts are obtained from barley, *Lycium barbarum* Linn., radish, etc. The salts have been therapeutically shown to be very effective. The procedure followed for the extraction of the minerals is as follows:

The plant or the part of the plant containing minerals is incinerated and the ash stirred in water is kept standing for 2-3 days. This liquid is then strained with a muslin cloth. A basin is placed below, so that the water containing the minerals may keep on dripping and collecting in the basin. This filtrate is again poured on the ash and the process is repeated twice or thrice. Almost all the minerals are thus extracted. The water containing the minerals is then evaporated and the salts are then dried and stored.

Another procedure is to put the ash into a basin and to pour water upon it, agitating it by hand or mechanically. The ashy water is then left undisturbed for some time and then filtered. The water is boiled, leaving the salts which are then dried.

Both procedures are virtually the same but for small differences. Salts from *Lycium barbarum* Linn., barley, and radish are obtained in this way.

Hamdard has modified the process according to modern bulk methods employed for filtration, boiling, etc.

The process is now known as the Hamdard process. Salts obtained by this process are effective against jaundice.

These minerals have been analyzed in the laboratories of Hamdard and the results are as follows:

Icterene is an inorganic chemical compound which Hamdard obtained from *Tamarix dioica*. Years of chemical research and therapeutic evolution have proved *Icterene* to be clinically

a scientific cure for jaundice. This it probably achieves by expelling the obstruction of the bile.

Icterene has also been successfully employed in oliguria or wherever diuresis is required. In mild infection and febrile states it acts as a diaphoretic and lowers the body temperature.

Clinical experiments of Hamdard have led to the same result, i.e. the disappearance of yellow colour within 3-4 days and it is hardly ever necessary to continue the treatment for another three days.

The chemical analysis of *Icterene* carried out by Prof. Dr. Georg Hahn in the PCSIR Laboratories at Karachi has shown the composition of the compound to be as follows:

1. Moisture, 79%
2. Organic matter, 2%
3. Cations:
 - Iron, 8.07%
 - Cobalt, 1.50%
 - Calcium, 1.50%
 - Magnesium, 0.17%
 - Sodium, 1.70%
4. Anions:
 - Chloride, 28.9%
 - Sulphate, 31.7%

11. ICTERENE DOSAGE

A course of two tablets three times a day for adults in between meals for three days is usually enough to bring about clinical cure, but in many cases 8 tablets in 24 hours can be given without causing any harm. In the event of a satisfactory response not being obtained, the period of treatment may be enhanced by another 3 days.

The patient should, while under treatment, drink plenty of liquid material, e.g. fruit (particularly citrus) juices, glucose water, etc. Meat and fats are to be totally avoided.

The drug has not given to known toxic or adverse side-effects.

The presentation of the compound is in tablet form. Islamic medicine undoubtedly possesses efficacious treatment against jaundice, while allopathy has yet to find a therapeutic agent for its cure. We are all too well aware of the fact that the jaundice patient, whether treated by allopathy or Islamic medicine, has to be stashed up in a hospital or private clinic for weeks and, in certain cases, for months. The patient is given saline dextrose drips which at times affects the pancreas adversely.

The tamarix fruit (particularly that of *Tamarix indica* Linn.) is considered a refrigerant, digestive, carminative, laxative, and useful in diseases caused by deranged bile. Infusions of the fruits are also given as draughts in febrile diseases.

From what therefore has been observed about tamarisk we are led to arrive at the following conclusions:

(i) Nature has provided cure for diseases, and plants specific to certain regions offer therapy in particular regions against diseases that are prevalent in those regions. Thus the inhabitants of cold regions are prone to suffer from gout and rheumatism, and we have thus *Colchicum autumnale* (*Surinjan*) growing throughout the temperate regions, e.g. Central Asia and Western Europe. The climate of south and western India is hot and humid, and the wood of the sandalwood tree allays heat and pruritus, acting as a diaphoretic. Likewise, medicinal folklore has antidotes for scorpion and, snake-bite and alexipharmics. And this is what the practitioners of Islamic medicine have also said.

(ii) Treatment by means of natural drugs enshrines thousands of years of experience and rather than refuting them scientific studies have confirmed their efficacy. We have the example of tamarisk.

(iii) It has not been possible for us so far to investigate how the practitioners of Islamic medicine arrived at the idea of extracting salts from the ashes of certain plants. No doubt, one of the chief merits of wheat lies in the fact that, besides being a protein and vitamin source, it has magnesium, manganese, zinc, iron, and copper besides arsenic oxide present to the extent of 0.03 mg/one kg grains. *Sha'ir* (*Hordeum vulgare* Linn.) has 55 mg of arsenic per 100 g dry plant; these instances show that the presence of minerals is essential for proper metabolic functioning.

The extraction of mineral salts from plants may appear strange to Western science, but so mysterious are the workings of the human body that these salts inexplicably possess great therapeutic value. Dr. Georg Hahn, who was head of the Organic Chemicals Division at the Karachi Laboratories of the Pakistan Council of Scientific and Industrial Research, carried out work under the guidance of Dr. Salimuzzaman Siddiqui, F.R.S., and submitted a report upon the composition of salts from *Tamarix* spp. which we have summarized in the foregoing paragraphs.

The minerals which we have obtained from *Tamarix* spp. and which may be regarded as a patent, has been obtained according to the traditional methods, but for the fact that for mass production we have had to introduce unit operations calling for large-scale design. We have yet to see whether these minerals act (a) by effecting some change in blood and curing jaundice; (b) by the enlargement of the bile duct, thereby removing or evacuating the bile; or (c) whether it acts as a bacteriostatic agent. We need to carry out pharmacological studies upon this point, and these studies we have not been able yet to carry out.

All that I can say here is that I have so far tried *Icterene* on about 5,000 jaundice patients

and in not one patient have I been able to trace side toxic effects. It has no toxic effects, and I know for certain that allopathic practitioners have prescribed *Icterene* to patients in Karachi and elsewhere.

(iv) It is well-known that in control experiments upon animals, especially dogs, jaundice cannot be induced. When we therefore conduct *in vivo* experiments, we shall have to experiment upon human beings.

(v) The work on tamarisk gives rise to a series of questions: How much work has been done on other plants in the manner of the work done upon *Tamarix* spp.? Where has such work been done or is being done? Who has done it? Not only are these questions important, but a far more important question is as to how many plants there are on the earth on which such work ought to be done for the well-being of mankind. We have not even taken the trouble of identifying the plants described by the Masters comprehensively.

This point demands the full attention of scientists and chemists.

I would deem it a privilege if the scientists, chemists and doctors, present at this representative gathering make this extremely effective and efficacious drug which is a product of ancient wisdom and modern research, an object of their deliberations.

I feel that, if the participants of this Conference, express their views about the possible mechanism through which this drug acts, we should be in a position to stimulate interest in Islamic medicine and the venues it opens for further research. We know, for example, that in modern Western therapy, mineral salts are gaining in importance and the objective is to administer mineral salts with vitamins in an absorbable form; we have the examples of ferrous fumarate and ferrous sulphate. Many

salts like zinc sulphate act as potent antifungal agents; the same is true of certain sulphur compounds. Homeopathy, to a considerable extent and Biochemie almost, depend upon the administration of mineral salts. Perhaps *Icterene* through a biochemical process permits the evacuation of bile and promotes diuresis. Many other plants rich in minerals like radish also act as diuretic agents, Modern medicine employs citric acid compounds for diuresis in jaundice. Once the mechanism has been worked out, it might be possible to work upon other diuretic agents like water-melon and *Ribes nigrum* Linn., the latter being used as a diuretic and detergent in Germany. These are only two cross-

examples. There are other plants which require investigations upon their diuretic properties and use in jaundice. I feel sure that, if work is continued upon plant drugs, we should be able to come across many potent therapeutic agents from the Vegetable Kingdom.

There are thus infinite possibilities for drug research, which, so to say, has the sky as its limit.

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Anxiolytic Activity of Bark Extract of *Salacia reticulata* Wight

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Abstract

Salacia reticulata Wight, member of family *Celastraceae*, is a traditional antidiabetic drug. Salacinol, kotalanol, ponkorinol, salaprinol, and their corresponding de-o-sulfonated compounds, mangiferin, kotalagenin 16-acetate and various proanthocyanidin oligomers are the major chemical components present in its bark. The neuro-pharmacological studies on *S. reticulata* Wight included open field, cage crossing, rearing, traction time, stress induced swimming, light and dark exploration tests and compared with diazepam. Significant anxiolytic activity of bark extract of *S. reticulata* Wight at 300 mg dose affecting central nervous system was noticeable. The CNS effects in these experiment may possibly be regulated through gamma-amino butyric acid (GABA) receptor.

Keywords

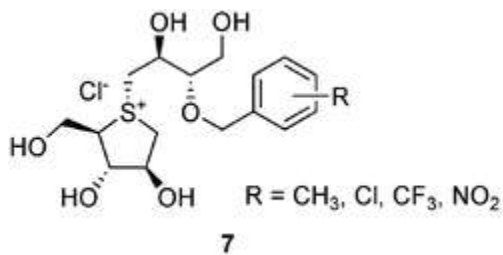
Salacia reticulata Wight, *Celastraceae*, diazepam, Anxiolytic activity, gamma-amino butyric acid (GABA) receptor.

1. INTRODUCTION

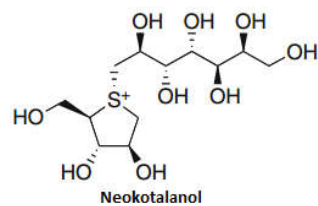
Salacia reticulata Wight (*Celastraceae*)

is a woody climbing shrub with greenishbrown bark, indigenous to India and Sri Lanka. It is also cultivated in Pakistan and other countries. Roots, stems, and leaves extracts of *S. reticulata* have been used in Asia from centuries for the cure of hyperglycemia and other ailments including asthma, amenorrhea, gonorrhea, hemorrhoids, inflammation, rheumatic and skin diseases (Arunakumara *et al.*, 2010). *S. reticulata* has also been used as a dietary supplement in Japan as preventive care for hyperglycemia and for weight loss (Eriko Kahinao *et al.*, 2006). The phytochemicals and their structure are presented in Fig. 1 and in Tables 1 and 2. Constituents having hypoglycemic activity includes kotalanol, ponkorinol, salacinol, salaprinol, and their corresponding de-O-sulfonated compounds. Other major chemical constituents which have been isolated from different parts of plant includes kotalagenin 16-acetate, mangiferin, and various proanthocyanidin oligomers (Akase *et al.*, 2011).

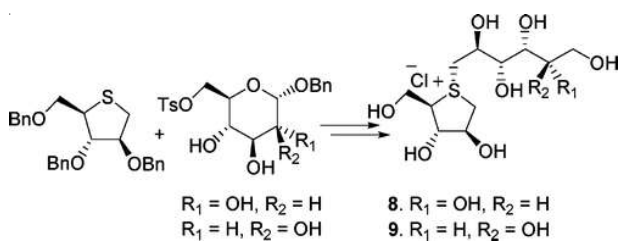
Various *in-vivo* and *in vitro* research on *Salacia* extracts revealed that it affect the enzymes that influence carbohydrate and lipid metabolism including α -glucosidase, aldose reductase and pancreatic lipase (Koga *et al.*,



A) 3'-O-Benzylated Salacinol



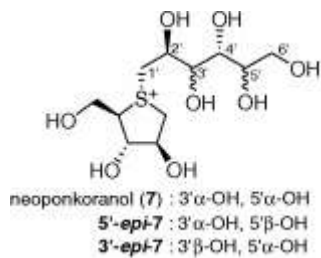
B) Neokotalanol



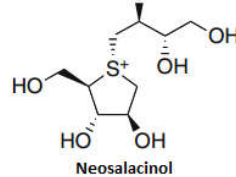
C) De-O-sulfonated Ponkoranol



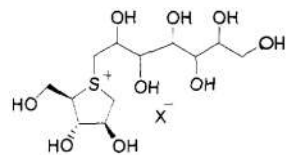
D) Neosalaprinol



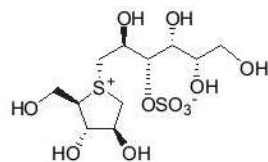
E) Neoponkoranol



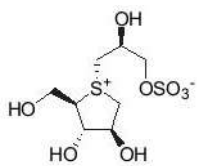
F) Neosalacinol



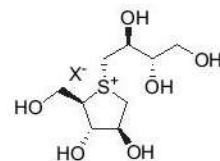
G) Ponkoranol



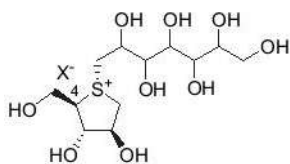
H) Ponkoranol



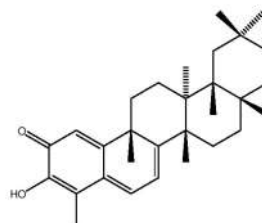
I) Salaprinol



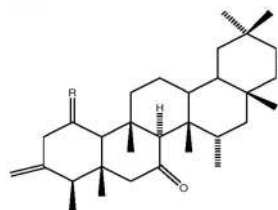
J) Salacinol de-O-sulfonate



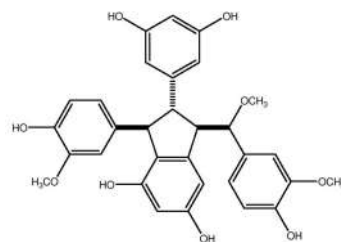
K) Kotalanol de-O-sulfonate



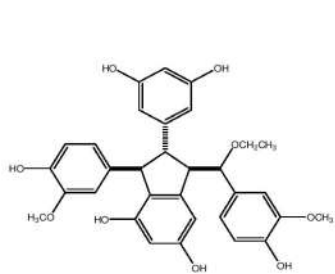
L) Quinonemethide



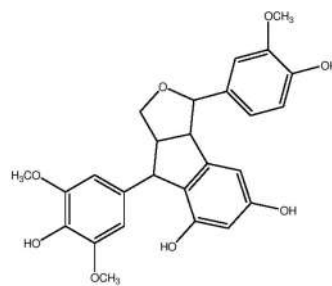
M) 15-α-hydroxyfriedeelan-3-one



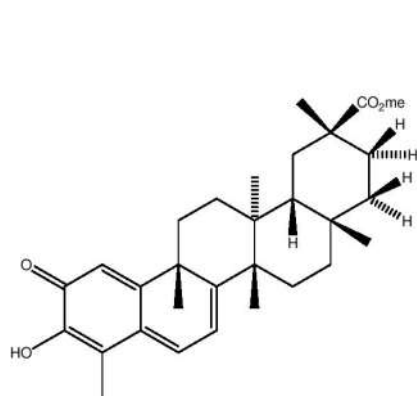
N) Lembachol A



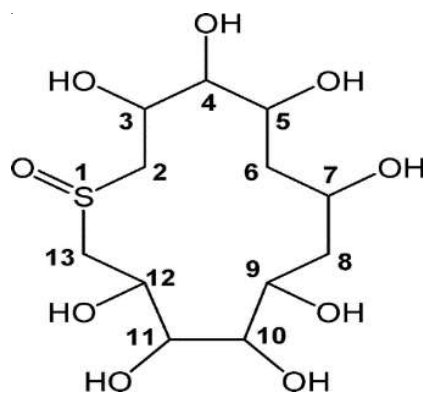
O) Lembachol C



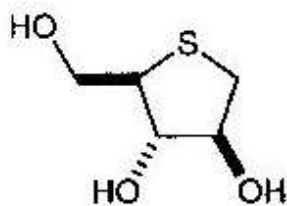
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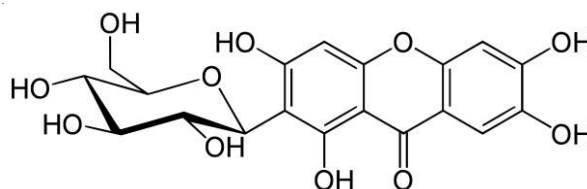
Q) Pristemirin



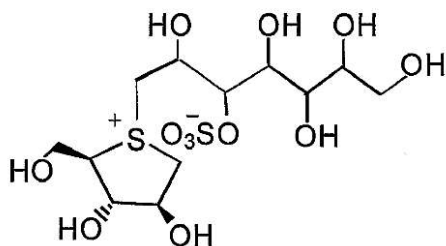
R) 13-membered sulfoxide



S) 1-deoxy-4-thio-darabinofuranose

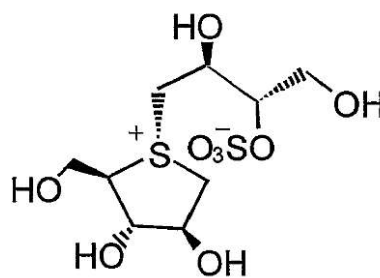


T) Magniferin



Kotalanol
(C₁₂H₂₄O₁₂S₂)

U) Kotalanol



Salacinol
(C₉H₁₈O₉S₂)

V) Salacinol

Fig. 1: Structures of different chemical constituents from *Salacia reticulata* Wight

A) Tanabe *et al.*, 2012; B, F, G) Muraoka *et al.*, 2011; C) Eskandari *et al.*, 2011; D, E) Xie *et al.*, 2011; H, I, J, K) Muraoka *et al.*, 2010(I); M, N, O, P, Q) Ramamoorthy *et al.*, 2010; R) Ozaki *et al.*, 2008; S) Yoshikawa *et al.*, 2002; T) Yoshikawa *et al.*, 2001; U, V) Yoshikawa *et al.*, 1998.

Table 1: Chemical Constituents of *S. reticulata* Wight

S.No.	Chemical constituents	References
1.	Celasterol	Dhanabalasingham <i>et al.</i> , 1996
2.	De-O-sulfonated Ponkoranol	Eskandari <i>et al.</i> , 2011
3.	Isoiguesterinol	Dhanabalasingham <i>et al.</i> , 1996
4.	Kotalanol	Muraoka <i>et al.</i> , 2010 and Yoshikawa <i>et al.</i> , 2002
5.	Kotalanol de-O-sulfonates	
6.	Lehmbachol A	
7.	Lehmbachol C	Ramamoorthy <i>et al.</i> , 2010
8.	Lehmbachol D	
9.	Neokotalanol	Xie <i>et al.</i> , 2013
10.	Neoponkoranol	Xie <i>et al.</i> , 2011
11.	Neosalacinol	Muraoka <i>et al.</i> , 2011
12.	Neosalaprinol	Xie <i>et al.</i> , 2011
13.	Ponkoranol	Muraoka <i>et al.</i> , 2010
14.	Pristimerin	Ramamoorthy <i>et al.</i> , 2010
15.	Quinonemethide	
16.	Salacinol	Muraoka <i>et al.</i> , 2010 and Yoshikawa <i>et al.</i> , 2002
17.	Salacinol de-O-sulfonate	Muraoka <i>et al.</i> , 2010
18.	Salaprinol	
19.	Tingenone	Dhanabalasingham <i>et al.</i> , 1996
20.	β -amyrin	
21.	13-membered sulfoxide	Ozaki <i>et al.</i> , 2008
22.	15- α -hydroxyfriedeelan-3-one	Ramamoorthy <i>et al.</i> , 2010
23.	1-deoxy-4-thio-darabinofuranose	Yoshikawa <i>et al.</i> , 2002
24.	22 β -hydroxytingenone	DhanabalaSingham <i>et al.</i> , 1996
25.	30-hydroxypristimerin	
26.	3'-O-benzylated salacinol	Tanabe <i>et al.</i> , 2012

Table 2: Pharmacological Activities of *Salacia reticulata* Wight

S.No.	Activity/ Parts used	Model of Study	Pharmacological activities	Reference
1.	Anti-inflammatory activity			
	Leaves hot-water extract	Arthritic mice Mice (<i>in-vitro</i>)	Anti-rheumatic activity and Anti-inflammatory	Sekiguchi <i>et al.</i> , 2012
	Bark extract	<i>In-vivo</i> and <i>in vitro</i> trials were done using mice as models	Anti-inflammatory	Sekiguchi <i>et al.</i> , 2010
2.	Antimicrobial			
	Chloroform and methanolic extract	<i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Pseudomonas aeruginosa</i> and <i>Escherichia coli</i> were used in antibacterial activity testing	Antimicrobial	Choudhary <i>et al.</i> , 2005
3.	Anti-obesity effect			
	Whole Plant extract	Differentiation of 3T3-L1 adipocytes (<i>in-vitro</i>)	Inhibition of fat accumulation in adipose tissues	Shimada <i>et al.</i> , 2011
	Plant extract powder (Kothalahim Japan Co. Ltd., Tokyo)	Obese TSOD mice (metabolic syndrome model) and non-obese TSNO mice (Control of TSOD)	anti-obesity	Akase <i>et al.</i> , 2011
	Leaves extract	<i>In-vivo</i> and <i>in-vitro</i>	Fat accumulation preventive effect and anti-obesity effect	Shimada <i>et al.</i> , 2010
	Aqueous extract aerial parts	Male Wistar fatty rats	Anti-obesity Hypo cholestreamic Hypoglycemic	Kishino <i>et al.</i> , 2009
	Aqueous extracts of root and stems	Male mice for a period of 9 weeks	Anti-obesity	Im <i>et al.</i> , 2008
	Water soluble extract	<i>In vitro</i> study by analyzing the per-uterine fat storage of female Zucker fatty rats and male rats	Anti-obesity	Yoshikawa <i>et al.</i> , 2002

S.No.	Activity/ Parts used	Model of Study	Pharmacological activities	Reference
4.	Anti-Oxidant			
	Aqueous and methanolic extract of roots and stems	<i>In vitro</i> study using oxidative stress-induced liver injury in mice	Anti-oxidant and Hepatoprotective	Yoshikawa <i>et al.</i> , 2002
5.	Hypoglycemic activity			
	Combination with valerian and black cohosh	Mice (<i>in-vivo</i>)	Hepatic Enzyme Inhibition	Yokotani <i>et al.</i> , 2013
	Leaves and root bark extracts	Double blind placebo-controlled study	Prediabetes management and hypolipidemic	Shivaprasad <i>et al.</i> , 2013
	Diastereomers isolated from leaves	Rats (<i>in-vivo</i>)	Hypoglycemic	Tanabe <i>et al.</i> , 2012
	Aqueous extract	<i>In-vivo</i> investigation using male wistar fatty rats for 6 weeks	Hypoglycemic and hypolipidemic	Kishino <i>et al.</i> , 2009
	Aqueous extract of stem part	<i>In vitro</i> investigation of the liver cells of KK-Ay diabetic mice	Hypoglycemic	Im <i>et al.</i> , 2009
	Thiocyclitol isolated from the water extract of the plant	<i>In-vivo</i> investigation using Wistar rats	Hypoglycemic	Oe <i>et al.</i> , 2008
	Extract of the roots	15-day and 30-day treatment of the extract	Hypoglycemic	Chandrashekar <i>et al.</i> , 2008
	Aerial parts	Clinical trial	Antidiabetic	Jayawardena
6.	Immune modulation activity			
	Leaves extract.	Rat small intestine.	Increase in cell-mediated immunity	Oda <i>et al.</i> , 2011
7.	Lipid lowering activity			
	Ethanollic extract of aerial parts	Pancreatic lipase activity <i>in-vivo</i>	Lipid-lowering activity	Koga <i>et al.</i> , 2013

S.No.	Activity/ Parts used	Model of Study	Pharmacological activities	Reference
	Leaves, root and bark extracts	Clinical trial	Anti-hyperlipidemic	Shivaprasad <i>et al.</i> , 2013
	Proanthocyanidin oligomers isolated from leaves	Mice (<i>in-vivo</i>)	Anti-hyperlipidemic	Koga <i>et al.</i> , 2012
8.	Safety			
	Plant extract	Mice for a period of 3 weeks	Safe, non-toxic	Im <i>et al.</i> , 2008
	Water soluble extract	Guinea pigs	Safe, non-antigenic and non-phototoxic	Shimoda <i>et al.</i> , 2001

2013). Anti-inflammatory (Sekiguchi *et al.*, 2010 and 2011), immunomodulatory (Oda *et al.*, 2011) antioxidant (Yoshikawa *et al.*, 2002) and antimicrobial activities (Choudhary *et al.*, 2005) have also been reported.

2. MATERIAL AND METHODS

2.1. Sample Collection

The research specimen *Salacia reticulata* Wight bark was procured from local market at Karachi, Pakistan in November-December 2012.

Prof. Dr. Mansoor Ahmad, Department of Pharmacognosy, Faculty of Pharmacy, University of Karachi Pakistan identified the plant. Voucher specimen (SR-1112/2012) was deposited in the herbarium of University of Karachi.

2.2. Animals

Mice (25-30 g) were purchased from animal house of Research Institute of Pharmaceutical Sciences (RIPS).



Fig. 2a: Dried bark of *Salacia reticulata* Wight



Fig. 2b: Dried bark of *Salacia reticulata* Wight

2.3. Drug

Valium (Diazepam, Roche Pakistan Ltd.) was used as standard drug.

2.4. Sample Preparation

The neuropharmacological experiments of *S. reticulata* were performed on bark extract of drug.

Dry plant (5 kg) material was comminuted into small fragments and macerated in 2.5 liters of methanol for 15 days at room temperature. The extract was filtered and residue was re-soaked in methanol. This procedure was repeated thrice. The methanol extract was evaporated under reduced pressure in a rotary evaporator to acquire residue, which was used for various experiments.

2.5. Instrumentation

The following instruments were used for the neuropharmacological research of *S. reticulata*. Rotary evaporator (Eyela, Japan) was used for evaporation of plant extract and shaker (SS-80 Japan) for shaking the extract prior to evaporation. Physical balances (Libror AEG-120 Shimadzu, Japan and Libror EB-3200 D Shimadzu, Japan).

3. ASSESSEMENT OF NEUROPHARMACOLOGICAL ACTIVITY

CNS activity was studied by Open field test, Head dip test, Cage crossing test, Rearing test, Traction time, Forced swimming test and Light and dark exploration test. All the CNS related tests were performed in a calm and peaceful environment.

In each test, animals were divided into 4 groups: Group-A for control, Group-B and Group-C were treated with 300 mg/kg and 500 mg/kg doses of crude extract, respectively, while Group-D was treated with diazepam

(2 mg/kg) served as standard. Each group contain 5 animals. The crude drug and diazepam were diluted in distilled water and administered orally. The control animals were also treated orally with the same volume of saline as the crude extract. In all the tests observations were made after 30 to 40 minutes of treatment.

3.1. Open Field Test

The open field apparatus designed in the laboratory consisted of 76×76 cm square area with opaque walls 42 cm high. The floor was divided into 25 equal squares. Testing was performed by method as described earlier (Kennett *et al.*, 1985 and Turner 1965). Animals were transferred from their home cages and placed in the center square of the open field (one at a time). The open field test was noted in the control and treated animals in numbers for 30 minutes.

3.2. Head Dip Test

It is an exploratory test which was performed according to the method described previously (Sanchez-Mateo *et al.*, 2002; Kasture *et al.*, 2002 and Debparsad *et al.*, 2003). The head dip box was also designed in laboratory. The head dip test was noted in the control and treated animals in numbers for 30 minutes.

3.3. Cage Crossing Test

The test performed on mice in a specifically designed apparatus with rectangular shape. The experiment was performed according to the method described by Florence *et al.*, 2000. The cage crossings were noted in the control and treated animals in numbers for 30 minutes.

3.4. Rearing Test

Rearing is also an exploratory behavior test which was executed following methods described earlier (Sanchez-Mateo *et al.*, 2002; Kasture *et al.*, 2002 and Sakina *et al.*, 1990).

The rearing was noted in the control and treated animals in numbers for 30 minutes.

3.5. Traction Time

Mice (25 to 30 g) were used. Traction time was evaluated following the method by Sanchez-Mateo *et al.*, 2002; Kasture *et al.*, 2002 and Debprasad *et al.*, 2003. The traction time was noted in the control and treated animals in seconds.

3.6. Forced Swimming Test

It was performed according to Sanchez *et al.*, 2002 and Turner 1965. The swimming time was noted in the control and treated animals in minutes. Mobility and immobility time of control and treated animals were noted for 6 minutes.

3.7. Light and Dark Exploration Test

The apparatus consisted of a Plexiglas box with two components 20×20 cm each. Experiment was performed by method described by Crawley and Goodwin, 1980. The light and dark exploration time was noted in the control and treated animals for 10 minutes.

4. RESULTS AND DISCUSSION

4.1. Open Field Test

Results showed significant activity (141.4 ± 5.37) at 300 mg dose in comparison to diazepam (96.83 ± 40.09), standard drug and control (203.66 ± 4.15).

4.2. Head Dip Test

Head dip test showed the highly significant activity (21.67 ± 3.242) at 300 mg dose and significant value (32.33 ± 3.084) at 100 mg dose in comparison to diazepam (19.83 ± 1.307) and control (59.17 ± 0.982).

4.3. Cage Crossing Test

This activity results were slightly significant

(15.958 ± 3.084) at 100 mg dose and (16.191 ± 3.242) at 300 mg dose in comparison to diazepam (17.333 ± 1.307), standard drug and control i.e. (40.166 ± 0.982).

4.4. Rearing Test

This activity displayed highly significant value (6.833 ± 1.471) at 100 mg dose and at 300 mg dose (7.33 ± 1.751) in comparison to diazepam standard drug (12.1666 ± 1.722) and control (32.333 ± 3.723) as shown in Fig. 6.

4.5. Traction Time

This activity exhibited highly significant results (24.66 ± 2.423 sec.) at 300 mg dose and significant value (16.10 ± 1.466 sec.) at 100 mg dose in comparison to diazepam (21.50 ± 0.245 sec.) and control (7.17 ± 0.375 sec.) as indicated in Fig. 7.

4.6. Forced Swimming Test

This activity displayed highly significant results (3.23 ± 0.018 min.) at 300 mg dose in comparison to diazepam (4.46 ± 0.002 min.), standard drug and control i.e. (2.39 ± 0.002 min.).

4.7. Light and Dark Exploration Test

In light exploration activity, test no significant results were obtained Fig. 9a. The dark exploration activity displayed highly significant results (7.01 ± 0.021 min.) at 300 mg dose and significant results (6.59 ± 0.028 min.) at 100 mg dose, in comparison to diazepam (7.49 ± 0.007 min.), standard drug and control (6.29 ± 0.003 min.) as shown in Fig 9b.

In the present study, neuropharmacological, effects of *S. reticulata* was investigated in mice to determine its anxiolytic and antidepressant potential. *S. reticulata* Wight is a member of family *Celastraceae* is a woody climbing shrub which have long been used in India and Sri Lanka to treat diabetes and other health problems

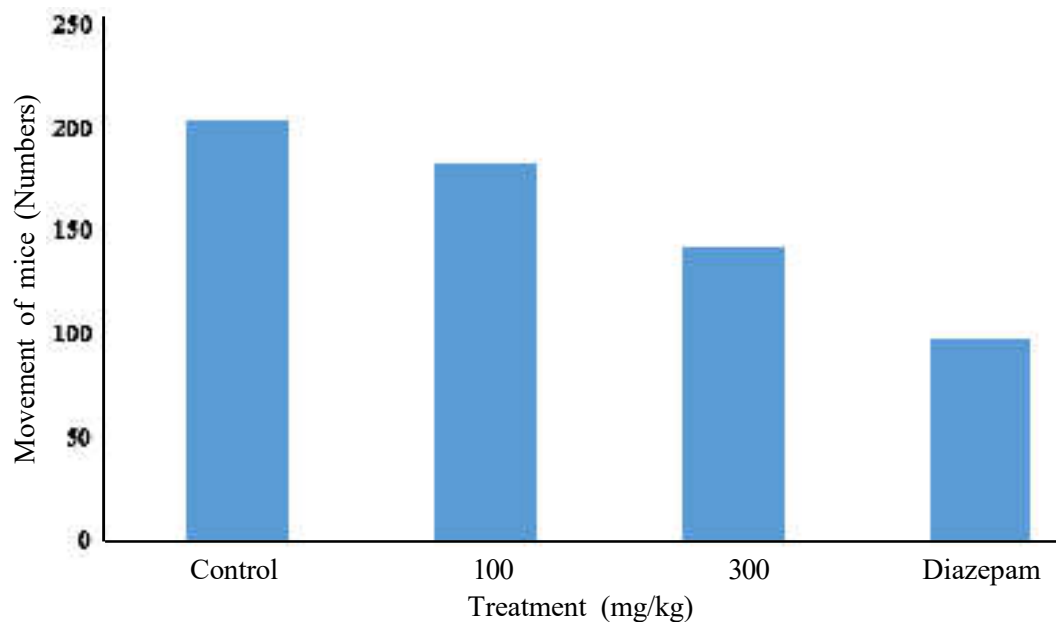


Fig. 3: Assessment of extract of *S. reticulata* on neuropharmacological activity by open field method
Control (0.5 ml Saline), Treated (*S. reticulata* extract) and standard drug (Diazepam 2 mg/kg)

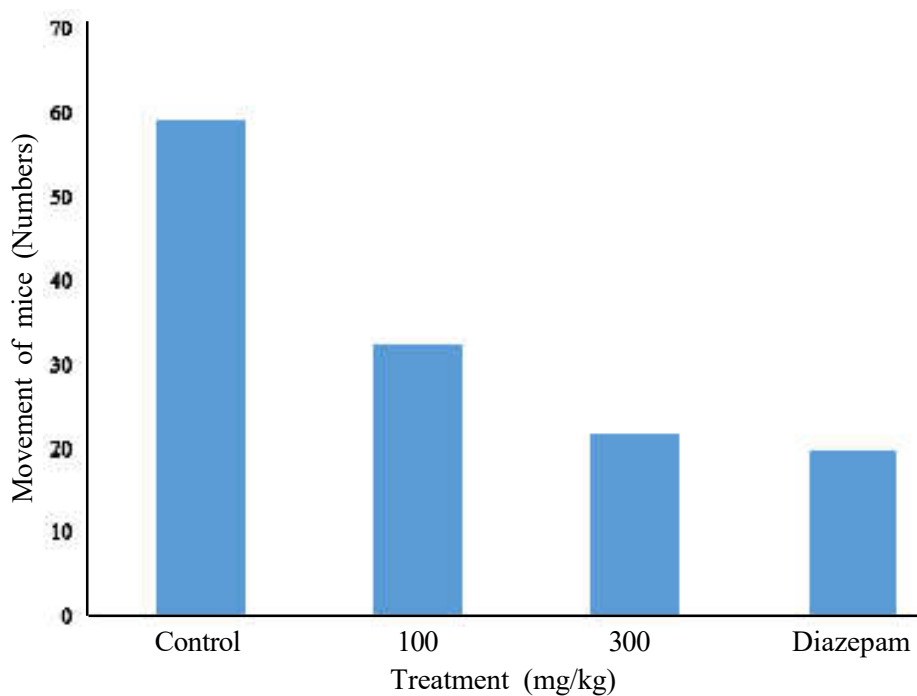


Fig. 4: Assessment of extract of *S. reticulata* on neuropharmacological activity by head dip test
Control (0.5 ml Saline), Treated (*S. reticulata* extract) and standard drug (Diazepam 2 mg/kg)

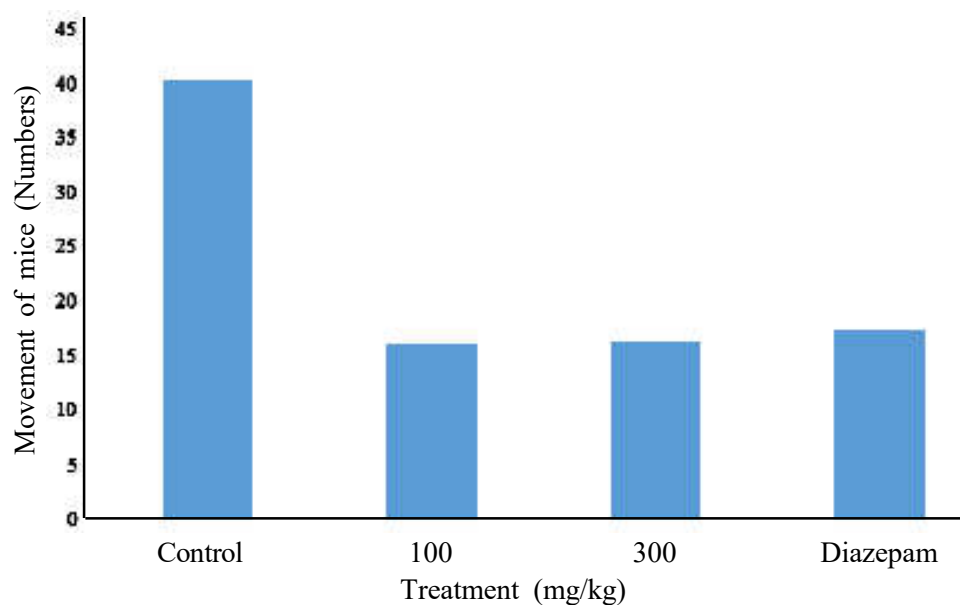


Fig. 5: Assessment of extract of *S. reticulata* on neuropharmacological activity by Cage crossing test
Control (0.5 ml Saline), Treated (*S. reticulata* extract) and standard drug (Diazepam 2 mg/kg)

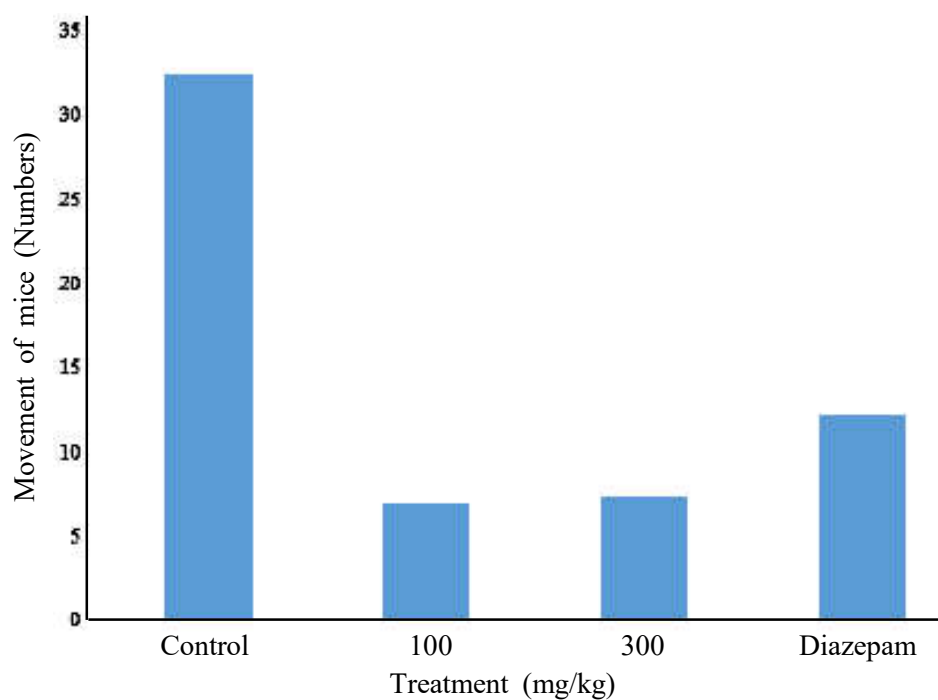


Fig. 6: Assessment of extract of *S. reticulata* on neuropharmacological activity by rearing test
Control (0.5 ml Saline), Treated (*S. reticulata* extract) and standard drug (Diazepam 2 mg/kg)

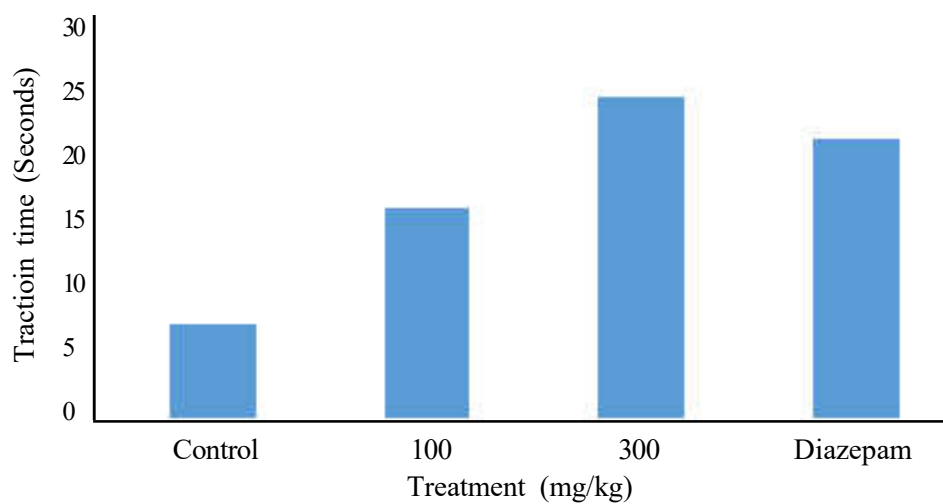


Fig. 7: Assessment of extract of *S. reticulata* on neuropharmacological activity by traction time test

Control (0.5 ml Saline), Treated (*S. reticulata* extract) and standard drug (Diazepam 2 mg/kg)

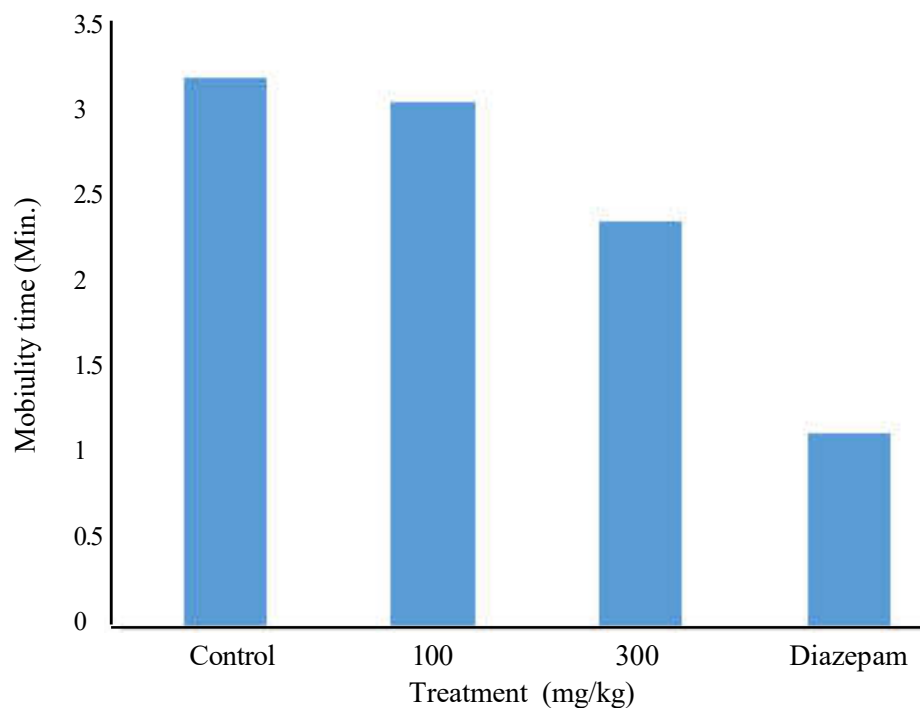


Fig. 8a: Assessment of extract of *S. reticulata* on neuropharmacological activity by forced swimming test (mobility time)

Control (0.5 ml Saline), Treated (*S. reticulata* extract) and standard drug (Diazepam 2 mg/kg)

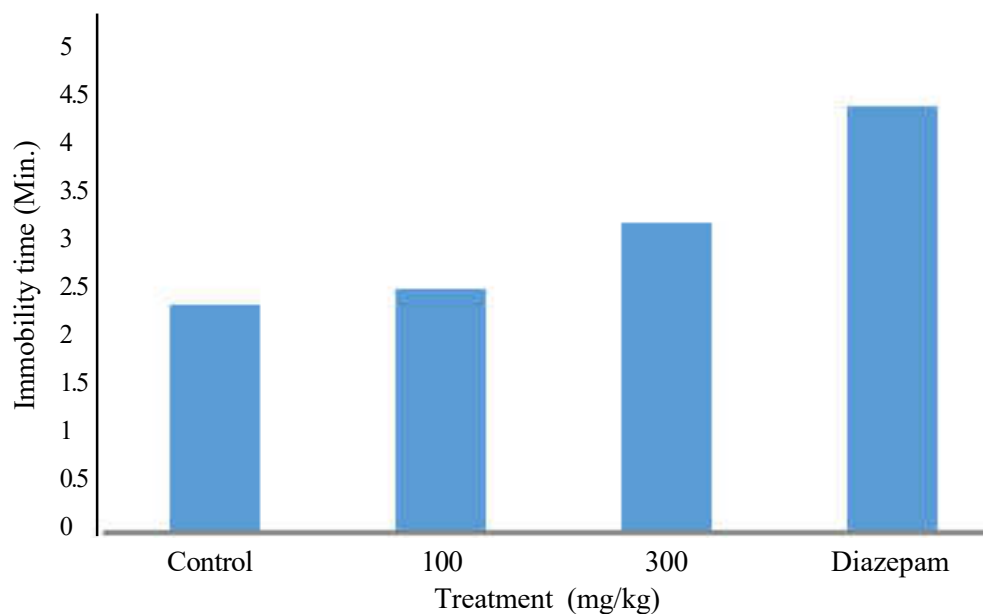


Fig. 8b: Assessment of extract of *S. reticulata* on neuropharmacological activity by forced swimming test (immobility time)

Control (0.5 ml Saline), Treated (*S. reticulata* extract) and standard drug (Diazepam 2 mg/kg)

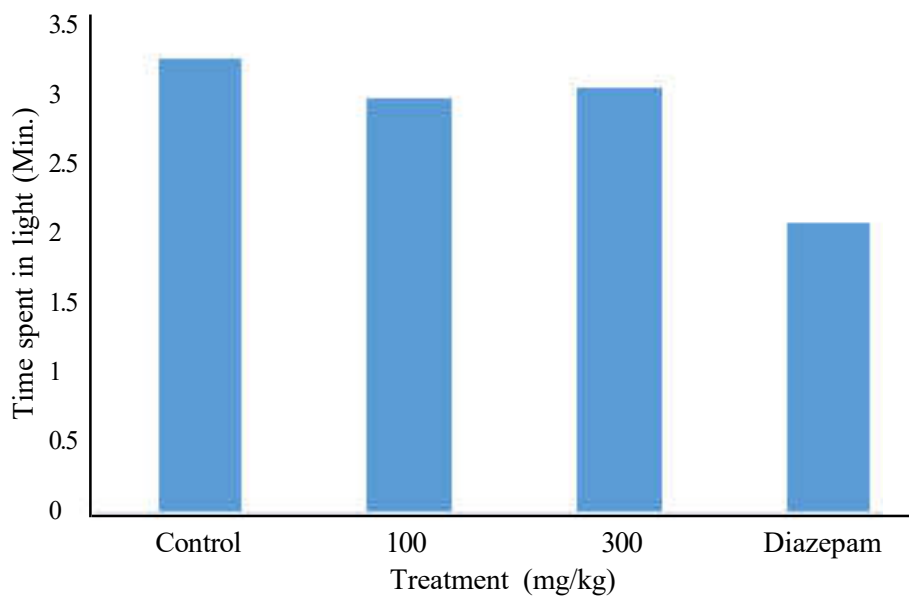


Fig. 9a: Effect of crude methanolic extract of *S. reticulata* on mice in light exploration test

Control (0.5 ml Saline), Treated (*S. reticulata* extract) and standard drug (Diazepam 2 mg/kg)

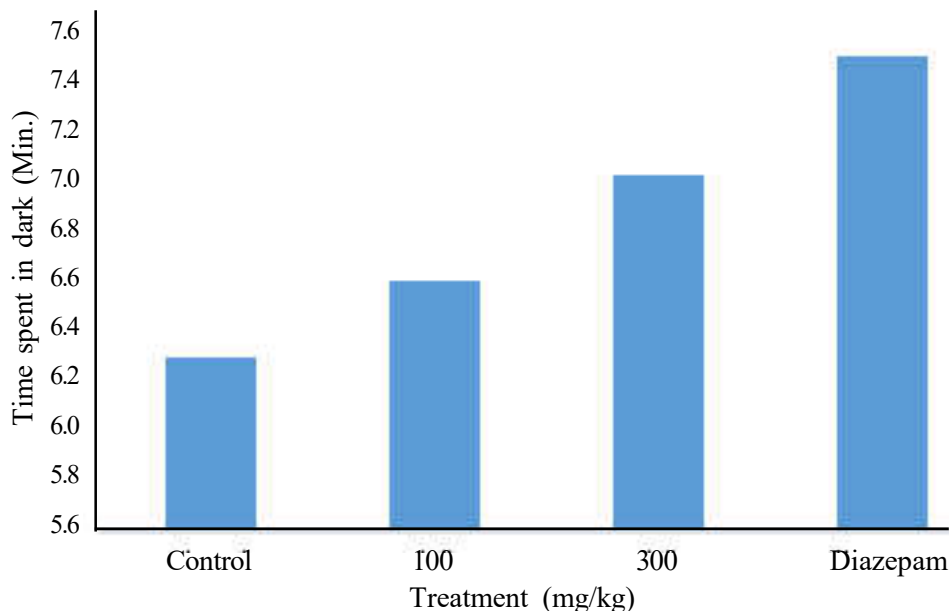


Fig. 9b: Effect of crude methanolic extract of *S. reticulata* on mice in dark exploration test

Control (0.5 ml Saline), Treated (*S. reticulata* extract) and standard drug (Diazepam 2 mg/kg)

like asthma, amenorrhea, gonorrhea, hemorrhoids, inflammation, rheumatic and skin diseases. In Japan *S. reticulata* is a famous dietary supplementary for the management of diabetes and obesity. It consists of kotalagenin 16-acetate, kotalanol, mangiferin, ponkorinol, salacinol and salaprinol which contributes to its medicinal action.

The open field activity showed significant activity (141.5 ± 5.37) at 300 mg dose in comparison to diazepam (96.83 ± 40.09) and control (203.66 ± 4.165). The same activity in other parameter, head dip test exhibited highly significant activity (21.66 ± 3.242) at 300 mg dose and significant value (32.33 ± 3.084) at 100 mg in comparison to diazepam (19.83 ± 1.307), standard drug and control (59.166 ± 0.982); in cage crossing activity results are highly significant (15.958 ± 3.084) at 100 mg dose and

SEM (16.191 ± 3.242) at 300 mg dose in comparison to control (40.166 ± 0.982) and standard drug (17.333 ± 1.307), respectively. Rearing test displayed highly significant value (6.833 ± 1.471) at 100 mg dose and (7.333 ± 1.751) at 300 mg dose in comparison to standard (12.1666 ± 1.722) and control (32.333 ± 3.723); traction time activity exhibited highly significant results at 300 mg dose (24.66 ± 2.423 sec.) and 100 mg dose (16.101 ± 1.466 sec.) in comparison to standard (21.50 ± 0.245 sec.) and control (7.166 ± 0.375 sec.); force swimming test displayed highly significant results (3.23 ± 0.018 min.) at 300 mg dose in comparison to standard (4.46 ± 0.002 min.) and control (2.39 ± 0.002 min.); in light exploration activity test no significant results were found. The dark exploration activity displayed highly significant at 300 mg dose (7.01 ± 0.021 min.) and significant results at

100 mg dose (6.59 ± 0.028 min.) in comparison to standard drug (7.49 ± 0.007 min.) and control (6.29 ± 0.003 min.). These results indicate that anti-depressant action of the extract of *S. reticulata* affects CNS. This is because in some cases extract results are very significant as compared to diazepam. Moreover, its effects on contraction and relaxation of muscles are also quite prominent. The CNS action in these experiments may be regulated through Gamma amino butyric acid (GABA) receptor.

5. CONCLUSION

The present research indicated the presence of significant anxiolytic potential of *S. reticulata* bark extract. This plant may be used as an alternative natural treatment of existing drugs available to cure anxiety and depression. However, it should be used with the precaution by hypoglycemic patients because of its strong sugar lowering property.

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Assessment of Knowledge, Perceptions and Attitude of Patients and Their Care Givers Towards Pulmonary Tuberculosis in Pakistan

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Abstract

Majority of the people are not aware of causes of tuberculosis (T.B) disease, its mode of transmission and the consequences of not receiving treatment. Beside this perception of (T.B.) society regarding the disease adds a social stigma for the patients that may influence TB patients' decision in health seeking behavior and adherence to its treatment. The foremost purpose of this study was to evaluate the knowledge attitude and perceptions of patients and their care giver regarding management of tuberculosis in twin cities of Pakistan. A descriptive cross-sectional study design was used. A semi-structured questionnaire was provided to 382 patients as well as their caregivers. The total sample size for the study was 764. Convenience sampling technique was used to selected sample. Data was cleaned, coded and evaluated using SPSS version 21. Patients (74%, n=284) and caregivers (27.4%, n=105) had correct knowledge regarding total course of treatment of TB. The results showed that 54.4% (n=208) of the patients and 69.6% (n=266) of caregivers had appropriate knowledge regarding use of Myrin-P for disease treatment. Significant association ($p < 0.05$) was

found regarding use of Myrin-P for TB with caregivers possessing better knowledge as compared to patients. These results led us to conclude that knowledge of TB patients and their caregivers regarding causes and transmission was adequate however knowledge regarding treatment of disease was poor. Patients as well as their caregivers had positive health seeking behaviors and preferred to visit health care facility after diagnosis of disease. Caregivers had feelings of sympathy for such patients.

Keywords

Attitude, Knowledge, Perceptions, Pulmonary tuberculosis, Pakistan.

1. INTRODUCTION

Tuberculosis is one of the prime public health challenge faced by developing countries at present (Ali *et al.*, 2003). Approximately 1/3rd of the world's total population has been anticipated to be accounted for pulmonary tuberculosis caused by *Mycobacterium tuberculosis* (Liefoghe and Muynck, 2001). Increased number of HIV patients, aging and issue of resistance to anti-tuberculosis drugs

worldwide has increased incidence at an alarming rate (Jurcev *et al.*, 2008). Misconception of early symptoms and overuse of antibiotics is leading towards drug resistance and increased healthcare costs (Munro *et al.*, 2007). Majority of the people are unaware of causes, mode of transmission and the consequences of not being treated. Beside this perception of society regarding the disease adds as a social stigma for the patients that may influence TB patients' decision in health seeking behavior and adherence to the treatment. People with TB tend to hide their disease out of fear of what others and the society may say and what will be the consequences if the people around knows about it (Kilale *et al.*, 2008). Beside this, lack of inadequate disease knowledge among caregivers, lack of adequate counseling by health personnel, low financial status and difficulty in accessing healthcare facilities for treatment are also important barriers for effective management of TB (Koay, 2004). Extensive research has been conducted in developed countries regarding accessibility, perceptions, acceptance and adherence of patients to their treatment regimen of pulmonary tuberculosis and barriers to adherence have also been identified which led to improved control of pulmonary tuberculosis in these countries. Whereas in developing countries including Pakistan limited data is available in this regard (Khurram *et al.*, 2011).

Tuberculosis is a major public health problem in our country but it has been one of the most neglected health areas in the past. Despite efforts by government the burden of TB in Pakistan is still high. It is responsible for 5.1% of the total national disease burden in Pakistan (Mushtaq *et al.*, 2010). The impact of this disease on socio economic status is substantial. The National TB Control Program is responsible for developing national guidelines, framing policies and generating resources for

implementation of TB control measures at Provincial and district levels. Despite of the international attention of TB and Directly Observed Treatment Strategy (DOTS), knowledge of patients and caregivers regarding it is still not well acknowledged in Pakistan (Qureshi *et al.*, 2008). There are still many misconceptions and cultural beliefs surrounding TB leading to ineffective disease management and control in the country. Most of the researches related to TB awareness are conducted in two provinces of Pakistan i.e. Khyber Pakhtunkhwa and Sindh. Keeping in view the location and operation of its control program in the capital city, the two main cities of Pakistan namely Islamabad and Rawalpindi were selected for the current study. The rationale of the study was to assess that National Tuberculosis Control Program being majorly operational in these two cities whether the program has been successful in promoting awareness and adherence among patients and general community. Caregivers can play an important role in disease management but unfortunately so far their knowledge has not been assessed. Thus, the main objective of the study was to assess knowledge, attitude and perceptions of patients and their caregivers regarding management of Tuberculosis.

2. MATERIAL AND METHODS

A descriptive cross-sectional study design was used to evaluate knowledge, attitude and perceptions of patients and their caregivers regarding management of Tuberculosis in twin cities of Pakistan. Approval was obtained for the study from the Ethical Committee of Hamdard University. Moreover in Pakistan, questionnaire-based studies do not need any endorsement from Ministry of Health. Despite that, prior information was sent to the Ministry of Health, Government of Pakistan for the

execution of this research. Beside this, approval for the data collection was also taken from incharges of hospitals. Informed verbal consent from the respondents was also taken.

2.1. Study Population, Sample Size and Sampling of Respondents

This study was conducted from June to September 2017. All the patients diagnosed with pulmonary tuberculosis and their respective caregivers seeking treatment from public or private healthcare facilities located in Rawalpindi and Islamabad were included. Sample size calculations were performed using Raosoft® sample size calculator to determine the size of sample that represents the population of patients and their care givers. The sample size $n=382$ patients as well as their care-givers to achieve 95% confidence level with 5% margin of error. The total sample size for the study was 764. Convenience sampling technique was used to selected sample.

2.2. Study Tool

A semi-structured questionnaire was developed through extensive review of literature and focus group discussions. The questionnaire comprised of 4 sections.

1. Included information regarding prescriber's demographic characteristics including age, gender, education level, profession, marital status, monthly income, rural or urban area and public or private setting.

2. Perceptions of patients and their caregivers regarding management of TB were explored.

3. Knowledge regarding signs and symptoms, cause, mode of transmission, treatment, preventive measure and source of information for TB was assessed.

4. It was related to performance of DOTs and suggestions for improving control of

disease. A 5-point Likert scale was used for assessment of sections 2 of the questionnaire. While in the third section, for the knowledge part responses were assigned as 1 = yes/correct and 2 = no/incorrect.

2.3. Reliability and Validity of the Tool

Four different groups of experts including clinicians, specialists, physicians and doctors from academia participated in two focus group discussions held at different time intervals for the development, finalization, face and content validity of the data collection tool. Patients ($n=38$) and their care givers (10%) of the total sample size were selected for pilot testing of the study. A Cronbach alpha value of 0.84 established the reliability and internal consistency of the questionnaire.

2.4. Data Collection and Analysis

Two teams, one in each city, with 10 data collectors in each team, were trained by the group of experts including the principal investigator. The questionnaires were self-administered to the respondents. Questionnaires were collected back on the same day to avoid study biasness. After data collection, data was cleaned, coded and entered in SPSS version 21. Skewness test was performed and histogram with normal curves was used to assess the normal distribution of data. Descriptive statistics comprising of frequency and percentages was calculated. Non-parametric tests Chi-square tests ($p \geq 0.05$) were performed to identify association among different variables.

3. RESULTS AND DISCUSSION

Out of 764 respondents, 60.2% ($n=460$) were males and 39.7% ($n=304$) were females. Nearly thirty three percent ($n=252$) had completed primary education, 19.8% ($n=152$) had completed secondary education, 17.6%

(n=135) were matric, 17.1% (n=131) were intermediate and 7.4% (n=57) had a bachelor degree. Out of the total respondents, 71.2% (n=544) were married whereas 30.3% (n=232) were unmarried. Regarding sector of treatment, 99.4% (n=760) of the respondents were undergoing treatment from public sector whereas 0.5% (n=4) from private sector Table 1.

Majority of the respondents (69 %, n=532) were satisfied with currently available TB treatment in Pakistan. Majority of the respondents (69.5%, n=531) agreed on the fact that understanding cultural beliefs and individual attitudes can help prescribers in improving adherence to anti-TB therapy. Majority of the respondents (84.1%, n=648) agreed that there is a need of more educational programs to increase knowledge & awareness of community regarding treatment of T.B. A detailed description is given Table 2.

Majority of the patients had correct knowledge regarding symptoms of TB in terms of: Rise of temperature in evening (91.8%, n=351), weakness/weight loss (85%, n=325), headache (55.4%, n=212), blood in sputum (n=69.6%, n=266), continuous cough (75.9%, n=290) and loss of appetite (73.5%, n=281). Majority of the respondents had inadequate knowledge regarding causes of Tuberculosis: bacteria (63.6%, n=243), smoking (54.1%, n=207), alcohol consumption (n=46.3%, n=177) and polluted water (n=63.8%, n=244). Majority of the caregivers had correct knowledge regarding mode of transmission: Through cough (81.9%, n=313), sharing utensils (63.6%, n=243) and through airborne droplets (71.9%, n=275). Detail is given in Table 3.

The results of the current study highlighted that only 40% (n=153) of the patients and 48.6% (n=186) of the caregivers had correct knowledge regarding use of Isoniazid,

Rifampicin, Pyrazinamide and Ethambutol for first two months of treatment. Seventy four percent (n=284) of the patients and 27.4% (n=105) of caregivers had correct knowledge regarding total course of treatment of TB. The results showed that 54.4% (n=208) of the patients and 69.6% (n=266) of caregivers had correct knowledge regarding use of Myrin-P for treatment of TB. Significant association ($p<0.05$) was found in terms of use of isoniazid and rifampin in continuous phase with patients having better knowledge as compared to caregivers. Significant association ($p<0.05$) was found regarding use of Myrin-P for TB with caregivers possessing better knowledge as compared to patients. A detailed description is given Table 4.

Majority of the patients preferred to visit a health facility when treatment did not worked (63.8%, n=244), symptoms did not last for 3-4 weeks (63.87%, n=244) and as soon as they realized that symptoms are of TB (77.4%, n=296). The results of the study showed that when majority of the patients were sure about having TB symptoms they preferred to visit health facility (66.4%, n=254), pharmacy (37.6%, n=144) and traditional pharmacy (29.5%, n=113). Significant association ($p<0.05$) was found among patients and their caregivers in terms of action to be taken when TB symptoms were confirmed. Caregivers preferred to go to pharmacy and disapproved self-treatment of TB. A detailed description is given Table 5.

Majority of the patients were of the opinion that major reasons for not seeking medical consultation was being recovered (48.4%, n=185), lack of affordability (55.7%, n=213), self-medication (45.5%, n=174) and social stigma (62%, n=237). The results showed that majority of the caregivers agreed that the consequences of not seeking treatment for TB are complications from disease (78.5%, n=300),

(n=135) were matric, 17.1% (n=131) were intermediate and 7.4% (n=57) had a bachelor degree. Out of the total respondents, 71.2% (n=544) were married whereas 30.3% (n=232) were unmarried. Regarding sector of treatment, 99.4% (n=760) of the respondents were undergoing treatment from public sector whereas 0.5% (n=4) from private sector Table 1.

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Table 1: Demographic Characteristic of Respondents

Indicator		n (%)	Indicator		n (%)
Age (years)	<20	161 (21)	Qualification	Primary	252 (32.9)
	21-30	347 (45.4)		Secondary	152 (19.8)
	31-40	178 (23.2)		Matric	135 (17.6)
	41-50	78 (10.2)		Intermediate	131 (17.1)
Setting	Rural	214 (28)		Bachelors	57 (7.4)
	Urban	550 (71.9)		Others	37 (4.8)
Sector	Public	760 (99.4)	Monthly Income (Pak Rs.)	<10,000	481 (62.9)
	Private	4 (0.5)		10000-20000	207 (27)
Gender	Male	460 (60.2)		21,000-30,000	40 (5.2)
	Female	304 (39.7)		31,000-50,000	26 (3.4)
Marital Status	Married	544 (71.2)		>50,000	10 (1.3)
	Unmarried	232 (30.3)			

Values within parentheses represent the percentages

Table 2: Perceptions of Tuberculosis Patients and Their Caregivers Regarding Its Management in Pakistan

Indicators	Disagree n (%)	Neutral n (%)	Agree n (%)
TB is well controlled with currently available TB treatment in Pakistan	139 (18.1)	93 (16.4)	532 (69.6)
An understanding of cultural beliefs and individual attitude of patient by clinician can help in improving adherence to anti TB therapy	124 (16.2)	109 (14.2)	531 (69.5)
There is need for more educational program to increase knowledge and awareness of community regarding treatment of T.B	64 (8.3)	57 (7.4)	643 (84.1)

Values within parentheses represent the percentages

Table 3: Knowledge of Tuberculosis Patients and Their Caregivers Regarding Sign and Symptoms, Causes and Its Mode of Transmission

Indicators	Correct n (%)	Incorrect n (%)	Correct n (%)	Incorrect n (%)	p-value
Sign and Symptoms					
Rise of temperature in evening	351 (91.8)	31 (8.1)	363 (95)	19 (4.9)	0.23
Weakness/Weight loss	325 (85)	57 (14.9)	362 (94.7)	20 (5.2)	0.227
Headache	212 (55.4)	170 (44.5)	254 (66.4)	128 (33.5)	0.384
Blood in sputum	266 (69.6)	116 (30.3)	281 (73.5)	101 (26.4)	0.416
Continuous cough for more than three weeks,	290 (75.9)	92 (24)	326 (85.3)	56 (14.6)	0.625
Loss of appetite	281 (73.5)	101 (26.4)	310 (81.1)	72(18.8)	0.87
Causes					
Bacteria	243 (63.6)	139 (36.3)	272 (71.2)	110 (28.7)	0.44
Smoking	207 (54.1)	175 (45.8)	255 (66.7)	175 (45.8)	0.65
Alcohol consumption	177 (46.3)	205 (53.6)	182 (47.6)	200 (52.3)	0.784
Polluted water	244 (63.8)	138 (36.1)	244 (63.8)	138 (36.1)	0.416
Mode of Transmission					
Bacteria	243 (63.6)	139 (36.3)	272 (71.2)	110 (28.7)	0.44
Smoking	207 (54.1)	175 (45.8)	255 (66.7)	175 (45.8)	0.65
Alcohol consumption	177 (46.3)	205 (53.6)	182 (47.6)	200 (52.3)	0.784

Patients and caregivers (n=382) for each group
 Values within parentheses represent percentages
 Chi-Square $p \geq 0.05$

Table 4: Knowledge of Tuberculosis Patients and Their Caregivers regarding Treatment of Tuberculosis

Indicators	Correct n (%)	Incorrect n (%)	Correct n (%)	Incorrect n (%)	p-value
Isoniazid, Rifampicin, Pyrazinamide and Ethambutol used for first two months of treatment	153 (40)	229 (59.9)	186 (48.6)	196 (51.3)	0.292
Isoniazid and Rifampicin continuously used for next four to six months	157 (41)	225 (58.9)	132 (34.5)	250 (65.4)	0.006
Total course of treatment 6 to 9 months	284 (74.3)	98 (25.6)	336 (87.9)	46 (12)	0.158
Myrin P is used for treatment of TB	208 (54.4)	174 (45.5)	266 (69.6)	116 (30.2%)	0.048

Patients and caregivers (n=382) for each group
 Values within parentheses represent percentages
 Chi-Square $p \geq 0.05$

Table 5: Practices of Tuberculosis Patients and Their Caregivers Regarding Tuberculosis

Indicators	Correct n (%)	Incorrect n (%)	Correct n (%)	Incorrect n (%)	p-value
When would you prefer to go to health facility after getting TB?					
When treatment on my own does not work	244 (63.8)	138 (36.1)	238 (62.3)	144 (37.6)	0.658
If symptoms last for 3 to 4 weeks	244 (63.8)	138 (36.1)	243 (63.6)	139 (36.3)	0.007
As soon as I realize that my symptoms are of TB.	296 (77.4)	86 (22.5)	302 (79)	80 (20.9)	0.231
What would you do if you are sure about having TB symptoms?					
Go to health facility	254 (66.4)	128 (33.5)	324 (84.8)	58 (15.1)	0
Go to pharmacy	144 (37.6)	238 (62.3)	287 (75.1)	95 (24.8)	0.013
Go to traditional pharmacy	113 (29.5)	269 (70.4)	147 (38.4)	235 (61.5)	0.768
Self-treatment	106 (27.7)	276 (72.2)	150 (39.2)	232 (60.7)	0.001
Others	113 (29.5)	269 (70.4)	145 (37.9)	237 (62)	0.04

Patients and caregivers (n=382) for each group
 Values within parentheses represent percentages
 Chi-Square $p \geq 0.05$

Table 6: Attitudes of Tuberculosis Patients and Their Caregivers towards Tuberculosis

Indicators	Yes n (%)	No n (%)	Yes n (%)	No n (%)	p-value
In your opinion what are the reason for not seeking medical consultation for TB management?					
Recovered	185 (48.4)	197 (51.5)	210 (54.9)	172 (45)	0.442
Lack of affordability for the treatment	213 (55.7)	169 (44.2)	238 (62.3)	144 (37.6)	0.169
Self-Medication	174 (45.5)	208 (54.4)	296 (77.4)	86 (22.5)	0.751
Lack of access to health care facility	218 (57)	164 (42.9)	238 (62.3)	144 (37.6)	0.759
Social stigma	237 (62)	145 (37.9)	261 (68.3)	121 (31.6)	0.669
Consequence of not seeking treatment					
Complication from the disease	283 (74)	99 (25.9)	300 (78.5)	82 (21.4)	0.884
Would transmit disease to other	247 (64.6)	135 (35.3)	300 (78.5)	82 (21.4)	0.01
Death	247 (64.6)	135 (35.3)	296 (77.4)	86 (22.5)	0.56
What would be your reaction if you found out you have TB?					
Feel shame and/or embarrassment	216 (56.4)	166 (43.4)	252 (65.9)	130 (34.2)	0.144
Feel frightened and/or hopeless	242 (63.3)	140 (36.6)	291 (76.1)	91 (23.8)	0.01
Positively accept the disease and seek for treatment	222 (58.1)	160 (41.8)	300 (78.5)	82 (21.4)	0
How is a TB patient perceived in the community?					
Most of the people reject them.	190 (49.7)	192 (50.2)	230 (60.2)	152 (39.7)	0.041
Most of the people are friendly but avoid them.	192 (50.2)	190 (49.7)	231 (60.4)	151 (39.5)	0.208
Mostly people are friendly and help them	221 (57.8)	161 (42.1)	259 (67.8)	123 (32.1)	0.36
Changes in your Relationship if close family members acquire TB					
Sympathy	261 (68.3)	121 (31.6)	296 (77.4)	86 (22.5)	0.497
Hatred	149 (30)	233 (60.9)	304 (79.5)	78 (20.4)	0.003
Friendly but avoid	261 (68.3)	121 (31.6)	270 (70.6)	112 (29.3)	0.507

Patients and caregivers (n=382) for each group
 Values within parentheses represent percentages
 Chi-Square $p \geq 0.05$

regarding mode of transmission of tuberculosis with cough and inhalation of airborne droplets being the most common modes as in India where knowledge of patients regarding symptoms and mode of transmission were satisfactory (Yadav, *et al.*, 2006).

Most of the respondents possessed incorrect knowledge regarding use of drug isoniazid and rifampin in initial and continuous phase of Tuberculosis (Freitas *et al.*, 2012). Majority of the respondents knew the duration of treatment of TB. Our results highlighted that majority of the caregivers had better knowledge regarding use of Myrin-P for treatment of TB. Similar findings were reported in a study conducted in Uganda (Buregyeya *et al.*, 2011).

Care-seeking behavior of patients and their caregivers play an important role in treatment adherence. The majority of TB patients as well as caregivers preferred to visit health facility for seeking treatment when symptoms lasted for 3-4 weeks or when patients had started feeling TB symptoms. Similar findings were reported in a study conducted in China (Xu *et al.*, 2004). Furthermore majority of the patients and caregivers preferred visiting a health facility for treatment of TB. Majority of the caregivers preferred visiting a pharmacy for seeking treatment as compared to TB patients. The results of the present study showed that majority of the TB patients also considered self-treatment for TB as in India where majority of the patients considered self-treatment as the first option for TB (Saranya *et al.*, 2016). Various barriers result in delayed health seeking behavior by patients and their caregivers. The results of the current study highlighted that majority of the TB patients and caregivers were of the view that the major reasons for not seeking medical consultation for TB management were lack of affordability, access to health care facilities and social stigma. The

results are in line with study conducted in China and Pakistan where affordability and accessibility was found to be a major factor for not seeking care for TB (Khan *et al.*, 2013; Xu *et al.*, 2004). The results of the study highlighted that majority of the TB patients and their caregivers were of the view that consequences of not seeking treatment for TB are complications from disease, transmission of disease and death. Fear and stigmatization of the disease has an impact on health seeking behavior of TB patients. The results of the current study highlighted that majority of the patients as well as caregivers were of the view that they would have felt ashamed and frightened or hopeless if they were diagnosed with the disease. The results of this study are in line with a study conducted in India which concluded that feelings of hopelessness and anxiety are common in TB patients (Manoharam *et al.*, 2001). Majority of the caregivers were of the view that they would have positively accepted disease and sought treatment. The results of the current study highlighted that most of the respondents were of the view that mostly people are friendly towards TB patients and help them in seeking treatment. Similar findings were reported in a study conducted in Uganda (Buregyeya *et al.*, 2011). The results of the current study showed that most of the patients and caregivers were of the view that they had feelings of sympathy for their relatives which have acquired the disease. Similar results were reported in a study conducted in Pakistan (Ali *et al.*, 2003).

4. CONCLUSION

The results of the present study concluded that knowledge of TB patients and their caregivers regarding causes and transmission of disease was adequate while knowledge regarding treatment of disease was poor.

However, both TB patients and their caregivers had positive perceptions towards the current anti-TB treatment available in the country. Patients as well as their caregivers had positive health seeking behaviors and preferred to visit health care facility as soon as they were diagnosed with disease. Caregivers had a positive attitude towards individuals diagnosed with tuberculosis and had feelings of sympathy for such patients. There is a need to design educational interventions by National TB control program in the country in order to improve knowledge levels and increase awareness of TB patients and their care givers. Counseling sessions for healthy dietary pattern and hygiene should be conducted with patients as well as their caregivers in order to help them cope with disease and its complications. Patient centered approach should be adopted by healthcare professionals to improve adherence to anti-TB treatment. Public-private partnerships in TB control should be strengthened to reduce the rising prevalence of disease in the country.

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Causes of Non-Communicable Diseases: A Case Study of Karachi City

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Abstract

The advance world is in the focal point of a chivalrous health development. In numerous advance groups, the industrious weight of irresistible diseases is presently combined with the rising tide of non-communicable disease (NCD), in Pakistan 25% deaths are caused by such diseases. The focus of this investigation is to distinguish and analyze those components that are reason for non-communicable disease in cosmopolitan city of Karachi. The examination depends on exploratory investigation through information gathered by family unit overview in Karachi. This family unit study was directed in 2015 for reason of distinguishing issues of the city. Study uncovers that approximately 45% family units are getting water which is fit for drinking. Strategic relapse investigation presumed that 22 times augmentation in non-communicable diseases level with the ascent in every unit of low quality drinking water provided. Ascend in populace because of migration having effect of 6.2 times and insufficient seepage framework also affecting augmentation of NCDs. It is concluded that supply of low quality drinking water is causing diseases that are non-communicable. Alongside this over weight of

populace due to migration is likewise having profound effect on non-communicable diseases.

Keywords

Non-communicable disease (NCD), Quality of drinking water, Quality healthcare.

1. INTRODUCTION

The present Advance world is amidst circumspect health advancement. A large portion of creating countries bear the weight of irresistible diseases with the disturbing augmentation in non-communicable disease (NCD). Perpetual, diseases are of long term and by and large consistently in succession or a disease that is non-irresistible with advance gradually with the long stretch. The four principle kinds of such diseases included are cardiovascular diseases (like heart assaults and stroke), growth, interminable respiratory diseases, (for example, endless impeded pneumonic disease and asthma) and diabetes (World Health Organization, 2013). As indicated by current measurements of World Health organization, around 38 million individuals kick the bucket each year because of NCD. The

70-80% deaths happen in low income nations (World Health Organization, 2014). The Deaths due to NCDs now far dwarf deaths due to communicable disease. As indicated by WHO NCD Country Profiles 2014, Pakistan is at present confronting the twofold Burden of Communicable (38%) and Non-Communicable Diseases (half).

In Pakistan 25.3% people had high BP, 19% had CVD diseases, 3% had diabetes, 6% had constant respiratory diseases, 8% had growths, 23% were tobacco smokers and 0.1% were liquor customers (World Health Organization, 2014). Besides, Diseases that reason the most deaths in Pakistan incorporate cardio vascular disease (CVD) 25%, growths 7%, respiratory diseases 5%, diabetes 1%, wounds 8%, and other different NCDs 8% (Agha Khan University, n.d.). In the meantime, the profitable workforce of the economy bears the vast majority of NCDs; these diseases irritate a huge financial cost on healthcare arrangement of the social orders at entirety. They are the rising issue in megacities like Karachi for general society healthcare of the general public. Karachi is the Pakistan's financial center point with 21.7 million populaces speaking to all real ethnic gatherings. The dreariness weight of non-communicable diseases can be seen from the certainties that one of every three grown-ups beyond 45 years old experiences hypertension, and predominance of diabetes is accounted for at 10 percent. In Low center salary nations (LMICs), 80% of all demises happened because of NCDs (Global Status gives an account of NCDs, 2012). As per the World Economic Forum, the evaluated cost of this reason the world in 2030 will come to the level of \$47 trillion. The report presented that it will be a noteworthy risk to both the worldwide health and the worldwide economies amid 21st century (Bloom, 2012). The

accessibility of garbage handled sustenance with unhealthy fats economically available in the market for shoppers and pull them in towards languid way of life. In any case, overweight and corpulence are on disturbing level in creating world (Swinburn, 2011). Interactive hazardous elements to expand NCDs are because of quick urbanization, financial change and rising way of life in Asian megacities (Ham, 1973). According to current insights, over 60% of the expansion in the world's urban populace throughout the following three decades will happen in Asia, where it will surpass 2.6 billion by 2030, and where 16 of the world's 24 megacities are discovered (McGee, 2001). The recurrence of diabetes has climbed quickly in South Asian nations than any other part of world. Moreover, the cardiovascular disease, as of now, is spreading much speedily in the world (King H, 1998).

The impact of this research is that the factors for augmentation of non-communicable disease in the largest megacity of Pakistan i.e. Karachi.

The low quality of drinking water, over weight of populace because of movement and lacking seepage framework are the significant determinants that reason to increment in non-transferable illness in the Karachi city. As per Karachi Megacity Survey, just 45.5% family units in Karachi are getting water which is fit for drinking. The objective of this study is to analyze those factors that are responsible for increase in non-communicable disease in specially in this region.

This research work depends on exploratory investigation through information gathered by family unit study in Karachi. This family unit overview was directed in 2015 for motivation behind distinguishing issues and dynamics of Karachi city which based on dependent variable i.e. increase in non-communicable disease and

independent variables i.e. supply of poor quality drinking water and over-burden of population due to migration towards this place.

The fast development of a few urban areas with improvement in formal part is one of the major urban test in the 21st century. Non-communicable diseases have a significant toll on people, social orders and health frameworks (World Health Organization, 2014). They ordinarily cause in untimely grown-up mortality, deep rooted handicap that put serious effects on healthcare arrangements of the economy (Alwan, *et al.*, 2010). Situated in South Asia, Pakistan has a populace of more than 190 million and for every capita of health uses US \$25 (World Health Organization, 2014).

NCDs and wounds are among the best ten reasons for mortality and bleakness in Pakistan. Karachi reports one of the most noteworthy occurrences of bosom tumor for any Asian populace (Bhurgr *et al.*, 2008). Furthermore, gauges demonstrate that there are one million seriously rationally sick and more than 10 million people with psychotic dysfunctional behaviors inside the nation (Planning Commission of Pakistan, 2010). All through the most recent couple of years there has been a steady move from communicable to non-communicable diseases, for example, cardiovascular diseases (counting stroke and coronary illness), diabetes, emotional wellness issue, tumors, and endless aviation route diseases (Jafar *et al.*, 2013). A significant writing is accessible in the examination world, which bolster the analyst goal of this investigation. The quality and standard drinking water is basic need for each human life. She reported in the investigation additionally reasons that sully of drinking water is one of the extreme issues looked in urban and rustic zones of Pakistan (Ameen, 2014). Additionally, Zafar and Malik (2014) deduce in their examination that

Healthcare framework for NCDs ought to be the rethink and remake of whole health framework to gain from benefit arrangement to healthcare financing with enhance administration and execution checking (Zafar and Malik, 2014).

The Non-communicable diseases could be considered as contaminations that have cause in colossal part of way of life of individuals. Notwithstanding, a vast piece of NCDs are owing to operational and upstream factors (Blackshaw, 2011). The investigation of Thakur (2011) features the social and financial ramifications of NCDs in India. The examination uncovered that NCDs in India represent a financial weight around 5-10% of GDP of the nation that is hampered monetary improvement of the nation. The investigation additionally presumed that health part alone can't handle the "perpetual crisis" of NCDs, however multi-sectorial activity is required to reinforcing the health framework (Thakur, 2011). Gohari (2015) found in their investigation the five driving reasons for death in Tehran. The investigation uncovered that Tehran is a developing megacity with populace of 8 million individuals which is further isolated into 22 locales. The investigation intended to perceive high or generally safe bunches for five NCDs driving reason for death in 22 regions of Tehran. The investigation reasons that every one of the five causes has distinctive conveyance in various regions of the city. They additionally uncovered that this error maybe is the stun of disparity in healthcare offices in various regions of the city (Gohari, 2015).

According to 2014 statistics, In Pakistan, around 62% % disease are Non-communicable and injuries and 38% are communicable. The data reveals that 82% of total deaths are occurred due to Non-communicable diseases and 18% are due to injuries.

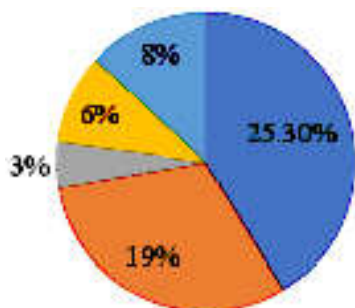


Fig. 1: Percentage of people suffered from NCD, 2017

■ Blood Pressure, ■ Cardiovascular Diseases, ■ Diabetes, ■ Chronic Respiratory Diseases, ■ Cancer

In the year 2014, 25.3% patients of NCD in Pakistan were suffering from blood pressure, 19% from cardio vascular disease, 8% from cancer, 6% chronic respiratory disease and 3% diabetes. Blood pressure is the most common prevailing NCD in Karachi. Research is attempted to reveal the reason of this augmentation (Fig. 1).

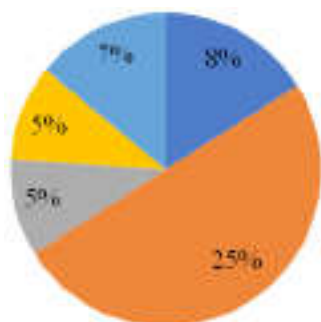


Fig. 2: Death occurred due to NCD in 2014

■ Blood Pressure, ■ Cardiovascular Diseases, ■ Diabetes, ■ Chronic Respiratory Diseases, ■ Cancer

Study reveals Blood pressure is most significant NCD but cardio vascular disease has caused more deaths in Karachi than Blood pressure. In 2014, Cardio vascular caused 25% of all deaths by NCD. Beside this, 8% due to

Blood pressure, 7% due to cancer, 5% diabetes and chronic respiratory disease each (Fig. 3).

3. RESEARCH METHODOLOGY

The city of Karachi was ordered into stratum as indicated by its 18 authoritative towns and 6 cantonments zones. Every town and cantonment were partitioned into squares and each piece includes 200 to 250 family units, by and large; every town and cantonment has distinctive block sizes in view of their populace as recorded in the 1998 census. As per the Pakistan Bureau of Statistic (PBS), Karachi has 13,233 squares. A two-arrange stratified inspecting was utilized to draw test. At first stage 1% squares were chosen through orderly irregular testing after an arbitrary begin. Amid the review, 1991 family unit were gone by and head of the family unit i.e. driving individuals were interviewed through close ended survey.

4. RESULTS AND DISCUSSION

4.1. Quality of Water Supplied to Household

Analysis showed 46% households are receiving drinking water, which is not fit for drinking. 45% respondent agrees they are receiving quality drinking water and 7.68% have no idea about quality of water they are receiving from their house tap (Fig. 3).

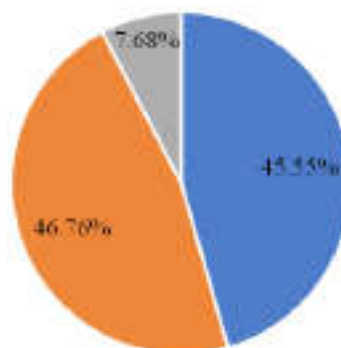


Fig. 3: Water supplied to household is fit for drinking

■ Yes, ■ No, ■ Don't Know

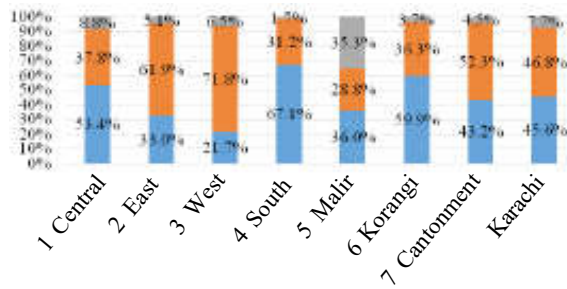


Fig. 4: District Wise Analysis: Supply of quality drinking water to districts

■ Yes, ■ No, ■ Don't Know

The supply of quality of drinking water varies area wise. As indicated by overview result, most of the occupants of Central, South and Korangi area are satisfied by the quality of drinking water provided to them that is 53.4%, 67% and 59.9% individually. Then again, 62%, 72% and 52.3% occupants of East, West and Cantonment individually are not fulfilling quality of drinking water supply to them (Fig. 4).

4.2. Analysis on Causes of NCD in Karachi City

4.2.1. Poor Quality of Water

Water is necessity of life. No-one can survive without water. 70% of human body weight is comprised of water. According studies a human body needs to consume up to 20 liters of water on daily basis to maintain health. Deficiency of water may cause many diseases in human body. As indicated by investigation of reliant and free factors, the examination found that 87% of review respondents said that supply of low quality of water is the fundamental driver that would figure the level of NCDs in the Karachi city.

4.2.2. Overburden of Population

We always have limited resource to fulfil

needs of our society. Karachi as the city of more 20 million population is also facing problem of scarcity of resources. Population growth of the city is affected by two factors: one is birth rate and second is immigration from different areas of country. And the people coming from different areas are not aware about the problems of Karachi. The analysis of over weight of populace in Karachi, which is happened because of outsiders and its effect on expanding volume of NCDs in Karachi, demonstrated that just about 94% respondents comprehend that the expanding pattern of NCDs is a direct result of the overburden of populace in Karachi.

4.2.3. Inadequate Drainage

Adequate drain system of water plays an important role to maintain sanitation in the locality. We can save society from many diseases by constructing and maintaining a good sanitation system but unluckily in the city of millions of people, we are unable to see such water drainage system. As per the bivariate investigation of insufficient seepage framework in Karachi and its effect on NCDs in the city result, 86% of the respondents understand that lacking waste framework is a noteworthy reason for NCDs in Karachi.

4.2.4. Logistic Regression

The binary logistic investigation is helpful research tool to break down dichotomous information. It has three presumptions; initially, the result must be watchful and the factors (Dependent and Independent) are ought to be as dichotomous. Also, the information ought not to have any anomaly and thirdly, there is no multicollinearity between logical variables. All factors are recorded in the request of twofold numbers (0,1) e.g. 0 = no Over Burden of Population because of movement and 1 = Over

Burden of Population because of migration. Model explains 21.2% variation in dependent variable caused by independent variables.

Table 1

Step 1 Variables in equation	df	Sig.	Exp (B)
Poor quality drinking water (1)	1	.000	21.82
Over Burden of Population due to immigration (1)	1	.000	6.2
Constant	1	.000	0.077

Logistic regression analysis shows significant impact of 22 times on non-communicable diseases with the rise in each unit of poor quality drinking water supplied. The impact of poor quality water is very high as mostly respondent agree with this the water quality is leading factor among all other significant impacting factors. As people in Karachi migrate from all over the Pakistan they are also more likely to affect NCDs as shown in Table 2. It has impact of 6.2 time with its rise in 1 time. Therefore, as result of this research it is recommended that the awareness programmes on hygiene and civic issues must be conducted on Governmental level.

To avoid medical problems government should initiate/organise awareness programmes on hygiene and civics issues via conducting awareness programs on hygiene and civic issues via seminars, workshops etc. and initiate campaigns of mindfulness programs for the improvisation of knowledge at public level.

Government should take appropriate

measures for ensuring the supply of quality drinking water and its check and balance, alongwith proper and perfect arrangement of drainage system in the city to ensure satisfied sanitation and people should also be educated in this regard. Moreover the harmonization and facilitation of general public needs and necessities according to the basis of demographical survey reports and population planning and development (settlers and emigrants) at the Governmental level in Karachi city.

Government should pay attention to problems of immigrants in the city and provide them opportunities so that they can avoid low quality products.

5. CONCLUSION

Low quality drinking water is causing more sicknesses that are non-transmittable. Next to this over weight of populace due to movement is likewise having solid effect on non-transferable maladies. Individuals originating from various zones of Pakistan don't know about health issues problems in Karachi city. Particularly, foreigners are more influenced by such medical problems as a result of low quality of drinking water. Insufficient waste is causing sway alongside contaminated drinking water and overburden of populace however not noteworthy. Unthinkable investigations demonstrated 93.8% settlers have experienced non-transmittable illnesses. 87% of non-transmittable infections are caused by low quality of drinking water and 86.1% because of insufficient seepage framework in the city. Area insightful investigations demonstrated that 92.8% respondents realize that non-transmittable infections are caused on account of such water which is hygienically unacceptable, while 74.8% endorsed that the real reason is overburden of populace because of migration towards this region from the entire country.

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Commonly Used Medicinal Herbs in Pakistan – A Pharmacognostic Appraisal

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Abstract

Nature always stands as a golden mark to exemplify the outstanding phenomena of symbiosis. As the public are becoming aware of the potency and side effect of synthetic drugs, there is an increasing interest in the natural product remedies with a basic approach towards the nature. Medicinal herbs as potential source of therapeutics aids has attained a significant role in health system all over the world for both humans and animals not only in the diseased condition but also as potential material for maintaining proper health. The current review focused on the pharmacognostic studies of eight most commonly available medicinal herbs of Pakistan (*Cuminum cyminum* L., *Curcuma longa* L., *Foeniculum vulgare* Mill., *Lawsonia inermis* L., *Nigella sativa* L., *Symplocos racemosa* Roxb., *Trigonella foenum-graceum* L. and *Withania somnifera* L.).

Keywords

Medicinal plants, Histology, Microscopy, Pharmacognosy, Pakistan.

1. INTRODUCTION

Medicinal plants are the potential source of therapeutic agents. They attained a significant role in health care system all over the world for humans not only in diseased condition but also for maintaining their proper health. As the people are becoming aware of the side effects of synthetic drugs, generally there is an increasing interest in the natural product remedies with a basic approach towards the nature. Medicinal plants and condiments are affordable, accessible to the most of the population in the world. There has been as highly increased interest for herbal remedies in several parts of the world. Thus, there is need to encourage the use of medicinal plants and condiments as potential sources of new drugs (Rachinger 1981; Zargari 2001).

Larger number of medicinal plants are predominantly used to treat cardiovascular problems, liver disorders, central nervous system, digestive and metabolic disorders and also useful as supplement in the treatment or management of various diseases. Condiments served as

coloring, flavoring agents, preservatives, food additives as well as medicine and aesthetic in cosmetology. The active phytochemicals derived from these condiments have provided the molecular basis for these actions.

Since from the beginning of this century, there has been an increasing interest in the study of medicinal plants and their traditional use in different parts of the world. With the chemically synthesized drugs for number of diseases, natural products of plant origin has its own importance and has maintained the most important resource for developing new drugs to treat various diseases (Ahmed, 2006). Adulteration or substitution of original plant with alternate plant material or intentional addition of any foreign substance to increase the weight or potency of the product or to decrease its cost is alarming and may lead to serious consequences. It is established that therapeutic efficacy of medicinal plants depends upon the quality and quantity of chemical constituents. The misuse of herbal medicine or natural products begins with incorrect identification. The main error is one common vernacular name assigned to two or more entirely different species. All these problems can be resolved by pharmacognostic studies of medicinal plants. It is essential to lay down pharmacognostic specifications of medicinal plants which are used in various drugs (Peter and Tassou, 2000). There is an urgency to expeditiously utilize and scientifically validate medicinally useful plants. Therefore, the current review provide strategy for identification of most commonly occurring medicinal plant in Pakistan (*Cuminum cyminum* L., *Curcuma longa* L., *Foeniculum vulgare* Mill., *Lawsonia inermis* L., *Nigella sativa* L., *Symplocos racemosa* Roxb., *Trigonella foenum-graceum* L. and *Withania somnifera* L.). All these medicinally important plants are depicted in Table 1.

2. AUTHENTICATION METHODS

There are many methods employed currently for authentication and evaluation of herbs used as raw material by herbal drug industries. Most common methods include organoleptic, microscopic, biological, taxonomic, chemical and pharmacological evaluations.

3. PHARMACOGNOSTIC EVALUATION

Pharmacognosy basically deals with standardization, authentication and comprehensive study of natural drugs and all gathered informations from every point of view about the specific object of health related aspects. Most of the researches in pharmacognosy have identified controversial species of plants, authentication of commonly used traditional medicinal plants through morphological, phytochemical, physicochemical and microscopic analysis to establish the standards according to the WHO guidelines. The importance of pharmacognosy has been widely felt in recent times. Unlike taxonomic identification, pharmacognostic study has additional parameters which help in identifying adulteration in dry powder form. This is again necessary because once the plant is dried and made into powdered form, it loses its morphological identity and sensory characteristics and easily prone to adulteration or admixing. Pharmacognostic studies ensure plant identity, lays down standardization parameters which will help and prevent adulterations (*WHO Monograph*, 1999).

4. DESCRIPTION AND MICROSCOPIC AUTHENTICATION OF HERBS

The process of standardization can be achieved stepwise via pharmacognostic studies which help in identification and authentication

Table.1: Medicinal Important Plants

S.No.	Scientific Names	Urdu names	Pictures	Fig. No. (A and B)
1.	<i>Cuminum cyminum</i> L.	<i>Zeera</i>		1
2.	<i>Curcuma longa</i> L.	<i>Haldi</i>		2
3.	<i>Foeniculum vulgare</i> Mill.	<i>Sounf</i>		3
4.	<i>Lawsonia inermis</i> L.	<i>Hina</i>		4
5.	<i>Nigella sativa</i> L.	<i>Kalongi</i>		5
6.	<i>Symplocos racemosa</i> Roxb.	<i>Lodhpathani</i>		6
7.	<i>Trigonella foenum-graceum</i> L.	<i>Methi</i>		7
8.	<i>Withania somnifera</i> L.	<i>Asgand</i>		8

of the plant material. Such information can act as reference information for accurate identification of a particular plant and will be useful in parathion of its monograph. Further, it will act as a tool to detect adulterants and substituents and will help in maintaining the quality, reproducibility and efficacy of natural drugs.

Microscopic authentication is indispensable in the initial identification of medicinal plants as well as identification of small fragments or powdered herb (Rizwani and Zahid, 2014). Microscopic examination and transverse sections of medicinally important plants used in Pakistan are showed in Figs. 1-8 A and B.

4.1. *Cuminum cyminum* L.

Cuminum cyminum L. belongs to the family Apiaceae. It is one of the old cultivated medicinal food herbs in Asia, Africa and Europe. Globally, seeds have been commonly used for culinary and flavoring purposes and folklore therapy since antiquity (Rachinger, 1981; Zargari, 2001). *C. cyminum* is cultivated and distributed in almost all parts of the world. In Pakistan it is cultivated in Baluchistan and Kashmir (Ahmed, 2006). Fruit is the mixture of united and separate mericarps, yellowish green or yellowish brown elongated ovoid, 3-6 mm in length (Peter and Tassou, 2000).

The main characteristic features of powder drug are epicarp, trichomes, vittae, sclerids, endocarp, calcium oxalate crystals, endosperm and fibro vascular tissue. Transverse section of the drug shows the following features, epicarp consisting of colorless layer of cells containing thin walled sinuous with polygonal surface along with irregular striated cuticle and stomata. Trichomes attached with small fragments of epicarp. Vittae contain yellowish brown fragments composed of large, thin walled polygonal cells. Endocarp composed of large

thin walled elongated cells while endosperm was thick walled containing aleuron grains and microrostte calcium oxalate crystals. Fibrovascular tissues were thin walled. The pitted fibers, vessels with spiral and annular shaped and attached with sclerids of mesocarp (Figs. 1A and B).

4.2. *Curcuma longa* L.

Curcuma longa L. belongs to the family Zingiberaceae, is an erect perennial herb, the medicinal part obtained from underground stem (Ahmed, 2006). The origin of the plant is not certain; however the plant is a native of Southern Asia and is cultivated throughout the warmer parts of the world (*WHO Monograph*, 1999). *C. longa* is an aromatic perennial herb with tuberous rootstock without leafy stem above ground (Peter and Tassou, 2000).

The diagnostic characteristics of drug are parenchyma, epidermis, unicellular trichomes, cork tissue, rectangular vessels and starch grains which are seen abundantly. Histology showed rounded to oval parenchyma with slightly irregular walls filled with gelatinized starch which containing bright yellow color. Cork tissue consists of several layers of rounded stomata and cicatrices. Trichomes are unicellular and elongated. Vessels are prominent with rectangular pits and few were spiral and contain gelatinized starch granules (Fig. 2A and B).

4.3. *Foeniculum vulgare* Mill.

Foeniculum vulgare Mill. belonging to the family Apiaceae (Diaaz *et al.*, 2005). The plant is easily grow anywhere widely distributed all over the world. In Pakistan it is mainly cultivated in Punjab and Maharashtra and Assam in India. *F. vulgare* is a thick, perennial root-stock, stout stem, 4 to 5 feet or more in height, erect and cylindrical, bright green color and so smooth as to seem polished, much branched leaves cut

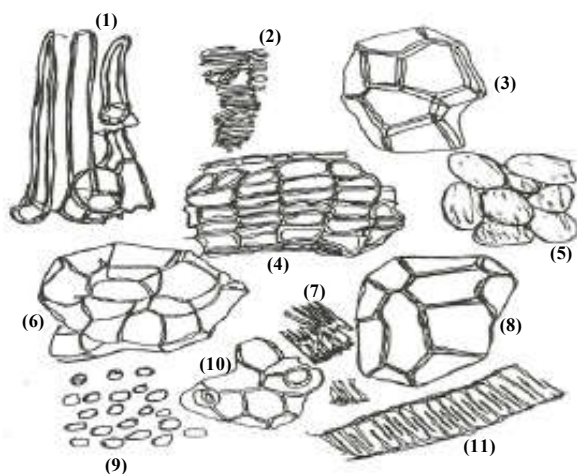


Fig. 1A

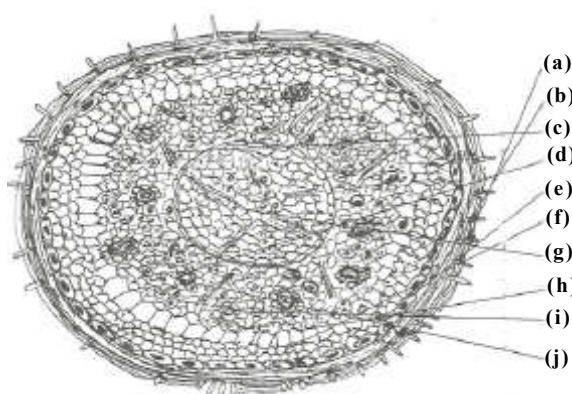


Fig. 1B

Fig. 1A) Powder fruit drug of *Cuminum cyminum* in chloral hydrate, glycerine and iodine solution: (1) endocarp; (2, 3) group of sclerids from mesocarp; (4) microrosette of calcium oxalate crystal; (5) endocarp; (6) endocarp with palisade, vascular tissue, sclerids and parenchyma; (7) endosperm containing microrosette of calcium oxalate crystal; (8, 10) covering trichrome attached to fragment of epicarp; (9) group of sclerids from the sclerenchymatous layer of mesocarp; (11) epicarp with stomata; (12) fragment of vittae, and **Fig. 1B)** (a) vascular tissues; (b) fragment of vittae; (c) cortical tissue; (d) sclerenchyma cells with tannin deposition; (e) stomata; (f) epidermal granular trichome; (g) epidermis; (h) endospermic cells

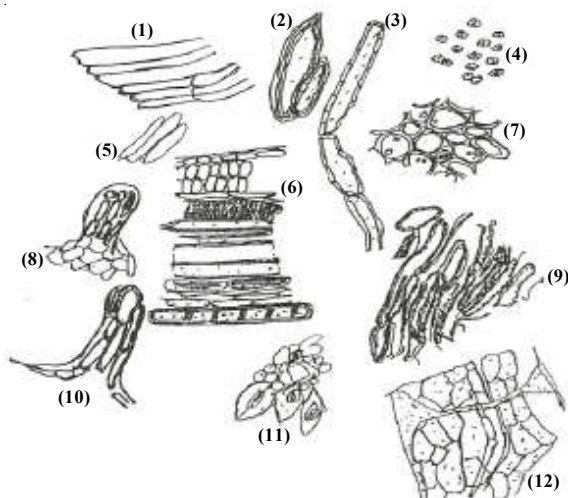


Fig. 2A

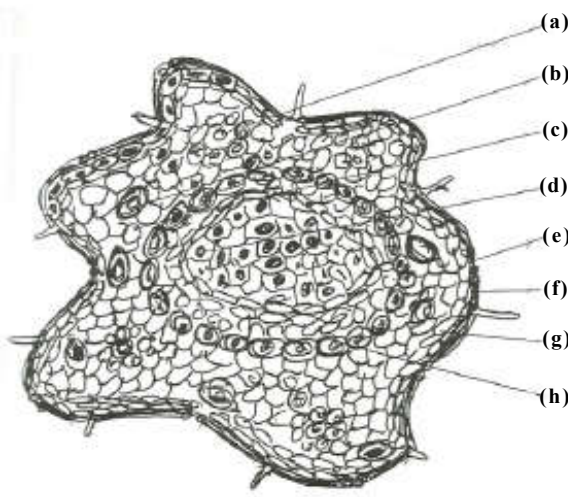


Fig. 2B

Fig. 2A) Powder rhizome drug of *Curcuma longa* in chloral hydrate, glycerine and iodine solution: (1) covering trichome attached to the fragment of epidermis; (2) spirally thickened vessels; (3) cork in oblique; (4) outer tissue with epidermis, cork, cortex, layer of collapsed cells; (5) parenchymatous cell filled with gelatinized starch and yellow coloring matter; (6) parenchymatous cells; (7) reticulate thickened vessel; (8) cork cell; (9) starch granules; (10) epidermis with stomata and cicatrix, and **Fig. 2B)** (a) glandular trichome; (b) cork tissue; (c) phloem vessel; (d) oil containing cells; (e) epidermal cells; (f) small cortical tissue; (g) pericycle tissue; (h) curcumin and color containing cells; (i) vascular tissue; (j) pith region with cells contain thick lignin and tannin deposition

into the finest of segments (Ahmed, 2006; Peter and Tassou, 2000).

In the powder microscopy of comphoraeous aromatic powder, some prominent features are more abundantly observed such as thread like steroids fragments of vittae. Oil globules which are comparatively larger than coriander powder, microspenoidal calcium oxalate crystals and reticulate and annular vessels and fibro vascular tissues were seen more prominently. Transverse section of fruit showed almost closer cellular arrangement as like that of coriander except sclerids which are present in fennel fruit (Fig. 3A and B).

4.4. *Lawsonia inermis* L.

Lawsonia inermis L., belongs to the family Lythraceae. It is a small, elegant bush with fragrant flowers, cultivated and naturalised all over the country (Kirtikar and Basu, 2005; Nadkarni, 1982). It is much branched, deciduous, glabrous, sometime spiny shrub or small tree with grayish brown bark, attaining a height of 2.4-5 m (Khare, 2007).

The main diagnostic features of powdered leaves are fragments of cuticle, parenchyma, collenchyma, granular mucilage sacs; oil globules palisade tissues having chloroplast, epidermal cells with anomocytic stomata. The cluster of calcium oxalate crystals, large trachied, pericycle fibers dominates. The transverse section revealed that the leaves are covered with thick cuticle. The upper epidermis contains stomata and the middle of section fibro vascular bundle is present surrounded by pericycle (Figs. 4A and 4B).

4.5. *Nigella sativa* L.

Nigella sativa L. belongs to family Ranunculaceae. It is native to Southern Europe, North Africa and Southwest Asia and it is cultivated in many countries around the world

(Khare, 2007). *N. sativa* is small beautiful perennial herb and about 30-60 cm in height. The seed are trigonous, inflated, aromatic black and rugulose-tubercular (Ahmed, 2006).

Microscopic study of powder showed sclerenchyma cells, oil cells and numerous starch grains. Seeds are jet black in color and cuneate shaped with rough seed testa; raised ridge called raphe is present on the concave surface. Longitudinal surface of seed shows that the outer most surface is thick black seed cast followed by rough white endosperm. An anterior end small embryo is also visible (Figs. 5A and 5B).

4.6. *Symplocos racemosa* Roxb.

Symplocos racemosa Roxb. belonging to the family *Symplocaceae* is a small evergreen tree (Kirtikar and Basu, 2005). *Symplocos* is a genus of flowering plants in the order Ericales, containing about 250 species native to Asia, Australia and the Americas (Rao *et al.*, 2011; Anonymous, 1976; Bhattacharjee, 1998).

Reddish brown powder of the root bark of *S. racemosa* has characteristic spicy odor and slightly bitter taste. Main diagnostic feature of the drug powdered are stone cells, coloring matter containing rectangular cells, thin walled oil cell, sheet of cork tissue some of them having lignin and tannin contents. Rosette calcium oxalate and numerous starch grains (simple and compound) are the prominent features. Noticeable fragments in cross transverse section of root of *S. racemosa* include sclerids and thread like single small cellular arrangement with phloem and phelloderm. Upper and lower zone of pericycle, stone cells, two layers of thick lignified cells, thickened cork cells, secondary cortex having bast mucilage cell, thick oil gland seen in this region. Medullary rays, occasional soft bast also present in the drug (Figs. 6A and 6B).

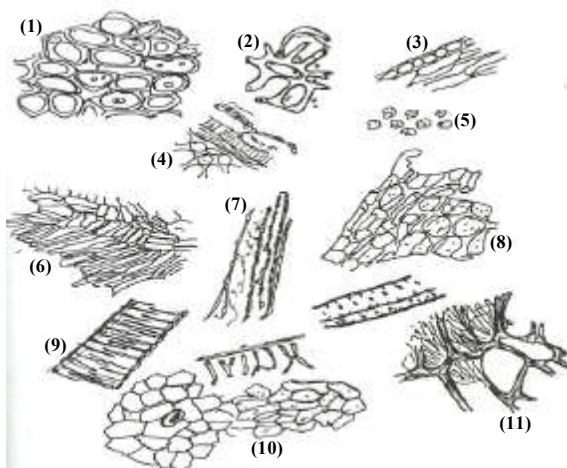


Fig. 3A

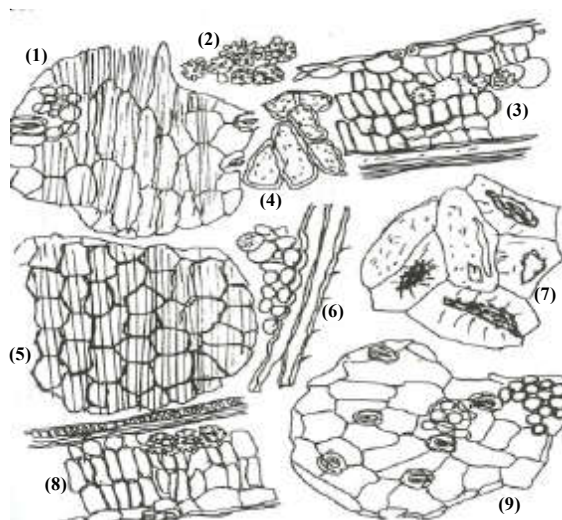


Fig. 4A

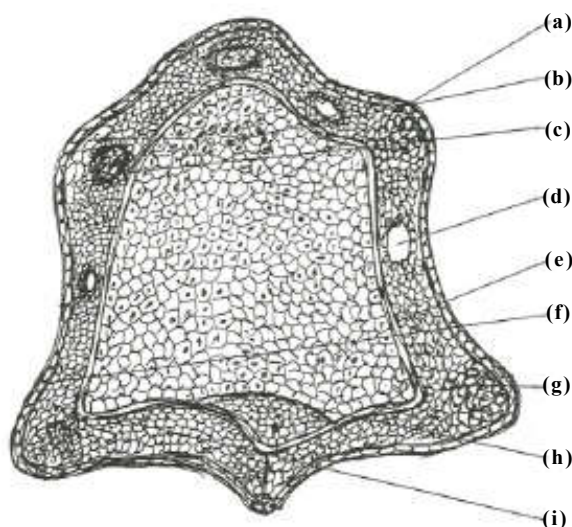


Fig. 3B

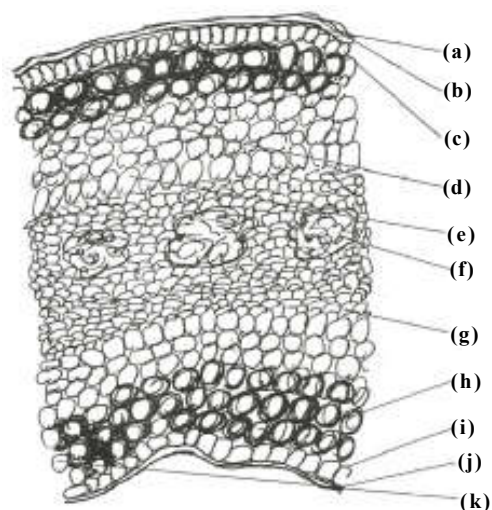


Fig. 4B

Fig. 3A) Powder fruit drug of *Foeniculum vulgare* in chloral hydrate, glycerine and iodine solution: (1) epidermis containing microrosette calcium oxalate crystal; (2) thick walled endosperm cell; (3) epicarp and parenchyma of mesocarp; (4) epicarp with parenchyma, endocarp, testa and endosperm; (5) calcium oxalate crystal; (6) endocarp; (7) fibrovascular tissue; (8) vittae with thick walled mesocarp; (9) vascular tissue; (10) epicarp with stomata; (11) endocarp with overlying cells of mesocarp, and **Fig. 3B)** (a) advance pith region; (b) reticulate lignified parenchyma; (c) fragment of vittae; (d) oil globules; (e) cortical cells; (f) epidermal cells; (g) vascular tissue; (h) endospermic cells; (i) mesodermal cells

Fig. 4A) Powder leaf drug of *Lawsonia inermis* in chloral hydrate, glycerine and iodine solution: (1) lower epidermis of lamina with anomocytic stomata; (2) cluster of calcium oxalate; (3) lamina with lower epidermis, spongy mesophyll with cluster of calcium oxalate crystals; (4) thin walled sclerids from epicarp; (5) epidermis of petiole; (6) pericycle fibre containing cluster of calcium oxalate crystals; (7) thick walled sclerids; (8) lamina with upper epidermis; (9) lamina of epidermis with anomocytic stomata, and **Fig. 4B)** (a) stomata; (b) cuticle; (c) upper epidermis; (d) upper pigmented hypodermis; (e) mucilage sac; (f) fibro vascular bundle; (g) pericycle; (h) collenchyma; (i) lower epidermis; (j) cuticle; (k) lower pigmented hypodermis

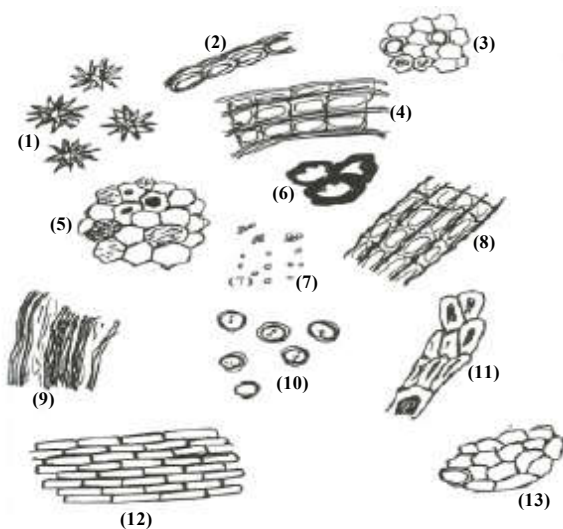


Fig. 5A

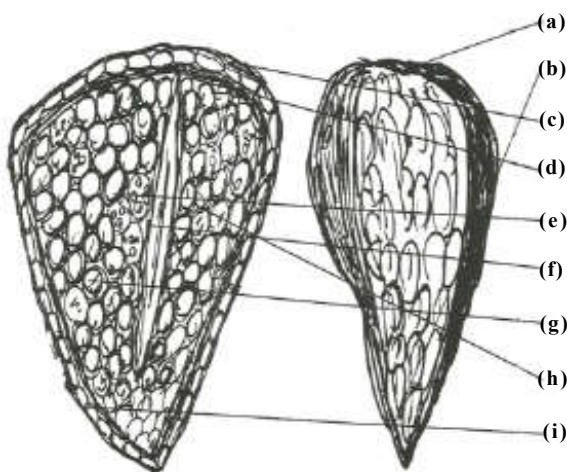


Fig. 5B

Fig. 5A) Powder seed drug of *Nigella sativa* in chloral hydrate, glycerine and iodine solution: (1) calcium oxalate (rosette); (2) epidermis of testa; (3) sheet contain oil cell; (4) group of fibres of epidermis of testa; (5) sheet of sclerenchyma containing tannin, starch and oil; (6) sclerenchyma cells of testa in surface view; (7) starch grain; (8) surface view of thick walled cells; (9) group of fibre; (10) parenchymatous oil cells of endosperm; (11) endospermic longitudinal view; (12) sheet of cork cells; (13) parenchyma of testa surface view, and **Fig. 5B)** (a) embryo; (b) raphe; (c) seed coat; (d) endosperm; (e) oil granules (starch grain); (g) cortical tissue; (h) tannin containing cells; (i) epidermal cell

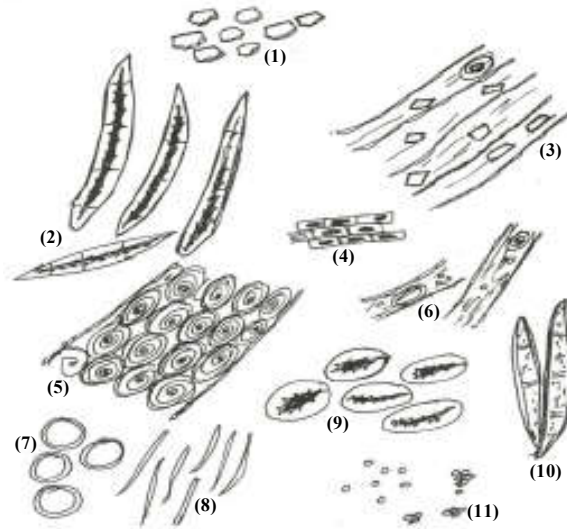


Fig. 6A

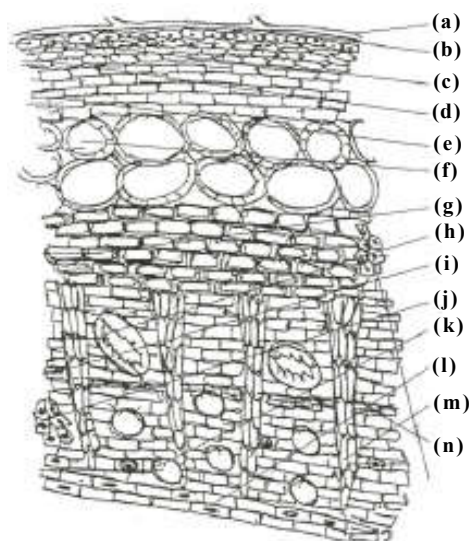


Fig. 6B

Fig. 6A) Powder root drug of *Symplocos racemosa* in chloral hydrate, glycerine and iodine solution: (1) calcium oxalate prism; (2) elongated sclerids; (3) group of fiber with calcium oxalate and starch deposit; (4) cork tissue; (5) sheet of starch grain on surface view; (6) oil and starch containing vessels; (7) thin walled oil cell (8) thread like fibre; (9) stone cell; (10) phloem fiber; (11) starch grain (simple and compound), and **Fig. 6B)** (a) phelloderm; (b) lenticle; (c) thick lignified cell; (d) upper zone of pericycle; (e) lower zone of pericycle; (f) stone cell; (g) thick walled cork cell; (h) oil gland; (i) secondary cortex; (j) medullary ray; (k) sieve tubes; (l) group of bast tissue; (m) mucilage cell; (n) cambium; (o) bast cell

4.7. *Trigonella foenum-graceum* L.

Trigonella foenum-graecum L. belonging to the family Fabaceae. It is native to Western Asia. Mild Mediterranean climates are most suitable. Fenugreek seeds are small (5 mm. long), hard, and brownish yellow the color may varies. They are flattened and have a very characteristic rhomboidal outline. Nearly in the center of one of the long, narrow sides is a small depression in which hilum and micropyle are situated, the former being distinctly visible as a whitish point; this depression is continued in the form of a furrow running diagonally across part of each of the adjoining sides, thus dividing the seed into two unequal lobes (Petropoulos, 2002; Flammang *et al.*, 2004).

Powder microscopic study of seed revealed the presence of palisade cell, parenchymatous cell of cotyledons, aleuron grains, oil cells, cuticle, epidermis and hypodermis of testa. Histological examination of seed showed prominent cuticle cells of epidermis. Palisade consists of single row of columnar cells containing chloroplast. Hypodermal cells are polygonal in shape just beneath the palisade cells. Two layers of thin walled parenchyma cells resides near the endospermic region enriched with rich numerous cell containing mucilage and aleuron grains (Figs. 7A and 7B).

4.8. *Withania somnifera* L.

Withania somnifera L. belonging to the family *Solanaceae* that reaches about 30-150 cm in height (Anonymous, 1998; Bhattacharya *et al.*, 2001). *W. somnifera* has been in use for over 2500 years to treat all kind of diseases and human ailments. The species name *somnifera* means “sleep-bearing” in Latin, indicating it was considered as sedative.

Diagnostic microscopic cellular fragments of powder of *W. somnifera* are oval shaped

starch granules which are most abundant. Parenchyma, small trachieds, lignified sclerids, stone cells, single layered group of medullary rays, cell filled with starch grains and parenchyma cells in beaded form. Fragment consists of group of spiral vessels and sclerids, wide lumen stone cell are frequent but narrow lumen stone cells are also found occasionally. Group of phloem fiber having tannin and starch grains were rich with scattered fragment of cork tissue. Transverse section of *W. somnifera* root have scattered vascular bundles where cambium is missing. About 4-5 layers of cork tissue, epidermal thickly isodimetric shaped cells beneath the layer of cork tissue. Middle region covered with large rectangular mesodermal zone consisting of 3-4 layers; most of them have deposition of tannin, resins and starch grains. A compact layer of starchy oval shaped also found before pericycle region. While central region covered with conducting tissue such as phloem, xylem and medullary rays. Especially medullary rays are numerous (i.e, consist of 20-25 single layered cells) and in between xylem and trachieds, 2-3 cells and phloem fragment in rows (Figs. 8A and 8B).

5. CONCLUSION

The vast majority of quality-related problems are associated with unregulated herbal products. There is substantial evidence that many traditional medicine, give rise to serious public health concerns due to lacking of effective quality control measures. Sometimes mal agriculture practice, seasonal variation, processing and methodology also influence the toxicity of medicinal plants. This review article represents simple but reliable microscopical measurements which are useful to a lay person in using the investigated plants as herbal drug and home remedy. It is not only helpful for the pharmaceutical manufacturers to identify and

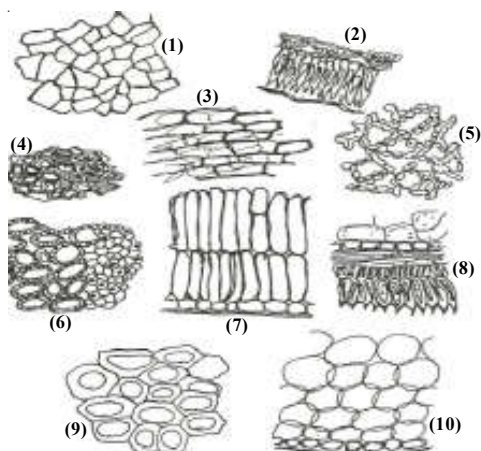


Fig. 7A

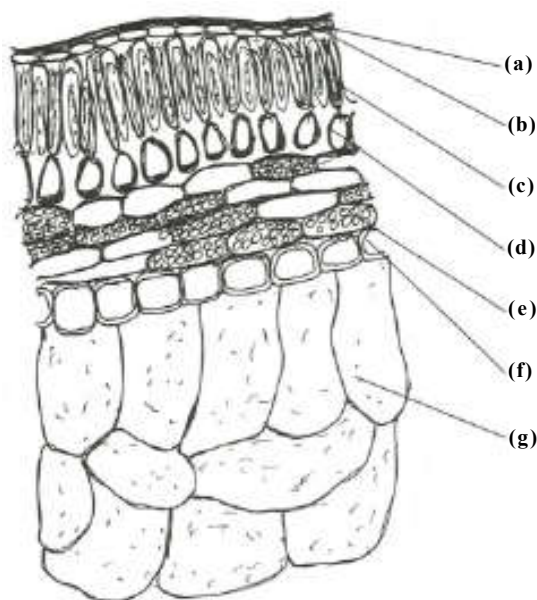


Fig. 7B

Fig. 7A) Powder seed drug of *Trigonella foenum-graceum* in chloral hydrate, glycerine and iodine solution: (1) undifferentiated parenchyma of testa; (2) cuticle, epidermis and hypodermis of testa; (3) epidermis of testa; (4) parenchyma of testa; (5) outer most layer of endosperm; (6) endosperm containing hypodermis of testa; (7) endosperm with palisade of cotyledons; (8) epidermis and hypodermis of testa; (9) hypodermis of testa; (10) epidermis with parenchymatous cell of cotyledons, and **Fig. 7B)** (a) cuticle; (b) epidermis; (c) hypodermal cell; (d) epidermis of testa; (e) starch grains; (f) endospermic cells; (g) group of mucilage cells

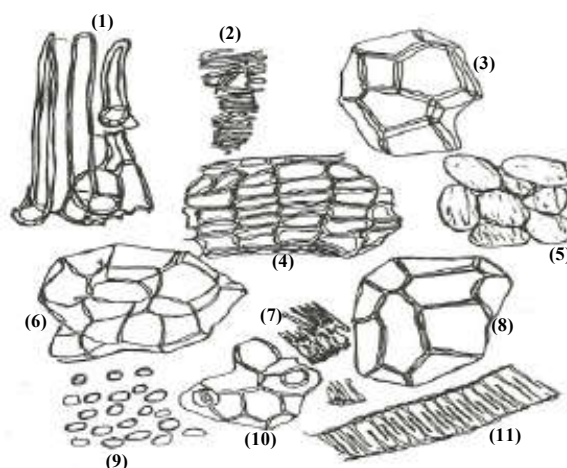


Fig. 8A

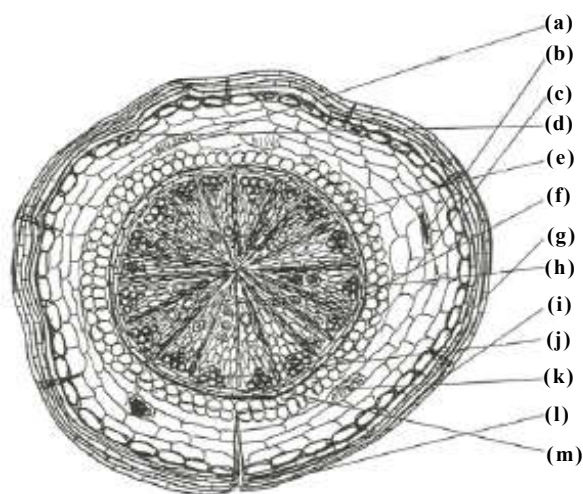


Fig. 8B

Fig. 8A) Powder root drug of *Withania somnifera* in chloral hydrate, glycerine and iodine solution: (1) group of phloem fibers with starch grain; (2) oil cell; (3) small spiral vessel; (4) group of small spiral vessel; (5) simple starch grain; (6) sclerids; (7) beaded parenchyma cell; (8) sheet of beaded parenchyma with rich starch; (9) group of fiber having starch; (10) narrow lumen stone cell; (11) cork tissue, and **Fig. 8B)** (a) withanolide alkaloids; (b) tannin containing cell; (c) primary cortex; (d) bast; (e) pericycle; (f) secondary cortex; (g) outer layer of dermal cell; (h) trachieds; (i) multiple layer of cork; (j) medullary ray; (k) starch cell; (l) primary phloem arch; (m) secondary phloem

selection of the raw material at preliminary stage for herbal drug production but also beneficial for the manufacturers of cosmetic and food products. While for definite determination of raw material at any stage according to seasonal variation more sophisticated and advanced techniques along with good agriculture practices are helpful to establish the quality standard of herbal drugs.

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Evaluation of Medication Errors and their Contributing Factors – A Source of Preventable Adverse Drug Events

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Abstract

Medication errors are the most common preventable source of ADE (Adverse drug event) that may result in burdening of public health. Consequences of medication errors may lead to increased cost of treatment, prolonged course of therapy and increased risk of death. A descriptive questionnaire-based survey study was conducted in different regions of Hyderabad city. Finding of the study shows that among 467 respondents, 295 (63.2%) were nasal drop users, 384 (82.2%) were eye drop users and 131(28.1%) were MDI (Metered dose inhaler) users. It was found that every respondent committed medication errors in at least one step of medication administration. Scarcity of pharmacists in pharmacies, provision of only verbal information instead of written and lack of practical demonstration are considered to be the contributing factors for the occurrence of high rate of medication errors.

Keywords

Medication errors, Eye drops, Nasal sprays, Meter dose inhaler, Adverse drug events.

1. INTRODUCTION

Medication error is “any avertable incident which might cause or lead to indecorous utilization of medicine which may or may not cause patient’s injury, it is in the control of the health care professional or being handled by the patient himself” According to European Union these are unintended mistakes and are the most communal avertable source of (ADE) and lead to a noticeable burdening of public health (2017). There are mainly three types of medication errors: 1) Errors in written medication order, 2) dispensing, 3) and its administration (Barber *et al.*, 2003). Consequences of medication errors are: 1) Increased cost of treatment (Cost has been undoubtedly a major barrier in seeking appropriate health care in Pakistan (Fatmi and Avan, 2002; Stephenson and Hennink, 2004), 2) Prolonged treatment and 3) Almost double the risk of death (Lustig, 2000).

According to a study 34% of all errors resulting in preventable ADEs, are due to the medication administration errors (Bates *et al.*, 1995). Out of every 100 errors of medication

38 occur during administration of medication. Several other reports also support to that medication administration errors occupy a major place in the list of errors incidents. The percentages are even higher while administering dosage forms like (MDI), eye drops or nasal sprays. A study was conducted to evaluate the technique used to administer MDI and only 21% of the participants performed all the steps correctly (Shrestha *et al.*, 1996).

An incident of *Serratia marcescens* keratitis was reported in three patients and the reasons associated were mishandling of the eye-drop bottle and inaccurate administration technique (Templeton *et al.*, 1982). Interaction and communication between the prescriber and the recipient of therapy has conspicuous effect on patient's adherence to the prescribed treatment. Although eye-drop is a conventional dosage form but there is a necessity to elaborate appropriate method of administration of these dosage forms to the patients (Taylor *et al.*, 2002).

Winfield *et al.*, (1990) conducted a survey to explore the reasons of non-adherence to prescribed therapy, among eye-drop users and found that a considerable number of patients were non-complaint. The cause of this high level of non-compliance was mainly due to the difficulty in its administration of the eye-drops (Winfield *et al.*, 1990) Several studies revealed that patients experience difficulty in administering intranasal dosage form (Strang *et al.*, 2016).

The awareness regarding nasal spray administration has been stressed as majority of the patients were not fully aware about correct administration techniques ultimately causing impediment in achieving targeted outcomes of therapy. Further it was found 44% of the patients could perform all the six steps of administration accurately (Loh *et al.*, 2004).

2. MATERIALS AND METHOD

This is a descriptive questionnaire-based survey study conducted in different regions of Hyderabad city.

2.1. Study Design

It is a second largest city of Sindh province in Pakistan. In this study (n=500) data was collected between January-2015 to April-2015. A total of 467 questionnaires were filled by using random sampling technique.

2.2. Exclusive Criteria

Subjects who were hospitalized, bed ridden, mentally retarded and those whose medicines were administered by others like pediatrics and geriatric were excluded from the study.

2.3. Inclusion Criteria

Both male and female patients ranging from the age groups of 18 to 60 years were selected for this study.

2.4. Data Assessment

The questionnaire comprised of two parts. The first part contained questions inquiring about demographic data and patient's knowledge about the method of administration of medicine. Questions about method of administration were structured referring (Pharmacists, 2013) In the second part respondents were questioned about their sources of drug related information.

2.5. Data Analysis

Collected data was analyzed by using IBM SPSS version 21 (Statistical package for social sciences version 21). Frequency and percentages were reported for categorical data. Chi-square test was executed to find the significant association of administrative techniques with study variables. P value < 0.05 was taken as level of significance to signify the association.

3. RESULTS AND DISCUSSION

A total of 467 patients of both genders agreed to fill the questionnaire, out of these 248 (53.1%) were males. Majority (69.6%) of the respondents belonged to age group between 18-30 years. Qualification wise distribution shows that 282 (60.4%) were educated having graduate degree education and remaining were below that educational level (Table 1).

Among the respondents 384 (82.2%) were eye drop users, 295 (63.2%) were nasal drop users and 131 (28.1%) were MDI (Metered dose inhaler) users as shown in Tables 4, 5 and 6 respectively.

Upon inquiring the method of administration it was found that patients were committing errors while administering the medicine (Tables 4, 5 and 6). Only a diminutive percent of respondents did not commit any error that is, 4.7% for eye drops, 16.9% for nasal spray and 6.9% for metered dose inhaler.

Wrong administration technique was practiced by, 64.9%, 49.5% and 36.3% MDI, eye drops and nasal spray users respectively (Tables 4, 5 and 6). Nearly half 48.55% patients contaminate their eye drop by touching the tip of the container. This can cause eye infections. As it was seen in a study conducted by William et al, where patients contaminated their eye drop bottle while using. Later patient got infected from that contaminated bottles (Templeton et al., 1982).

One of the reasons of such a high rate of errors may be the lack of drug related information. Provision of ample information about the medicine can improve patient safety and adherence (Bates et al., 2001; Ponnusankar et al., 2004).

Most of the patients (90.8%) were receiving drug related information from doctors and in our country contact time of doctor per patient is less than 2 minutes (Hafeez et al.,

2004). In such a little time duration confusions regarding the therapy remain unclear. This can lead to medication errors.

Further it was found that only 2.6% of the patients were guided by the pharmacist (Table 2). This is because of the ratio lack of pharmacists in public health services and the less number of pharmacists in the community pharmacies of Pakistan (Khan, 2009). There are several studies reporting improvement in patient's administration technique after being guided by the pharmacists (Foland et al., 2002; Giraud et al., 2011).

Upon inquiring about mode of information a noticeable dearth was found in the provision of practical demonstration about the administration of medicine, which was given to only 3.4% of patients. Further 67.9% were given drug related information in verbal mode only (Table 3). The verbal information is likely to be forgotten or misunderstood (Kessels, 2003; Tebbi, 1993).

There is no significant correlation was found between source of information and medication errors.

A correlation between administration of eye drops and mode in which medication related information received, was found. Among the patients who were given medication related information verbally only, less than half (45.2%) could administer correctly, whereas the values increased up to 67.7% with written information. When method of administration was explained practically it was found that all the patient were capable of administering their medication correctly (Table 7) (P value=.000).

4. CONCLUSION

This led us to conclude that the occurrence of medication administration errors is quite frequent. Usually the information provided is in verbal mode and few patients received practical demonstration due to lack of qualified drug

Table 1: Demographic Details of the Respondents

Parameters	Background Charactersistic	Frequency	Percentage
Gender	Male	248	53.1
	Female	219	46.9
Age in years	18 to 30	325	69.6
	31 above	142	30.4
Marital status	Single	301	64.5
	Married	166	35.5
Qualification	Degree education	282	60.4
	Below degree education	185	39.6

Table 2: Source of Information

Source	Frequency	Percentage
Doctor	424	90.8
Pharmacist	12	2.6
Friends and family	31	6.6
Total	467	100

Table 3: Mode of Information

Variable	Frequency	Percentage
Verbal	317	67.9
Written	110	23.6
Practical	16	3.4
Verbal and written	24	5.1
Total	467	100

Table 4: Eye Drops Use and Errors in Its Administration

Parameters	Performance	n	Percentage
Respondents Eye-drops users	No	83	17.8
	Yes	384	82.2
Number of correct steps in eye-drops administration out of 6 steps	0	9	2.3
	1	46	12.0
	2	121	31.5
	3	135	35.2
	4	41	10.7
	5	14	03.6
	6	18	4.7
Hand washing before administration	No	126	32.8
	Yes	258	67.2
Inspection of the dropper	No	75	19.5
	Yes	309	80.5
Touching the tip of dropper	Wrong	188	49.0
	Right	196	51.0
Position of patient during administration of eye drop	Wrong	344	89.6
	Right	40	10.4
Position of head of patient after administration	Wrong	344	89.6
	Right	40	10.4
Instillation into eye	Wrong	190	49.5
	Right	194	50.5

Number of individuals (n)

Table 5: Nasal Spray Use and Error in Its Administration

Parameters	Performance	n	Percentage
Respondents nasal spray users	No	172	36.8
	Yes	295	63.2
Number of correct steps in administering nasal spray out of 5	0	9	3.1
	1	22	7.5
	2	48	16.3
	3	76	25.8
	4	90	30.5
	5	50	16.9
Washing hands before administration	No	61	20.7
	Yes	234	79.3
Blowing nose before administration	No	113	38.3
	Yes	182	61.7
Position of patient during administration of nasal spray	Wrong	168	56.9
	Right	127	43.1
Administration technique	Wrong	107	36.3
	Right	188	63.7
Washing hands after administration	No	63	21.4
	Yes	232	78.6

Number of individuals (n)

Table 6: MDI Use and Errors in Its Administration

Parameters	Performance	n	Percentage
Respondents of inhalers	No	336	71.9
	Yes	131	28.1
Number of correct steps in administering inhaler out of 7 steps	0	2	1.5
	1	0	0.0
	2	6	4.6
	3	19	14.5
	4	42	32.1
	5	34	26.0
	6	19	14.5
	7	9	6.9
Washing hands before administration	No	36	27.5
	Yes	95	72.5
Shaking inhaler before use	No	2	1.5
	Yes	129	98.5
Breathe out	No	81	61.8
	Yes	50	38.2
Position of patient during administration of inhaler	Wrong	38	29.0
	Right	93	71.0
Administration technique	Wrong	85	64.9
	Right	46	35.1
Rinsing mouth after administration	No	61	46.6
	Yes	70	53.4
Gap between two puffs	Wrong	30	22.9
	Right	101	77.1

Number of individuals (n)

Table 7: Correlation Between Mode of Information and Error in Its Administration

Instillation into eye	Mode of information n			Total
	Verbal	Written	Practical	
Wrong	44 (54.8)	31 (32.3)	0 (0)	190 (49.5)
Right	119 (45.2)	65 (67.7)	7 (100)	194 (50.5)
Total	263 (100.0)	96 (100.0)	7 (100)	384 (100.0)

Values within parenthesis are percentages.

expert. Therefore it is suggested that efforts should be made to assure availability of pharmacists at pharmacies for the consultation guidelines and benefit of patients and minimization of administration and other medication errors. Secondly, the drug information provided to the patients should be supported with written guidelines. It is suggested that the health care providers should assure patient's understanding about the therapy.

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Pharmacognostic Studies on Different Morphological Parts of *Cissus quadrangularis* L.

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Abstract

Standardization and authentication of medicinal plants is of great importance for the prevention of adulteration substitution and safe therapeutic use. Although there are many advanced techniques for identification of medicinal plants but pharmacognostic evaluation (including sensory and physico-chemical characteristics) is still considered as a reliable tool. Pharmacognostical parameters are not only necessary for the identification and confirmation but also helpful to estimate the quality and safety of plant drug materials. In present investigation we performed detailed pharmacognostic evaluation of different morphological parts i.e. Stem, leaf, root and tendril of medicinal plant *Cissus quadrangularis* L. which is recently gaining popularity as a good therapeutic agent in Unani prescriptions and important raw material in pharmaceutical manufacturing against musculoskeletal diseases, as powder microscopy, histology, organoleptic evaluation, physico-chemical testing and fluorescence analysis that

will be helpful to establish the standard protocol according to USP/BP/WHO guidelines respectively.

Keywords

Cissus quadrangularis L., Pharmacognostic, Fluorescence analysis, Physico-chemical testing.

1. INTRODUCTION

Man found many of his needs from Plants including shelter, clothing, food, flavors and Fragrances. Most of important life saving and therapeutic drugs in use today are plant derived. Ancient people realized importance of herbal medicines and found cure from mother nature for their illness (Ashur, 1986). Hence, medicinal plants have been used for so many years for cure and treatment of most of diseases in routine all over the world (Anely *et al.*, 2007). Despite of the advancements and success of synthetic chemistry and progress towards rational drug design, Natural sources are still significant in contribution of provision of medicinally important compounds and also

provide lead compounds for successful designing and development of synthetic analogues. Therefore now it is highly required from researchers and clinicians to collaborate and extract the main active principles from medicinal plants and to study how they can be utilized in the synthesis and production of better effective drugs and also to address their roles in the prevention and cure of present day diseases (Rasool Hassan, 2012).

Cissus quadrangularis L. (*Vitis quadrangularis*) (see Fig. and Error! Reference source not found.) belongs to the family Vitaceae is a succulent plant. It is found in Pakistan, Bangladesh, Srilanka, Malaysia and throughout warmer parts of India. It is commonly known as “Bone setter” and “Edible stemmed Vine”. It is also called as Asthisamhara, Hadjod, Hadjora, Hadbhanga, Vedhari, Vajravalli, Kandvel, Perandai, Nalleru and Veldgrap in different Indian languages (Anitha and Suji, 2012). The plant resembles the shape of joints and bones in the human body and it is very effective in strengthening them. It is also known to have rich amounts of calcium, phosphorus and other leading mineral and vitamin contents along with mucilage. The whole plant is utilized in treatment of sprains, fractures, rheumatism,

dislocation of hip, in complains of back and spine, irregular growth of teeth, hematuria, anthrax, elephantiasis, wounds and cracked tails. Other plant parts such as stem and leaves are used as anthelmintic, dyspeptic, alterative, digestive, analgesic in ear and eye problems, irregular menstruation and in asthma (Ruskin *et al.*, 2014). The study was aimed to evaluate different pharmacognostic features to proper identification, confirmation and determination of purity and quality of this standards crude drug as reliable therapeutic agent.

2. MATERIALS AND METHOD

2.1. Plant Material

Fresh plant was collected from the premises of University of Karachi, Pakistan prior to the identification and authentication by Prof. Dr. Surriya Khatoon, Department of Botany, University of Karachi. A voucher specimen (No. 0101) (a-d) of plant was deposited in herbarium of the Botany Department and Herbal Meuseum, Department of Pharmacognosy, Faculty of Pharmacy(voucher specimen No.010a-d), University of Karachi, Pakistan. Leaves, roots, stems, tendrils of plant were separated, cleaned, washed with distilled water, dried under shade and weighed.



Fig. 1a



Fig. 1b

2.2. Macroscopic Evaluation

Macro morphological characteristics of *Cissus quadrangularis* L. were studied by sensory testing (Gowda *et al.*, 2009).

2.3. Histological Evaluation

Cellular sequences in transverse sections of root, stem, leaf and tendrils respectively were examined by preparing permanent slides according to the procedure of staining and glutening followed by complete histological examination and evaluation under electronic microscope via characterization of primary and secondary cellular arrangements distinguished by Safranin and Malachite green dye along with their prominently embedded ergastic cell contents (Brain and Turner, 1975).

2.4. Microscopy of Pulverized Samples

Separately dried leaves and stems of plant were ground in electric grinder to acquire each morphological part properly in pulverized form.

2.5. Fluorescence Analysis

Dried stem powdered material (1 pinch) was taken in different test tubes containing different reagents like aqueous sodium hydroxide, hydrochloric acid, sulphuric acid (50%), methanol, Iodine, Nitric acid (50%) and ammonia, Sodium hydroxide and methanol, ferric chloride (5%), and acetic acid. These solutions were observed for their characteristic color reaction under normal day light and short UV (256 nm) and long UV (366 nm) respectively.

2.6. Physico-chemical Testing

Total ash value and moisture content of powdered aerial parts of plant were determined.

2.7. Moisture Content

Loss of weight on drying (Moisture content) of powdered aerial parts was evaluated by placing silica crucible containing powdered

sample (1 g) in oven at 105°C until constant weight obtained.

$$\text{Moisture content (\%)} = \frac{\text{Loss in weight of sample}}{\text{Weight of sample} \times 100}$$

2.8. Total Ash Value

Powdered sample (3 g) in silica crucible was weighed and burnt till red hot to make sample carbon free and then flame was increased gradually until constant value was obtained.

$$\text{Total ash value (\%)} = \frac{\text{Weight of total Ash}}{\text{Weight of sample} \times 100}$$

3. RESULTS AND DISCUSSION

For correct identification and authentication of medically important plants preparation of monographs, standardization of plants; pharmacognostic studies are required as mentioned earlier. These pharmacognostic studies also help to detect substituents and adulterants in order to ensure the quality, efficacy and reproducibility of natural drugs. Results of moisture content indicates meagre chances of microbial growth and microbial degradation of crude drug during storage because in presence of excess moisture some of constituents may undergo degradation due to enzymatic activity and this breakdown encourage microbial growth in the crude drug during storage. Total ash value was calculated as 12.51% which indicates that plant possess normal complexes of organic and inorganic components within the acceptable range 22% (*British Pharmacopoeia*, 1980).

3.1. Macroscopic evaluation:

The stems were quadrangular, green colored, with pungent odor and caustic taste. Stems of different lengths ranges from 0.5-2 cm thick, containing internodes (3-16 cm) which were compressed at nodes. Leaves were lobbed

or simple and dentate. Fruiting and flowering period is May-June. Organoleptic features are depicted in Table 1.

Table 1: Organoleptic Features of *Cissus quadrangularis* L.

Organoleptic features	Observations
Color	Green
Odor	Pungent
Taste	Caustic
Appearance	Rough

3.2. Histological Evaluation

Stem

Stem has thick and long four wings, this four angled stem upon maturation forms sharp pointed projections at each angle. Transverse section of stem showed four long and thick wings, each wing is about 1.4 mm thick and 5.8 mm long while central part of stem was 1.8 mm thick. It contains Epidermal coating of Epidermis (Ep), Pith (Pt), externally covered with thick cuticle. Epidermal cells are circular, thick walled and tangentially elongated (Fig. 2a). Ground tissues are circular thin walled and compact parenchymatous. Epidermis is followed by cork than 8-16 layer of thin walled, circular to oval collenchymatous cells (Co) in angular

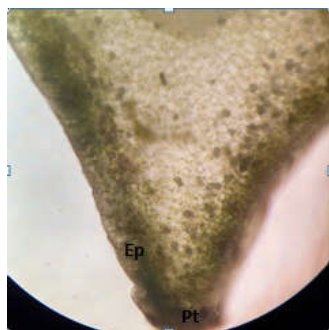


Fig. 2a: Transverse section of pointed projection of stem showing Epidermis (Ep) and Pith (Pt)

points that are embedded over vascular bundles (Vb). These vascular bundles are collateral, conjoint and of variable size also radially stretched and in each wing three vascular bundles are present, each of them is shielded with sclerenchymatous (Sc) sheath. Phloem (Ph) cells present around circular, wide, angular and thin walled xylem (Xy) which itself surrounded by thin walled fibers of xylem. Distinct cambium and interfascicular cambium and large central Pith (Pt) is present (Fig. 2b).

Acicular calcium oxalate crystals are present throughout this portion.

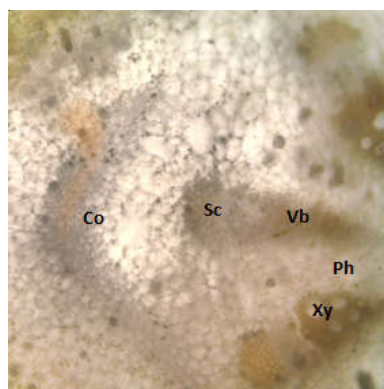


Fig. 2b: Transverse section of stem focusing Vascular bundles, Collenchyma cells (Co), Sclerenchyma (Sc), Vascular bundle (Vb), Phloem (Ph), Xylem (Xy)

Leaf

Thick walled, small and square shaped epidermal cells were found in midrib while ground tissues present were small, circular, thick walled and compact. Three vascular bundles were present from which one vascular strand was smaller and present on abaxial side. Phloem was located on outer end of xylem segment. xylem cells were narrow, circular and thick walled. Raphides are dispersed in spongy mesophyll tissue in lamina.

Transverse section of leaf through mid rib shows Epidermal cells (Ep), Vascular

bundle (Vb), Phloem (Ph), Xylem (Xy) and Ground tissues (Gt) (Fig. 3).



Fig. 3: Transverse section of leaf through Epidermal cells (Ep), Vascular bundle (Vb), Phloem (Ph), Xylem (Xy), and Ground tissues (Gt)

Root

Transverse section of secondary root is circular while main root is rectangular. Periderm of rectangular shape and multi layered cortex was present. Calcium and tannins deposited cells were distributed through main root with large portion of pith and almost three medullary rays at each corner while in secondary root these medullary rays were present with regular gaps

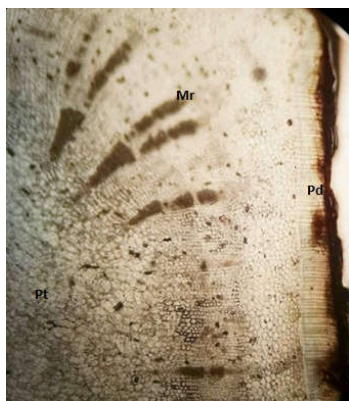


Fig. 4a: Transverse section of main root showing: Medullary rays (Mr), Periderm (Pd)

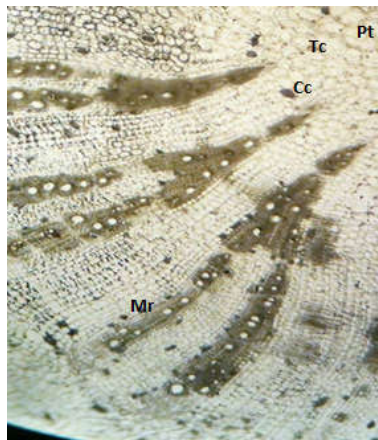


Fig. 4b: Medullary rays showing calcium containing cells (Cc), Tannins containing cells (Tc), Pith (Pt)

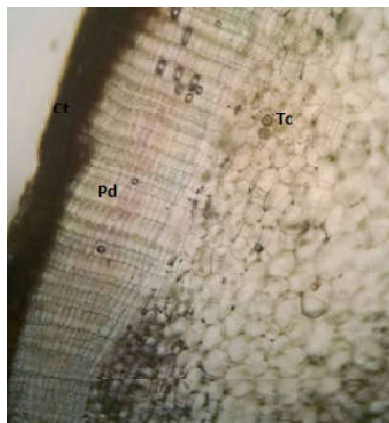


Fig. 4c: Periderm showing Cork tissues (Ct), Periderm (Pd), Tannins containing cells (Tc)

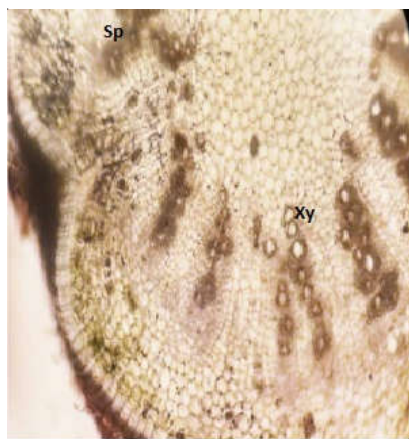


Fig. 4d: Secondary root showing Secondary phloem (Sp), Secondary Xylem (Xy)

Tendrils

Transverse section of tendril of *C. quadrangularis* L. demonstrate radial vascular bundles (13), Xylem, Phloem, hexagonal cells of Pith, mature epidermal cells and collenchyma cells in cortical region (Fig. 5).

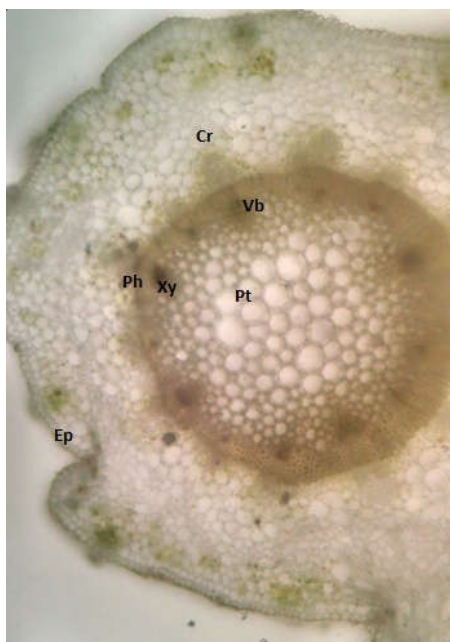


Fig. 5: Transverse section of Tendril, Epidermal cells (Ep), Cortical region (Cr), Radial vascular bundle (Vb), Phloem (Ph), Xylem (Xy), Pith (Pt)



Fig 6a: Fibers sheet



Fig 6b: Acicular calcium oxalate crystals

3.3. Microscopy of Pulverized Samples

The microscopic studies of various parts of pulverized samples of stems and leaves are described below:

Stem

Different types of calcium oxalate crystals, Epidermal cells, anisocytic stomata, parenchyma cells with mucilage, spiral xylem element, narrow vessel elements with seriated horizontally elliptical lateral wall pits and also partly scalariform pits are revealed from microscopic studies of *C. quadrangularis* L. powder (Figs. 6a, b, c, d, e, f and g).

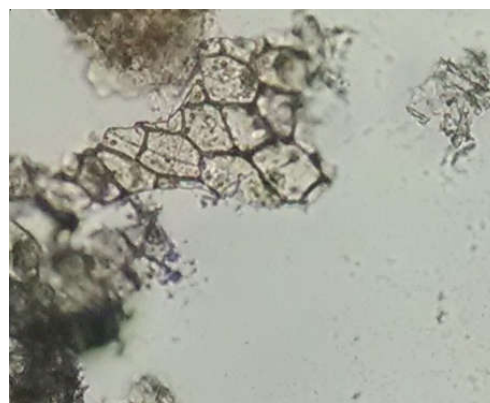


Fig 6c: Mucilage containing mesoderm



Fig 6d: Cells with calcium and other mineral deposition

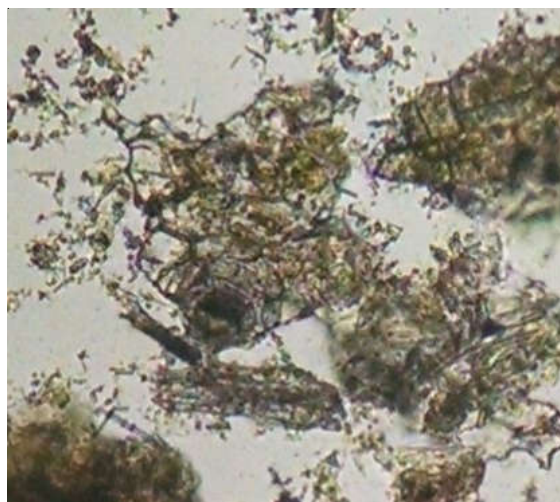


Fig 6g: Epidermal cells with anisocytic stomata

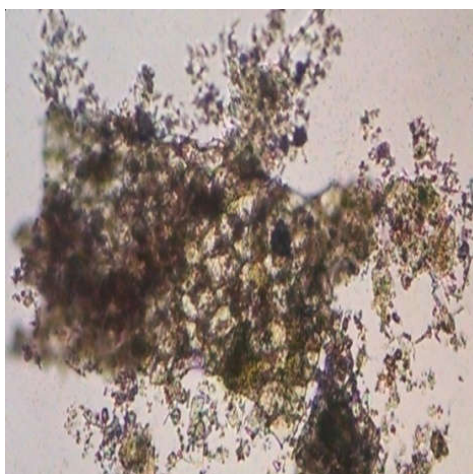


Fig 6e: Cells of mucilage in scleranchyma



Fig 6f: Sclerides with tannins deposition



Fig. 7a: Xylem vessel

Leaf

Microscopic studies of powdered leaf of *C. quadgrangularis* L. showed presence of numerous of acicular calcium oxalate crystals, raphides of calcium oxalate crystals, lignified xylem vessels and phloem fibers (Fig. 7a, b, and c).

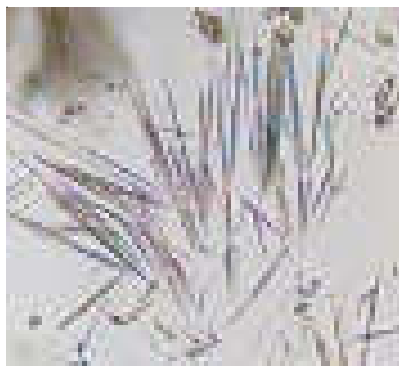


Fig. 7b: Acicular calcium oxalate



Fig. 7c: Group of phloem fibers

Fluorescence Analysis

Fluorescence analysis of powder of stems of *Cissus quadrangularis* L. revealed different colors after reaction with various solvents and then the powder was observed under day light and UV (254nm and 366nm). The observations are given in Table 2.

3.5. Physico-chemical Testing

Physico-chemical examination is prime

factor in determination of quality, adulteration and substitution in crude drug. Total ash value and moisture content of *C. quadrangularis* L. was 12.5 and 3.5 respectively.

4. CONCLUSION

Natural medicines have been the basis of prevention, treatment and control of most of human diseases. Nature always proves itself the best illustration to the great phenomenon of

Table 2: Fluorescence Analysis of Stem of *C. quadrangularis* L.

Solvents	Visible (400 nm)	Short Ultra violet (254nm)	Long Ultra violet (366nm)
Distilled water	Whitish yellow	Pale yellow	Light green
Methanol (98%)	Fluorescent green	Colorless	Pale brown
Hydrochloric acid (10%)	Light brown	Green	Deep brown
Sulphuric acid (50%)	Blackish green	Dark green	Reddish brown
Ferric chloride (5%)	Pale green	Green	Black
Aqueous sodium hydroxide	Light green	Brown	Pale brown
Nitric acid (50%) + Ammonia	Pale green	Yellowish green	Pale brown
Acetic acid	Pale green	Yellowish green	Pale brown
NaOH + Methanol (1:1)	Fluorescent green	Pale yellow	Yellowish brown
Iodine	Brown	Greenish brown	Black

symbiosis. In recent era our interest are rushing towards the use of natural medications as the undesirable outcomes of modern medicine are unfolding. Herbal drugs use is now getting popular all over the world not only as home remedies and as over the counter drugs but also as raw material in manufacturing number of pharmaceutical products in pharmaceutical industries, and it occupies a significant share in global drug market. Thus the prime responsibility of the regulatory authorities to satisfy consumers with guaranteed safety, purity, efficacy and potency of natural drugs. *C. quadrangularis* L. is an ornamental plant available in the market for safe use against musculo-skeletal disease as well as for development of body mass and body building in physical fitness and health centres. Present research work includes fluorescent and physico-chemical analysis and complete pharmacognostic studies of each morphological part of the plant will be helpful in the right identification. This kind of research will not only be helpful to ensure correct identification, detection of adulterants and setting of standard parameters to ensure reproducible quality of herbal drug material which will also further lead to efficacy and safety of herbal drug. Although plant is being used in India for edible purpose and our preliminary toxicological findings also prove this as a safe drug material.

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