



AZARAQI (*STRYCHNOS NUXVOMICA* L.): A NOVEL DRUG OF UNANI SYSTEM OF MEDICINE FOR THE MANAGEMENT OF NERVE AND PHLEGMATIC DISEASES

Mohd. Afsahul Kalam^{*1}, Aieman Yaqoob², Bazilah Majeed² and Ansar Ahmad³

¹Research Officer (Unani) & Lecturer Department of Ilmul Advia (Pharmacology Unani), Regional Research Institute of Unani Medicine, Habak, Naseem Bagh Campus, Hazratbal, Srinagar, J&K. 190006.

²PG Scholar Department of Ilmul Advia (M.D Pharmacology Unani), Regional Research Institute of Unani Medicine, Habak, Naseem Bagh Campus, Hazratbal, Srinagar, J&K. 190006.

³Professor Department of Ilmul Advia, Regional Research Institute of Unani Medicine, Habak, Naseem Bagh Campus, Hazratbal, Srinagar, J&K. 190006.

Corresponding Author: Mohd. Afsahul Kalam

Research Officer (Unani) & Lecturer Department of Ilmul Advia (Pharmacology Unani), Regional Research Institute of Unani Medicine, Habak, Naseem Bagh Campus, Hazratbal, Srinagar, J&K. 190006.

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ABSTRACT

Azaraqi is well known drug of Unani System of Medicine, obtained from the dried, ripe seed of *Strychnos nuxvomica* L. belonging to the family Loganiaceae. It is a small tree 12 meters tall widely distributed in India and also occurring in Ceylon, Syria, and Northern Australia. *Azaraqi* is well known for its anti-phlegmatic effect, nerve tonic and stimulant properties which makes it an important drug in treatment of insomnia, hysteria, epilepsy, paralysis, hemiplegia, arthritis, nocturnal incontinence of urine, emphysema, impotence, etc. These actions are attributed to hot temperament and bioactive compounds like strychnine and brucine present in its seeds. The seeds are used in various forms either alone or in compound formulations like powder, pills, *ma'jun* etc. Many pharmacological studies have been done on *Azaraqi* which include antidiabetic, anticonvulsant and analgesic properties. The chemical extracts of *nuxvomica* are interesting pharmacologically and is a valuable tool in physiological and neuroanatomic research. It is highly toxic, therefore used after detoxification.

KEYWORDS: *Strychnos nuxvomica* L., *Azaraqi*, *Muqawwi A'sab*, *Muharrrik A'sab*, Hemiplegia, nerve tonic.

INTRODUCTION

Unani System of Medicine is the ancient system of medicine introduced in India during 8th century and it got developed as an inclusive medical system because of its original contribution and new applications by the renowned learned persons of successive procreations. Unani Tib is based on doctrine of Buqrat (460-360BC) which includes dogma of four bodily fluids viz. *Dam*, *Safra*, *Balgham* and *Sawda*.^[1]

Unani Tib has sheer heterogeneity of plot of substantial medicinal herbs. Maximum portion of its medicinal source is derived from plants. *Azaraqi* or *Kuchla* (*Strychnos nuxvomica*) is one of the most popular drug used by Unani physicians. It was not medicinally used in ancient Greek and Ayurveda, but introduced first by Arab physicians in Unani System of Medicine.^[2,3] *Strychnos* is the Greek name for a number of poisonous plants; *Nuxvomica* is formed by two Latin words *Nux* and *Vomica* which means, a nut that causes vomiting.^[2,3] The Arabic name *Qatil al-Kalb* (*Qatil*=killer; *Kalb*=dog) and *Khaniq al-Kalb* (*Khaniq*=asphyxiate; *Kalb*=dog) stand for its seeds which are used to kill dogs that is why

it is also known as dog poison. Due to its killing property of crows it is called as *Habbul Ghurab* (*Habb*=seeds; *Ghurab*=crow). The characteristic features of its seeds like the fins of fish, it is also called *Fils-i-Mahi* (*Fils*=fins; *Mahi*=fish). *Azaraqi* is the ripe, dried seed of *Strychnos nuxvomica* L. and well known in Unani System of Medicine for its beneficial effect on various ailments related to brain and nerves. *Strychnos nuxvomica* L. plant is a small tree about 40 ft tall (see Fig. 1 a) that is endemic to East India and is also found in the forests of Srilanka, on the Malabar Coast and in Northern Australia. The fruit is a berry having 3-5 seeds (see Fig. 1 b, c, d) that are very hard and difficult to cut.^[2] They are freed from the bitter pulp by washing before exportation. The diameter of the seed is about 1 inch and thickness ¼ inch; shape like umbilicus; surface has tiny shiny, silky, hairy structures; inner part white; taste bitter and has no smell. The seeds are used medicinally, which possess *Mushtahi* (appetizer), *Muqawwi* (tonic), *Qabid Am'a* (astringent to bowels), *Dafi'-i-humma* (antipyretic) properties. The leaves when applied as poultice promote healthy action in sloughing wounds or ulcers, more especially in cases where

maggots are formed. Small doses of seeds are given with aromatics in colics. Wood is used as a popular remedy for dysentery, fevers and dyspepsia.^[2] Indian *Nuxvomica* seed contains 2.6-3% total alkaloids of which 1.25-1.5% is strychnine; 1.7% brucine and vomicine. Several of the *Strychnos* varieties furnish hunters with "curare", an extremely dangerous arrow poison.^[4] Studies have shown that the alkaloids present in *Azaraqī* occur in the large thick walled cells of the endosperm, but strychnine is concentrated in the cells near the centre of the seed and brucine in the outer cells near the epidermis. *Nuxvomica* is one of the ingredient of so many Unani compound formulation like *Ma'jun-i-Azaraqī*, *Ma'jun Lana*, *Habb-i-Azaraqī*, *Habb-i-Khas*, *Habb-i-Fawladi* those are used to treat many ailments like facial palsy, hemiplegia, gout, arthritis etc.^[5] The aqueous extract of drug exhibits significant cardio-tonic activity and is used in treatment of cardiovascular diseases.^[6] One more species *Strychnos ignatii* is used as *Papita vilayati* in Unani medicine for epidemic diseases especially cholera, and it has more quantity of strychnine than in *Azaraqī*.^[2,7]

MATERIAL METHOD

Relevant literature regarding *Strychnos nuxvomica* was retrieved from databases like Web of Science, Google Scholar, Researchgate, Baidu Scholar, Springer, PubMed, SciFinder, and Science Direct. Information was also collected from classic books of Unani medicine, like, *Khazainul Advia*, *Muheet-i-Azam*, *Makhzanul Mufradat*, National Formulary of Unani Medicine and unpublished materials and papers on *Strychnos nuxvomica*. The images of tree and its various parts are taken from the herbal garden of National Research Institute of Unani Medicine for Skin Disorder (NRIUM-SD), Hyderabad.

OBSERVATIONS

Mutaradifat (Vernacular Names)

Arabic: Khaniq al-Kalb, Habbul Ghurab, Qatil al-Kalb (2); *Bengali*: Kuchila,^[8] *Chinese*: Fan Mu Pich, Ma ta'ien tse; *Cannada*: Kasarkana Mara,^[4] *English*: *Nuxvomica* or strychnine tree, Quaker Button,^[4] Snake Wood, Poison Nut,^[9] Bachelors Button, Dog Buttons, Vomit Nut (2), Crow Fig, Semina strychni,^[3] *Gujarati*: Gajra,^[8] *Hindi*: Kajra,^[8] Kuchla,^[10] *Kashmiri*: Zaher beol,^[11] *Persian*: Fals-i-Mahi,^[2] *Sanskrit*: Kupilu, Kulaka, Vishamushti, Vishtindulca, Kaakatinduka, Kaakendu, Kaakapiluka, Vishamushtikaa, Vishatinka, Kuchilla, Ksachalaa,^[4,7,10] *Siddha*: Ettikottai,^[7] *Syrian*: *Azaraqī*,^[2] Others: Sleng thom, Kanjira, Kasarka, Brechnuss, Nanji-nakoradu, Krachenaugen, *Strychnoszaad*

Jae Waqu' (Distribution)

The tree is wild and plentiful throughout tropical India, commonly in the jungles about Manbhoom, in the Madras Presidency, Malabar and Coromandal Coasts, Cochin, Travancore, Southern India, Orissa.^[4] It is also

found in Ceylon, Asia, Malaysia, Jazira-Gharabul Hind and China.^[12]

Botanical Discription

Nuxvomica is a deciduous tree up to 15 meter tall, often with short, strong, axillary spines. Leaves are elliptic, orbicular and coriaceous. The flowers are greenish white, fragrant, in terminal compound cymes. Fruit a globose berry, thin shelled, orange when ripe, slightly rough but shining.^[9] The seeds are disc shaped, 20-25 mm long and the radicle 4mm. The seeds are almost colourless. The endosperm is composed of a thick walled cellulosic parenchyma.^[12]

Taxonomical Classification

Kingdom:	Plantae
Subkingdom:	Tracheobionta
Superdivision:	Spermatophyta
Division:	Magnoliophyta
Class:	Magnoliopsida
Order:	Gentianales
Family:	Loganiaceae
Genus:	<i>Strychnos</i>
Species:	<i>nuxvomica</i>

AJZA-I-MUSTA'MILA (PARTS USED)

Dried ripe seeds are used medicinally^[2]

MIZAJ (TEMPERAMENT)

It is dry in 2nd degree and hot in 3rd degree^[2]

AF'AL (ACTIONS)

Seeds are *Muhallil* (anti-inflammatory), *Musakkin-i-alam* (anodyne), *Mushil* (purgative), *Munaffith wa Mukhrij balgham* (expellant of phlegmatic matter), *Muqawwi-i-Bah* (aphrodisiac), *Musaffi-i-Khoon* (blood purifier), *Dafi'-i-Amrad 'Asbaniya* (useful in nerve disorders),^[8] *Muqawwi-i-A'sab* (nervine tonic), *Muharrik-i-A'sab* (nervine stimulant)^[13] *Dafi'-i-Ta'affun* (antiseptic), *Musakkin-i-Alam* (analgesic).^[14] It is also used as *Mudirr-i-Bawl* (diuretic), *Mudirr-i-Hayd* (emmenagogue), *Mufattit-i-Hasa* (lithotriptic) etc.^[2]

ISTE'MALAT (THERAPEUTIC USES)

In Unani System of Medicine, the seeds of *Azaraqī* are used after detoxification for the treatment of various ailments related to phlegmatic and nerve diseases viz; *Falij* (hemiplegia), *Laqwa* (bell's palsy), *Ra'sha* (tremor), *Iraq al-Nasa* (sciatica), *Istirkha-i-Mathana* (flaccidity of urinary bladder) and also for *Waja'al-mafasil* (arthralgia), *Dard-i-Kamar* (backache), *Du'f-i-Bah* (sexual impotence), *Du'f-i-Ishtiha* (loss of appetite), *Surfa* (cough), *Diq al-Nafas* (asthma), *Sil wa Diq* (tuberculosis), *Ta'un* (plague), *Kalaf* (melasma), *Bawasir* (haemorrhoids), *Ajzul Qalb* (bradycardia), *Ikhtilaj-i-Qalb* (palpitation due to cold), and diseases produced due to the *Fasad al-Dam* (impurity of blood) like, *Jarab* (scabies), *Dad* (ringworm) etc.^[2,8]

Tarkeeb Iste'mal (Method of Administration): Diseases of Head, Brain and Neck

Detoxified or purified seeds of *Azaraqī* 5 gm and sugar 125 gm are finely scuffed into fine powder and 75-250 mg along with *Momiya'i* is taken for the treatment of various diseases mentioned above.^[15] Due to its *Muqawwi-i-A'sab* (nerve tonic) and *Muharrrik-i-A'sab* (nerve stimulant) properties, it is used for the treatment of *Falij* (hemiplegia), *Laqwa* (bell's palsy), *Ra'sha* (chorea) etc. Some method of administration of the drug in various diseases are mentioned as follows:

In cases of unconsciousness and syncope occur due to Cholera, *Azaraqī* seeds rubbed along with *Arq-i-Gulab* (rose water), is licked accordingly.^[15]

Joint Disorders

Kuchla burnt in *Roghan Kunjad* is used as a massage to cure *Waja 'al Mafasil* (arthralgia).^[8]

To cure chronic arthralgia, it is used with *Arq-i-Ushba*.^[2]

In cases of arthralgia and neuralgia its paste along with *Sonth* (*Zingiber officinale*) and *Qarnul Aiyiyil* (stag horn) is applies locally.^[2]

Diseases of GIT

Irritable Bowel Syndrome: 125 mg powder of its detoxified seeds are taken with PAN to cure Irritable Bowel Syndrome and diarrhoea.^[2]

Abdominal pain: *Azaraqī* is taken with *Jaefal* and *Jawitri* (*Myristica fragrance*) to subside gastric pain.^[2]

Haemorrhoids: A paste of its seeds made with water is applied on haemorrhoids; it provides relief.^[15] Fumigation of its seeds on haemorrhoid is also very useful to stop the pain and bleeding.^[2]

Communicable diseases

In cases of *Ta'un* (plague) *Azaraqī* is used in the form of *Tila'*.^[8] In cholera it is used to lick after rubbing with *Arq-i-Gulab* (rose water).

Pills made with its bark powder in lemon juice is useful for the treatment of Cholera.^[2]

Skin Diseases

Paste of its seeds is applied to cure skin ailment such as *Kalaf* (melasma), low complexion of face, scabies, ringworm etc.^[2]

Poisonous bites

Its root is used orally to remove the toxicity that occurs due to snakebite.^[2]

Its paste is useful when applied on rat bite.^[2]

MIQDAR-I-KHURAK (DOSAGE)

The dose of its powder is 1\2-2 Ratti (1Ratti=125mg)^[8] or in quantity of 1 *Masha*/gm with proper correctives, as mentioned by Unani physicians.^[2]

Mazarrat (Toxicity and adverse Effects)

Toxic dose of *Azaraqī* initially cause backache and pain in limbs, temperature rises gradually. After sometime sweating, fatigue, shortness of breath and severe convulsions followed by bluish discolouration of face, bulging of eyes and feeling of fear. The specific feature of its toxicity is the paralysis of jaw muscles and *Risus sardonicus*.^[8,16]

DETOXIFICATION OF AZARAQI

Azaraqī being highly toxic, is first purified, then used. The way to purify is as: *Azaraqī* is placed in milk or water, milk is more preferred, for a week to moisten it. Once *Azaraqī* softens its covering is peeled off and discarded. The remaining part is then dried and converted to powder form called *Burada Kuchla*. This powder is placed in a thick cloth and tied. An earthen pot filled with milk is taken and the *Burada Kuchla* filled cloth is placed in that pot and cooked for some time. The leftover milk is discarded and *Kuchla* become purified by this way.^[8]

MUSLEH (CORRECTIVES)

Beekh Chaulayi (*Amaranthus* root),^[17] *Post Darakht Akol*,^[17] *Samar-i-Jamun* (*Eugenia jambulana* fruit),^[17] *Shira Gul-i-Kewda* (*Pandanus tinctorius*)^[17] are used as correctives for *Azaraqī* seeds. *Roganiyat* (oils), *Nabat-i-Safed* (sugar), *Ghee*, *Advia Mashmuma* (aromatic drugs) may also be given for the correction of its toxicity.^[18]

BADAL (SUBSTITUTE)

Bhalawan or *Baladur* (*Semicarpus anacardium* fruit) is used as substitute for the above mentioned diseases especially for phlegmatic (cold) and cerebral disorders.^[18]

Murakabat (Compound Formulations)**Table 1: Compound formulations of drug, their dosage, method of administration and indications.**

S.N.	Name of Compound	Dose & Method of Administration	Indications
01.	<i>Dawa-i-Azaraqi</i>	-	Hemiplegia, Bell's palsy Tremor. ^[5]
02.	<i>Dawa-i-Dipty Saheb</i>	125-250 mg with 10 gm butter	Gonorrhoea ^[19]
03.	<i>Habb-i-Azaraqi</i>	1 pill with <i>Arq Badyan</i> and <i>Arq Gaozuban</i> each 72 ml or <i>Arq Ajwain</i> and <i>Arq Sa'tar</i> each 120 ml	Cold diseases like, Nerve weakness, Neuralgia, Arthritis, Gout ^[5]
04.	<i>Habb-i-Fawladi</i>	1 pill kept in 6gm of <i>Khamira Gaozuban Ambari</i> is used orally	Cough, Cold,, Nervine tonic ^[19]
05.	<i>Habb-i-Khas</i>	1 pill OD with 25 ml milk	Appetizer, Cardiac tonic, Brain tonic ^[19]
06.	<i>Habb-i-Kuchla</i>	250mg	Nerve weakness Acute and chronic cold and catarrh, Bell's palsy, Hemiplegia ^[20]
07.	<i>Habb-i-Marwaridi</i>	1 BD with 250 ml milk	Leucorrhoea, General tonic ^[19]
08.	<i>Habb-i-Papita Vilayati</i>	250-500mg	Indigestion, Cholera, Loss of appetite ^[21]
09.	<i>Iksir-i-Azaraqi</i>	2-4 gm BD, Orally	Hemiplegia, Flaccidity of Urinary Bladder ^[22]
10.	<i>Ma'jun Azaraqi</i>	3 gm BD, Orally	Leprosy, Sciatica, Bell's palsy Hemiplegia, Gout, Tremors ^[2,22]
11.	<i>Ma'jun Lana</i>	3-5 gm, with <i>Arq-i-Badiyan</i> 125 ml BD, Orally	Hemiplegia, Bell's palsy, Tremor, epilepsy, Arthritis ^[21]
12.	<i>Roghan Azaraqi</i>	To be applied on the affected part	Rheumatic affection ^[2]
13.	<i>Roghan Kuchla</i>	To be shampooed on head and poured into ear and nose	Analgesic, Earache ^[19]
14.	<i>Roghan Surkh</i>	To be applied on the affected part and used as a poultice	Bell's Palsy, Gout, Gonagra, Podagra, Omagra ^[19]

Scientific Studies**Bioactive compounds**

There are 2.6-3% total alkaloids of which 1.25-1.5% is strychnine, 1.7% brucine. Vomicine, loganine, igasurine or impure brucine in combination with igasurine or strychnine acid are also present in small quantities. Another new alkaloid 3-methoxyicajine is synthesised from vomicine. bisnordihydrotoxiciferine, 11-methoxydiaboline and condensamine are isolated from rootbark of southern Vietnam.^[3,4,23]

Up to the present day, many chemical compounds including alkaloids, iridoid glycosides, flavonoid

glycosides, triterpenoids, steroids and organic acids, among others have been isolated and identified from *Strychnos nuxvomica*. There is also presence of protein, yellow colouring matter, a concrete oil or fat, gum, starch, sugars, wax, earthly phosphates and ash. Of these, the alkaloids are the principal chemical compounds in this plant with major bioactive and principal toxic compounds, Strychnine and Brucine. Brucine is present in wood, bark and leaves. A new alkaloid 15-hydroxystrychnine has been isolated from seed. Some of the chemical constituents of the plant are as below in Table-02.^[24]

Table 02: Showing chemical compounds, source part of the plant and chemical formula.

CHEMICAL COMPOUNDS	PART OF PLANT	CHEMICAL FORMULA
Strychnine	Processed seed	C ₂₁ H ₂₂ N ₂ O ₂
Brucine	Processed Seed	C ₂₃ H ₂₆ N ₂ O ₄
Pseudo strychnine	Processed Seed	C ₂₁ H ₂₂ N ₂ O ₃
Vomicine	Processed Seed	C ₂₂ H ₂₄ N ₂ O ₄
Icajine	Seed	C ₂₂ H ₂₄ N ₂ O ₃
Isostrychnine	Seeds	C ₂₁ H ₂₂ N ₂ O ₂
Isobrucine	Seeds	C ₂₃ H ₂₆ N ₂ O ₄
Stryvomitine	Seeds	C ₂₂ H ₂₂ N ₂ O ₃
Novacine	Seeds	C ₂₄ H ₂₈ N ₂ O ₅
5-Oxobrucine	Seeds	C ₂₃ H ₂₄ N ₂ O ₅

Strychnine-N-Oxide	Seeds	$C_{21}H_{22}N_2O_3$
Pseudobrucine	Processed Seeds	$C_{23}H_{26}N_2O_5$
15-Hydroxystrychnine	Seeds	$C_{21}H_{22}N_2O_3$
11-Hydroxyl-Icajine	Seeds	$C_{22}H_{24}N_2O_4$
Deoxy-isostrychnine chloromethochloride	Seeds	$C_{22}H_{24}ClN_2O$

Pharmacological Studies

Preliminary Studies on *Azaraqi* have shown it to be effective as:

Anti-diabetic

Hydro alcoholic, and aqueous extracts of *Strychnos nuxvomica* seed were evaluated for antidiabetic activity in alloxan induced diabetic rats, gliclazide as standard. The study suggested that *Strychnos nuxvomica* has anti-hyperglycaemic activity in experimental animals.^[25]



Fig. Showing tree (a); leaves and fruits (b, c); removing seeds from fruit (d); size of seed (e).

Anti-oxidant and Anti-bacterial

Mohesh et al. (2015) studied the anti-bacterial and anti-oxidant activity of *Strychnos nuxvomica* flower extract. The Methnolic extract of *Strychnos nuxvomica* flowers showed that the plant was able to inhibit all the microorganisms chosen, however its effects were higher with *Candida albicans* and *Klebsilla pneumonia* with chloramphenicol (10ug/ml) as the standard drug of choice. Further this study showed that the flowers of this plant can be used to treat against infections caused by these tested microorganisms.^[26]

Anti-inflammatory

Anti-inflammatory and anti-oxidant activity of *Strychnos nuxvomica* L. has been evaluated by Savita (2009) in albino rat model. Paw edema was induced in foster albino rats by alcohol extract of the *Strychnos nuxvomica*. Acute and chronic inflammation models were used to evaluate the anti-inflammatory activity (in vivo). In acute model carrageenan was used to induce inflammation in rat hind paw and cotton-pellet induced granuloma method was used for chronic inflammation model. SGOT and SGPT were monitored. After proper studies and experiments it was indicated that *Strychnos nuxvomica* possess potent anti-inflammatory activity with no detectable adverse effect. The results obtained confirmed the use of *Strychnos nuxvomica* traditionally for the treatment of Rheumatism and other inflammatory conditions.^[27]

Analgesic effect

Yin et al. (2003) carried out the study on the chemical constituents of *Strychnos nuxvomica* particularly Strychnine and Brucine by transdermal administration in albino rats and also in vitro and in vivo, transdermal absorption profiles showed the effective analgesic effects of the drug.in different phases, analgesic activities were exerted in formalin test.^[28]

Antiulcer activity

The major alkaloid strychnine when tested for antiulcer activity in Shay rat model, it reduced ulceration at an oral dose of 0.1 mg/kg body weight; strychnine at this dose acts as anti-secretory agent. At a dose of 0.25 mg/kg body weight there complete absence of ulceration compared to cimetidine was found.^[28]

Anti-Amnesic

In an experimental study, *Strychnos nuxvomica* extract inhibited acetylcholinesterase activity in the hippocampus and frontal cortex. These findings clearly suggest that, loganine possess anti-amnesic activity that may hold significant therapeutic value in alleviating certain memory impairment observed in Alzheimer's disease.^[29]

Anti-convulsion effect

In a recent research study, reported that ethanolic extract of *Strychnos nuxvomica* seeds reduced spontaneous motor activity and inhibited catalepsy. The seeds processed in milk exhibited marked inhibition of pentylenetetrazol (PTZ) induced convulsions and maximum potentiation of hypnosis, and were the safest LD50.^[29]

Anti-tumour

Major alkaloids present in *Strychnos nuxvomica* are effective against HepG2 cell proliferation. MTT assay was used to examine the growth inhibitory effects of the alkaloids on human hepatoma cell line. Brucine, Strychnine and Isostrychnine revealed significant inhibitory effects against HepG2 cell proliferation.^[29]

CONCLUSION

Azaraq (*Strychnos nuxvomica* L.) is known to be one of the important drugs in Unani Tib and has been used since long period of time either alone or in compound formulation for the treatment of various diseases like hemiplegia, paralysis, epilepsy, gout, sciatica, sexual debility, cardiac weakness etc. Pharmacological and scientific studies such as antidiabetic, anticonvulsant, analgesic, anti-inflammatory etc. effects have been proven its efficacy in various ailments as claimed by Unani Physicians in the past. Since this drug is highly toxic, hence used after proper detoxification.

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