Review Article Available online www.ijsrr.org ISSN: 2279–0543

International Journal of Scientific Research and Reviews

Atrilal (*Ammi majus linn*): Phytopharmacological Review of an Important anti Vitiligo Unani Drug

Misbahuddin Azhar

Research Officer Scientist-III, Regional Research Institute of Unani Medicine, Aligarh Uttar Pradesh –India

ABSTRACT

Atrilal (*Ammi majus* linn.) an important Unani antivitiligo medicine belong to the family Umbelifereae. It was in used since ancient time for vitiligo and mentioned in many unani classical texts. The previous pharmacological studies showed that atrilal (*Ammi majus* linn) was used effectively in the treatment of vitiligo, psoriasis, tinea and many other skin diseases. The aim of the present review is to collect the information of Atrilal (*Ammi majus* linn.) available in Unani classical literature, phyto-chemical and pharmacological studies and Unani formulations in which it is used as an ingredient also make an effort to prove the strength of action of drug mentioned in Unani classical literature. Fourteen Unani books were referred and eighteen pharmacological studies were recognized. This information gives the research question and guidance for future research.

KEYWORDS: Atrilal, Unani medicine, Phytochemistry, pharmacology, *Ammi majus* Linn. Vitiligo, Baras

***Corresponding author**
Dr. Misbahuddin Azhar
Research Officer Scientist-III
Regional Research Institute of Unani Medicine
Shahjahan Manzil, Near AMU Riding club
Qila Road, Aligarh-202001
Uttar Pradesh –India
Email: ccrum619@gmail.com
Mobile no +91 8383096715

INTRODUCTION

Unani system of medicine (USM), is one of the oldest forms of medicine known to mankind. It is still the most widely practiced form of medicine in many parts of the globe with different name. USM is presently practiced with different names e.g., Ṭibb Sunnatī (Traditional Medicine), Eastern Medicine, Uyghur Medicine Islamic Medicine or Arab Medicine etc in Different part of globe. USM offers four kinds of treatment modalities, pharmacotherapy is one of them. In which single and compound formulation from herbo-mineral and Animal Source are used for treatment. USM formulary and pharmacopeia is richest and most deserving therapy has a lot of herbs in its repository[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24]. Plants generally produce many secondary metabolites which are bio-synthetically derived from primary metabolites and constitute an important source of many pharmaceutical drugs[25,26,27,28,29,30,31,32,33].

Atrilal (*Ammi majus* linn.) is an important Unani medicine. Iranian Unani scholar Imamuddin Mehmood Sheerazi (1515-1592) wrote a short book entitled *Risala-e-Atrilal* on the medicinal properties in Persian. In Indian subcontinent three manuscripts of risala-e-atrilal were traced, one each in Khuda Bakhsh Library Patna, State library Hyderabad and Nizamia tibia college library Hyderabad. Founder of Ibn Sina Academy, Aligarh Hakim Zillur Rehman has translated the same into urdu after critical comparison of all the copies available. According to him many Unani Scholars has mentioned Atrilal (*Ammi majus* linn.) in their treatises e.g. Zakariya Raazi (854-925 AD) in *Al Hawi al Kabir*, Majoosi (930-994 AD) in *Kamil-us sana*, Ibn Sina (980-1037) in *Al qanoon fit tib*, Ibn Baitar (1197-1248) in *Al-Jami-ul-Mufradat-al-Advia-wal-Aghzia*, Daood Antaki (1543-1599 AD) in *Tazkira-Ulul-Albab*, Nooruddin Mohammad Abdullah (1646 d.) in *Alfaz-ul-Advia*, Yousuf bin Umar Ghasaani (1295 d.) in *Al-Motamid-fil-Advia-tul-Mufrada*, Mohd Husain Alvi Sheerazi (1790 d) in *Makhzan-ul-Advia*, Najmul Ghani (1859-1932) in *Khazainul Advia*, Hakim Abdul Haleem (1906-1954) in *Mufradat-e-Azizi*, Hakim Abdul Hakim (19th Century) in *Bustan-ul Mufradat* and many others[34]. Atrilal (*Ammi majus* linn.) is mentioned with different name in the above said text of unani medicine and names are mentioned in the list of common name. Unani System of Medicine offers successful treatment for various diseases especially the chronic ones. These include skin diseases like vitiligo, eczema, psoriasis where allopathic has minimal effects or causes some dangerous side effects.

Atrilal (*Ammi majus* Linn) is native of Egypt, it was imported to India. Due to its less availability, although it was in practice by many unani scholars, but many scholars of unani medicine have not mentioned this important drug of vitiligo in their text. There is a long list of text that has no description regarding the usefulness of atrilal for vitiligo. *Riyaz-ul-Advia*, *Jami-ul-mufradat* of

Hakim Sheikh Banda Hasan, *Mufradat-e-Azizi* of Hakim Abdul Haleem etc[1]. Similarly, many pharmacopeias are also free from its description or its usefulness in vitiligo e.g. *Qarabadeen-e-shifai* of Hakim Muzaffar bin Mohd Husaiani Shifai, *Qarabadeen Qadri* of Akbar Arzani. *In qarabadeen-e-Zakai* 15 formulations are mentioned for vitiligo only one formlation has atrilal as one of the ingredients. In *Qarabadeen Azam* more than 30 formulation has mentioned for vitiligo only one formulation of *Zimad* and one of *Majoon* has mentioned in which atrilal is One of the ingredient[34].

Many other important unani classical books on single drugs and compound formulations (qarabadeen=pharmacopeias) are free from its description because the physician's family kept this medicinal property in secret and not share with others and even not mentioned in the literature of that time. Because of this the drug atrilal even having a good quality in treating in vitiligo got neglected. A long list of unani classical literature that do not having any reference on this plant. Many unani pharmacopeias have mentioned formulation for vitiligo but they are free from Atrilal (*Ammi majus* Linn.).

MATERIAL& METHODS

Unani classical Literature was searched from recent to past available in different libraries of India, for phyto-chemical and pharmacological activities and computerized databases such as Medline, Pubmed, Ovid SP, Google Scholar and Science-direct were searched to identify all phyto-chemical, experimental and clinical trials carried out to prove the importance of Atrilal (*Ammi* majus Linn).

Botanical Description

Atrilal (*Ammi majus* Linn) belong to family Apiaceae[35]. English name is Bishop's Weed/ Greater Ammi[35] other common names are *Juz-ush-Shaitani, Rijl-ul-Ghuraab, Greater Ammi, Hashishatul Baras, Khella Shaitani, Shaitani Barrah, Tukhm-e-Talal, Atrilaan, Rijal-ul-Ghuraab, Rikl ul-Uqab, Rijl –ul Aqaq, Rijl-az-Zaagh, Kaak Changa, Missi*[34].

Description & Habitate:

Atrilal (*Ammi majus* Linn.) is an erect, branching annual herb, up to 1.5 m in height, sometimes grown as a winter ornamental. Leaves are oblong, 6.20 cm long, broad ternate or pinnate: leaflets lanceolate, obtuse to acute; flowers are white in colour with loose compound umbels. Its fruits are oblong, 1.5 - 2.0 mm long and 1 mm or less broad[35]. The plant is indigenous to Egypt and it grows in the Nile valley, especially in Behira and Fayoon[36]. In India its successful farming was conducted in plane of northern India, Jammu and Kashmir[34,36]. It is also found in the basin of

Mediterranean Sea, West Africa, in some regions of Iran and the mountain of Kohaz. It seeds are used for medicinal purposes and collected during the month of June to October In Unani Medicine Atrilal means its seeds, but some time its leaves called *Barg-e-murad* are also used for their medicinal values. Seed's longevity is 1 to 3 year after than that losses their strength[34-36]. According to a survey among the traditional healers and herbalist in all regions of the west bank of Palestine, it was found that *Ammi majus* Linn. was recommended for treatment of urinary tract infections[37].

Figure:1. Flowers of atrilal (*Ammi majus* Linn.)

Figure:2. Leaves of atrilal (*Ammi majus* Linn.)

Temperament:

In regards to its temperament Unani scholars have different opinions. According to some scholar it is Hot and Dry in second degree of temperament[38-41]; and some says it is Hot and Dry in third degree of temperament[40-43]. Author of *Muheet Azam* also said according to some unani scholars it is hot and dry in fourth degree of temperament[41,43].

Part used:

The seeds of the plant are used as medicine with the name of atrilal, sometimes it leaves also used as medicine with the name of *barg-e-atrilal*[38-42].

Action:

Unani scholars mentioned many actions in their treatises. All the actions mentioned are listed here in alphabetic order with English equivalent in brackets.

Daf-e-Baras (Vitiligo) & *Behaq* (Malesma)[35,37-43], *Jali* (Detergent)[35,38,41-46], *Kasir-e-Riyah* (carminative)[35,38,41-44]; *Mohallil* (Resolvent)[35,38,41-45], *Mudir-e-Baul* (Diuretics)[35,40-46], *Mudir-e-Haiz* (Emmenogogue)[35,40-41], *Mufattit-e-Hisat* (Lithotriptic)[40,43-45], *Mujaffif* (Desiccant)[41,45-47], *Mulattif* (Demulscent)[40], *Mufatteh* (Dilator)[41,43-46], *Mukhrij-e-Balgham* (Phlegmagogue)[41,43-44], *Mulayyan*

(Laxative)[39], *Musakkin-e-Alam* (Analgesic)[47], *Musaqqit-e-Janeen* (Abortifacient)[35,40-41,43-45], *Qatil-e-Kirm-e-Shikam* (Vermicidal)[35,40-43].

Potent Action:

Dafe-Baras wa Behaq (Antivitiligo & Anti-ptyriasis)[34,42-43].

Uses:

The indications in which the plant parts are recommended for therapeutic uses mentioned in Unani texts are arranged below:

- The decoction of seed is used as gargle for treatment of toothache[35]. Seeds of fruits were used for the treatment of skin disorders, psoriasis and vitiligo[35,38,40-41,43].
- The following prescriptions are mentioned in unani classics for vitiligo and malesma. Powder of seeds with honey and lukewarm water beneficial for Baras wa Behaq.
- It is also useful with aaqarqarha (*Anacyclus pyrethrum* DC.) and honey. Atrilal (*Ammi majus* Linn.), zanjabeel (*Zingiber officinale* Roscoe), aaqarqarha (*Anacyclus pyrethrum* DC.), nisoot (*Convolvulus turpethum*), and honey are used for baras (vitiligo)[38,40-41,43-44].
- Seeds of atrilal (*Ammi majus* Linn.), seeds of shaqaiq al-qahaan, aaqarqarha (*Anacyclus pyrethrum* DC.), jundbedaster (castorium) with honey orally thereafter honey water is of use for vitiligo.
- Atrilal (*Ammi majus* Linn.), barg-e-suddab (*Ruta graveolens* Linn.) and skin of snake with wine are beneficial for vitiligo.
- Paste of atrilal seed (*Ammi majus* Linn.) with vinegar applied on the affected part also helpful for vitiligo[39-40].
- Its leaf decoction orally is useful in dog's bite[40-41,43].
- Decoction of atrilal or with plain water orally is abortifacient[40,43].
- It is also used as an emmenogogue to regulate menstruation, as a diuretic, and for treatment of leprosy, kidney stone and urinary tract infections[35,38,40,43].
- Powder of seed of atrilal (*Ammi majus* Linn) one part and one part of powder of barg-e-suddab (leaves of *Ruta graveolens* Linn.) and skin of snake taken with wine of grapes[39-40].
- It was also advised for treatment of vitiligo after taking atrilal orally or locally at the site exposed the affected part of body to sunlight or sit in sun light for a period till the sweating start[35,37,39,].
- Powder of seeds are beneficial in niqras (gout), waja-ul-mafasil (polyarthritis)[38,40].
- It is also beneficial in disease of spleen, stomach and liver[40].

Dose:

2-3 gram[35,42]; 3-9 gm[38-41,43-44].

Substitute

In Unani classics it is also said that in case of non-availability of the drug substitute may be used.Baabchi (*Psoralea corylifolia* Linn.)[34,42], tukhm-e-karafs (*Apium graveolens* Linn.)[40,42], ajwain desi (*Trachyspermum ammi* (Linn.) Spragne)[40,44] could be substitute for kidney diseaseskateera (*Astragalus gummifer*)[39], kundush [*Schoenocaulon officinale* (Schl. & Cham.) A.Gray] and could be used[43-47].

Corrective

Unani scholars were well aware regarding the adverse and side effects of many unani drugs. So, they described about the corrective measures in terms of drugs and altenative measure in their treatments. Sometimes they add a corrective drug (muslehat) in prescriptions to counter the toxicity of the main drug. Daarchini (*Cinnamomum zeylanicum* Blume)[40-42,]zanjabeel (*Zingiber officinale* Roscoe)[40-42,]filfil siyah (*Piper nigrum* Linn.)[40-41]asl (Honey)[42] and for liver disorders. Sikanjabeen[40-41,43-44] and Sharbat banafsha[40-41] and for kidney disorders kateera (*Astragalus gummifer*)[40-41,43].

Chemical Constituents:

Its seeds contained amorphous glucoside, tannin, oleoresin, acrid oil, fixed oil, proteins and cellulose. The major constituents are furanocoumarins which included xanthotoxins, imperatorin, and bergaptens, marmesin, isoimperatorin, heraclenin and isopimpinellin. 6-hydroxy-7methoxy coumarin, nonfurocoumarin, umbelliprenin, glycosides of quercetin, luteolin, kaempferol, linoleic acid, methyl ester of oleic acid, palmitic acid, linolenic acid were also found[49-63].

Pharmacological studies:

Experimentation with *Ammi majus* Linn was started in Egypt in ancient period for its usefulness in vitiligo and other skin disorders[34,64]. In clinical studies it was found that *Ammi majus* Linn. is effective in cases of vitiligo, psoriasis and hypopigmentation tinea versicolor orally and locally[64-76]. It also has bactericidal, fungicidal, insecticidal, larvicidal, moluscicidal, nematicidal, ovicidal, and herbicidal activities[49,78]. It showed antiviral activity against vesicular stomatitis virus (VSV) and Herpes simplex virus (HSV)[50]. Its hot aqueous extract and petroleum ether extract reduced the *Schistosoma mansoni* worm burden in mice[57]. It also inhibited the growth of the *Neurospora crass* fungi *in-vitro*[79].

Antioxidant activity

Chloroform crude extract showed antioxidant activity in experimental study determined by the free radical scavenging by DPPH method[80-81].

Antimicrobial activity

Methanol and Chloroform crude extracts *A. majus* displayed antimicrobial activity against Gram positive bacteria, *Staphylococcus aureus* (*S. aureus*), and Gram-negative bacteria *Escherichia coli* (*E. coli*), *Haemophilus influenzae* (*H. influenzae*), and *Proteus spp* (*Proteus spp*)[80-81].

Cytotoxicity activity

Crude extracts of different solvent obtained from the seed of *A. majus* exhibited potent cytotoxicity activity by killing all the larvae in artemia lethality method (Artemia cysts) in dose dependent manner[80-81]. Pyrano-coumarin from atrilal plant showed cytotoxicity activity towards HCT116 cell line[82]. 8-methoxypsoralen inhibited cell growth in several cancer cell lines. The BrdU assay in neuroblastoma and metastatic colon cancer cells by induction of apoptosis via intrinsic and extrinsic pathways. They were the most sensitive to the compound. 8-MOP reduced the phosphorylation of AKT308, decreased the expression of Bcl-2, increased the Bax protein level, and activated caspases -8, -9, and -3 in both cell lines[83]. 4-hydro-7-hydroxy-8-methoxyfuroquinoline & 4-hydro-7-hydroxy-8-prenyloxyfuroquinoline showed antiproliferative and cytotoxic effects, with IC50 = 230.2 and 326.5 μM against HepG-2 and MCF-7, respectively[84]. Xanthotoxin from the seeds of *Ammi majus* found to decrease the osteoclast number, prevents bone loss, rescues bone microarchitecture, and restores bone strength in ovariectomized mice. In ovariectomy-mediated bone loss through the inhibition of receptor activator of nuclear factor-κB ligand-mediated osteoclastogenesis in mice. It may be considered to be a new therapeutic candidate for treating osteoporosis[85].

Antibacterial activity

Crude extract showed antibacterial activity against standard bacterial strains[86].

Antihyperlipidemic

The alcoholic extract of the *A. majus* seed significantly decreases the concentrations of cholesterol, triglycerides and low-density lipoprotein and increase in the concentration of high-density lipoprotein[87].

Anti-inflammatory activity

The alcoholic extract of the *A. majus* seed showed anti-inflammatory activity by significantly inhibiting the rat paw edema in dose dependent manner[88].

Analgesic activity

The alcoholic extract of the *A. majus* seed showed analgesic effect[88].

Antipyretic activity

The alcoholic extract of the *A. majus* seed lower the body temperature after one hour of treatment[88].

Other pharmacological actions

It also has bactericidal, fungicidal, insecticidal, larvicidal, moluscicidal, nematicidal, ovicidal, and herbicidal activities[49,79]. It showed antiviral activity against vesicular stomatitis virus (VSV) and Herpes simplex virus (HSV)[50]. Its hot aqueous extract and petroleum ether extract reduced the *Schistosoma mansoni* worm burden in mice[57]. It also inhibited the growth of the *Neurospora crass* fungi *in-vitro*[82].

Antidiabetic activity

Various extract showed hypoglycaemic activity in allaxon induced diabetic in experimental model animals[83]

Contraindicated and adverse effect:

It is contraindicated in diseases associated with photosensitivity, cataract, invasive squamous cell cancer, sensitivity to xanthotoxin, children under the age of 12, pregnancy, nursing, tuberculosis, liver and kidney diseases, human immune-deficiency virus infections and other autoimmune diseases[43,50,82,92].

Patient can develop bullous reactions of more or less severe, nervousness, insomnia, nausea and gastric burning even after first exposure[71]. Itching, edema, hypotension, vertigo, painful blistering, burning and peeling of the skin, pruritus, freekling, hypopigmentation, rash, cheilitis and erythema were also recorded with xanthotoxin therapy[90]. Phototoxic dermatitis and allergic rhinitis and contact urticaria is also reported due to exposure to fruits[90,93].

Unani Formulations

The Unani System of Medicine prescribes elaborate formulation or pharmaceutical processing of drugs for achieving stability, palatability, absorption and assimilability and for enhancing efficacy and safety. This pharmaceutical processing is applied to both single preparations and compound preparations, majority being of the later type. Some famous compound formulations of atrilal (*Ammi majus*) mentioned in Unani classical literature as: *Zimaad-e-Baras, Sofoof-e-Baras, Majon Atrilal*[94-95],*Dawa-e-Bars*[96], *Marham Atrilal*[97] etc.

CONCLUSION

Atrilal (*Ammi majus* Linn) is one of the oldest medicinal plants documented in *Eber's papyrus* of Egypt and used for vitiligo. In early era it was used by the scholars for de-pigmentation of skin and kept secrets with the family the procedure of its usefulness in skin disorders[34]. It also comes in the picture the Unani scholars who were well aware about its photosensitivity reactions[34]. As written by an Iranian Unani scholar Imamuddin Mehmood Sheerazi laid down a short book on this single unani medicine entitled *Risala-e-Atrilal* on the medicinal properties in Persian language. Hakim Zillur Rehman has translated the same into urdu and this translation were published from India, Pakistan and Iran. The drug atrilal is highly reactive medicine, it causes blistering on skin and Melanoprotective activity. In some animals their beeks were also changes the color after ingestion and expose to sunlight. So it may be concluded its temperament may be hot and dry in third degree due to its high reaction. Unani scholars i.e., Hakim Azam Khan, Hakim Najmul Ghani and Hakim Rafiquddin are among those who say it is hot and dry in third degree of temeperament[41-42].Ministry of AYUSH Government of India classified different system of medicine for a particular disease and system according to their strength. Central council for Research in Unani Medicine (CCRUM) has classified it for skin disorders. CCRUM is working in this area since last half century and designed many unani coded formulations under the name of UNIM-001, UNIM-002, UNIM-003, UNIM-005, UNIM-044, UNIM-045, UNIM-046, UNIM-047, DA_6, BSL_6 etc. Council conducted many clinical studies and got good results in cases of vitiligo[98-106]. It is also recommended that council must take up atrilal (*Ammi majus* Linn.) and its compound formulationfor vitiligo in future.

Many Phytochemical analyses of *Ammi majus* Linn.haveactive constituents imperatorin, bergaptens, marmesin, 8-methoxypsoralen Ammoidin (xanthotoxin) having depigmentation properties. Even it is native to Egypt, CCRUM is farming this plant in Aligarh and other regional centre. It is suggested that further research studies have been designed to reveal its unmasked potential in social stigmatic problem vitiligo.

ACKNOWLEDGEMENT

The author is thankful to Hakim Fakhre Alam, Research Officer (U), RRIUM, Aligarh for helping in translation of Arabic and Persian classical text of unani medicine.

REFERENCES

1. Akhtar F, Bari A, Aslam M, Azhar MU. Medicinal uses of amla (*Emblica officinalis*) A review, Ayurveda and All, 2004; 1(1): 26-28.

2. Akhtar J, Akram U, Azhar MU, Jamil SS. Anti asthamatic plants of unani system of medicine: a scientific review, Indian Journal of Unani Medicine, 2011; 4(2): 73-77.
3. Akhtar J, Azhar MU, Siddiqui KM, Siddiqui MK. Evidence based unani anti diarrhoeal drugs-a review, Indian Journal of Unani Medicine, 2010; 3(2): 97-103.
4. Akhtar J, Bi S, Azhar MU, Siddiqui KM. Supportive scientific investigations on usefulness of honey (*Asl Khalis*), Hamdard Medicus, 2012; 54 (4): 90-95.
5. Akram M, Akhtar S, Azhar MU, Ahmad M. Role of unani medicine in hyperlipidaemia, Indian Journal of Unani Medicine, 2008; 1(1): 22-28.
6. Akram M, Azhar MU, Anjum N, Quddusi N. Phytopharmacology of unani drug zeera siyah (*Carum carvi* linn.)- a review, Journal of Pharmacognosy and Phytochemistry, 2019; 8(1): 2772-2782.
7. Akram M, Azhar MU. Revand (rhubarb): an important unani drug for prevention of nephrotoxicity, International Journal of Pharma Professional's Research, 2016; 7(3): 1333-1340.
8. Anjum N, Quddusi N, Azhar MU. Phyto-pharmacological aspects of bisehri booti (*Aerva lanata*) and its uses in unani system of medicine: a review, Hippocratic Journal of Unani Medicine, 2017; 12(3): 51-64.
9. Azhar MU, Akhtar F, Aslam M, Anwer M, Tajuddin Jafri MA. Nephroprotective activity of some herbal preparations, Hamdard Medicus, 2005; 49(1): 110-115.
10. Azhar MU, Akhtar J, Akram U, Anjum N, Quddusi N. Pharmacological activity of holy drug zaitoon (*Olea europaea* linn.)-review, Indian Journal of Unani Medicine, 2011; 4(1): 85-91.
11. Azhar MU, Anjum N, Quddusi N, Akhtar J, Akram U, Yadav PK. Pharmacologically active nephroprotective plants-a review, Hamdard Medicus, 2013; 56(2): 56-76.
12. Azhar MU, Anjum N, Quddusi N. Pharmacological activity of khurma (*Phoenix dactylifera* linn.) a review, Hamdard Medicus, 2015; 58(2): 71-83.
13. Azhar MU, Anjum N, Quddusi N. Pharmacologically active cardioprotective plants at a glance, Hamdard Medicus, 2015; 58 (1): 51-83.
14. Azhar MU, Anjum N. Revand chini (chinese rhubarb) –a review on historical and unani classical prospect, International Journal of Unani and Integrative Medicine, 2019; 3(1): 11-18.
15. Azhar MU, Javed K, Jafri MA. Plant with nephroprotective activity, Hamdard Medicus, 2005; 48(4): 33-43.
16. Azhar MU, Khanam D, Aslam M, Tajuddin, Jafri MA. Plants with nephrotoxic activity, Journal Science and Pharmacy, 2004; 5(3): 97-103.

17. Azhar MU, Mustehasan, Alam M, Ahmad SG, Anjum N, Quddusi N. Nephroprotective unani drug *Khar-e-Khasak Khurd* (*Tribulus terrestris* linn.)-a review, International Journal of Scientific Research in Biological Sciences, 2020; 7(1): 24-36.
18. Azhar MU, Quddusi N, Akhtar J, Akram U, Anjum N, Hannan A. Pharmacological activities of salajit (asphaltum)-a unani drug, Indian Journal of Unani Medicine, 2011; 4(1): 5-8.
19. Azhar MU, Quddusi N, Parveen S, Tajuddin, Siddiqui KM, Siddiqui MK. Daa-us-sadaf (psoriasis) and role of herbal drugs, Hamdard Medicus, 2010; 53(1): 51-57.
20. Mustehasan, Azhar MU. Hajar ul Yahood (Jew's Stone) Anti-Urolithiatic Unani Mineral Drug-Review, World Journal of Pharmaceutical Research, 2020; 9(6): 1127-1133.
21. Mustehasan, Azhar MU, Naushin S. Kibreet (Sulphur) A Unani Mineral Drug- Review, IJSRBS, 2020; 7(3): 121-126,
22. Mustehasan, Azhar MU, Naushin S. Historical Ethnopharmacological Review of a Unani Mineral Drug–Samm al-Far (Arsenic Trioxide), HJUM, 2020; 15(2): 21-32.
23. Mustehasan, Azhar MU. Abrak (Mica) and its Unani Formulations-Review, WJPR, 2020; 9(8): 2475-2484.
24. Alam MI, Ahsan SM, Salam M, Ahmad T, Azhar MU, Arfeen S. Clinical evaluation of unani drugs Majoon Suranjan Safoof Suranjan and Raughan Suranjan in Waja Ul mafasil (Rheumatoid arthritis)-a preliminary study, Hippocratic Journal of Unani Medicine, 2014; 9(4): 73-84.
25. Alam MMA, Javed K, Jafri MA. Effect of revand (*Rheum emodi*) on renal functions in rats, Journal of Ethnopharmacology, 2005; 96(1-2): 121-125.
26. Azhar MU, Ahmad Z, Mustehasan. Effect of unani medicine in *Iltihab-e-Jild Huzaazi* (seborrheic dermatitis) of head: a case study, International Journal of Scientific Research in Biological Sciences, 2020; 7(2): 41-43.
27. Azhar MU, Alam M, Aslam M, Javed K, Jafri MA. Role of asgand (*Withania somnifera*) in cadmium chloride induced nephrotoxicity in rats, Hamdard Medicus, 2005; 48 (3): 48-51.
28. Azhar MU, Ansari RI, Ahmad S. Clinical effect of Barg-e-jhao (*Tamarix articulata* vahl.) in hepatosplenomegaly-a case study, International journal of AYUSH case reports (IJA CARE), 2019; 3(2): 128-135.
29. Azhar MU, Ayub S, Anjum N, Ahmad S. Effect of Jawarish bisbasa on dyslipidemia-a case study, International Journal of Scientific Research in Biological Sciences, 2020; 7(1): 20-23.
30. Azhar MU, Ayub S, Anjum N, Ahmad S. Role of dieto-therapy in weight and dyslipidemia management - a case study, International Journal of Scientific Research in Biological Sciences, 2020; 7(1): 17-19.

31. Azhar MU, Khan SA, Aslam M, Javed K, Jafri MA. Nephroprotective activity of kulthi (*Dolichos biflorus*) on gentamicin induced toxicity in rats, Journal Science and Pharmacy, 2004; 5(2): 50-53.
32. Azhar MU, Tajuddin, Jafri MA. Nephroprotective effect of Kulthi (*Macrotyloma uniflorum* (lam) verdc.) on acute renal failure in rats, Hippocratic Journal of Unani Medicine, 2008; 3(4): 97-102.
33. Azhar MU. Effect of herbal unani formulation on nephrotic syndrome: a case study, Indian Journal of Traditional Knowledge, 2018; 17(4): 807-810.
34. Rahman SZ. Risala Atrilal (urdu translation), publication division, Muslim university Aligarh, 1993; 32-63.
35. Anonymous. The Wealth of India-Raw material Vol. I, Council of Scientific Industrial Research, New Delhi, 1985; 225.
36. Hossain MA, Al Touby S. *Ammi majus* an Endemic Medicinal Plant: A Review of the Medicinal Uses, Pharmacological and Phytochemicals. Ann Toxicol, 2020; 2(1): 9-14.
37. Jaradat NA, Zaid AN, Al-Ramahi R, Alqub MA, Hussein F, Hamdan Z, Mustafa M, Qneibi M, Ali I. Ethnopharmacological survey of medicinal plants practiced by traditional healers and herbalists for treatment of some urological diseases in the West Bank/Palestine, BMC Complement Altern Med. 2017; 17(1): 255.
38. Kabiruddin, M. *Makhzanul Mufradat Almaroof Khawasul Advia*, Shiekh Mohammad Bashir & Son's Lohore, 1951; 48-49.
39. Ibn Baitar. *Al Jameul Mufradat Al Adwia wal Aghziya*, Vol-II, Central Council for Research in Unani Medicine publication, New Delhi, 1986; 288-290.
40. Ghani MN.*Khazinatul-Advia*, vol-I, Barqi Press Lahore, 1917; 368-370.
41. Khan A. *Muheet-e-Azam*, Vol-I, (Urdu translation), Central Council for Research in Unani Medicine publication, New Delhi, 2012; 198-201.
42. Rafiquddin M. *Kunzul Advia Mufrada*, University Publication Unit, Sarfaraz house, AMU Aligarh, 1985; 100-102.
43. Nabi MG. *Makhzan-ul-Mufradat-wa-Murakkabat*, Narayan Das Jangli mill, Dariba Kalan, Delhi, 1958; 175.
44. Antaki D. *Tazkira Ulul albab*, Central Council for Research in Unani Medicine publication, New Delhi, 2008; 62-63.
45. Ali N.*Nasir Al Moalajeen*, Matba Alvi, Lucknow, 1864; 37.
46. Haziq HMH. *Tauzeehul Advia*, Matba Iftikhar, Delhi, 1899; 7.
47. Ali HA. *Taleef-e-Ahsani*, Matba Mustafai, Lucknow, 1872; 5.

48. Ibn Hubal. *Kitab-al-Mukhtarat fit Tib*, Vol- II, (Urdu Translation), Central Council for Research in Unani Medicine publication, New Delhi, 1362H; .
49. Joy PP, Thomas J, Mathew S, Skaria M. Medicinal plants, Kerala Agriculture University, India, 1998.
50. Selim YA, Ouf NH. Anti-inflammatory new coumarin from *Ammi majus* L. Medicinal chemistry Letters, 2012; 2:1-4.
51. Balzek ZA. Pharmacognosy of the plants parts of *Ammi majus*Linn., FO, Ch , 1966; 35(1): 495-509.
52. Eisenreichoa E, Buckova L, Tomko J. Contents of *Ammi majus* Linn. l substances. Farm Obz Ch, 1980; 79(11):503-506.
53. Ekiet H, Gomolka E. Coumarin contents of *Ammi majus* Linn. l. callus cultures, Pharmazie, 2000; 55:684-687.
54. Abu-Mustafa, EA, Fayez MBE. Natural coumarins I. marmesin and marmesinin, further products from the fruits of *Ammi majus* Linn. L, Journal of Organic Chemistry 1961; 26: 161-166.
55. Hilal SH, Haggag MY. A thin layer chromatography (TLC)-colorimetric assay of furacoumarins. Egyptian Journal of Pharmaceutical Sciences, 1975; 16: 495-499.
56. Elgamal MHA, Shalaby NMM, Duddeck H, Heigemann M. Coumarins and coumarin glycosides from the fruits of Ammi species. PhytoChemisatry, 1993; 34(3): 819-823.
57. Abdulla WA. Preliminary stidies on the antischistosomal effect of *Ammi majus* Linn. L. Egyptian Journal of Bilharziasis, 1978; 4: 19-26.
58. Ivie GW. Linear furacoumarins (-soralens) from the seed of texas *Ammi majus* Linn. L. (bishop's weed). Journal of Agriculture and Food Chemistry, 1978; 26: 1394-1403.
59. Singab ANB. Acetylated falvonol triglycosides from *Ammi majus* Linn. L., Phytochemistry, 1998; 49: 2177-2180.
60. Abdul-Jalil TZ, Saour K, Nasser A. Phytochemical study of some flavoniods present in the fruits of two Ammi L. species wildly grown in Iraq. Iraqi J Pharm Sci, 2010; 19(1): 48-57.
61. Ashraf M, Ahmad R, Bhatty MK. Studies on the essential oil content of the Pakistani species of the family Umbelliferae. Part XXX *Ammi majus* Linn. seed oil. Park J.Sci. Ind. Res., 1979; 22(5): 255-257.
62. Al-Snafi AE, Chemical constituents and pharmacological activities of *Ammi majus* and *Ammi visnaga*. A review, International Journal of Pharmacy and Industrial Research, 2013; 3(3): 257-265.

63. Hussain I, Khan S, Khan MI, Rehman I, Ahmad M. Investigation of fatty acid composition of *Ammi majus* Linn. seed oil by gas chromatography mass spectrometry. J. Chin chem. Soc.,2012; 59: 1-4.
64. Becker SW. Psoralen phototherapeutic agents. Journal of the American Medical Association, 1967; 202: 422-424.
65. Collins P. 8-MOP PUVA for psoriasis: a comparison of minimal phototoxic dose based regimen with a skin type approach. British Journal of Dermatology, 1996; 135: 248-254.
66. De-Berker DA. Comparison of psoralen-UVB and psoralen UVA photochemotherapy in treatment of psoriasis, Journal of the American Academy of Dermatology, 1997; 36: 577-581.
67. El-Mofty AM. A preliminary clinical report on the treatment of leucoderma with *Ammi majus*Linn., J. Egypt Med. Assoc., 1948; 31: 651-665.
68. El-MoftyAM. Further study on treatment of leucoderma with *Ammi majus*Linn., J.R.Egypt Med. Assoc., 1952; 35: 1-19.
69. El-Mofty AM, El-Mofty M. Psoralen photochemoterapy in contrast to chemotherapy of psoriaisis, Med J Cairo Univ, 1980; 48: 71-83.
70. El-Mofty AM, El-Sawalahy H, El-Mofty M. Clinical study of a new preparation of 8-methoxypsoralen in photochemotherapy. Int J Dermatol, 1994; 33: 588-592.
71. El-Mofty AM, El-Sawalahy H, El-Mofty M. Photochemotherapy in the treatment of post tinea versicolor hypopigmentation. Med. J Cairo Univ, 1995; 61(4): 632-637.
72. Fahmy IR, Abu-Shady H. The isolation and properties of ammoidin, ammidin and majudin and their effect in the treatment of leukoderma. Q.J. Pharm. Pharmacol., 1984; 21: 499-503.
73. Kavli G, Volden G. Phytophotodermatitis. Photodermatology, 1984; 1: 65-75.
74. Parrish JA. Photochemotherapy of psoriasis with oral methoxsalen and long wave ultraviolet light, N Engl. J Med., 1974; 291: 1207-1211.
75. Parsad D, Saini R, Verma N. Combination of PUVAsol and topical calcipotriol in vitiligo. Dermatology, 1998; 197: 167-170.
76. Sidi E, Bourgeois J. The treatment of vitiligo with *Ammi majus*Linn., J Invest Dermatology, 1951; 391-395.
77. Al-Snafi AE. Chemical constituents and pharmacological activities of *Ammi majus* and *Ammi visnaga*. A review, International Journal of Pharmacy and industrial Research, 2013; 3(3): 257-265.
78. Mustafa MA, Al-Khazraji A. Effect of some plant extracts on the *Culex pipiens molestus* Forskal larvae. Iraqi Journal of Veterinary Science, 2008; 22(1):9-12.
79. Duke JA. Bishops weed (*Ammi majus* Linn. L., Apiaceae), Econ Bot,, 1988; 42(3): 442-445.

80. Rehab MSH, Hossain MA. Evaluation of antioxidant, antimicrobial and cytotoxic activities of seed crude extracts of *Ammi majus* grown in Oman. Egyptian Journal of Basic and Applied Sciences, 2016; 3: 329-334.
81. Rehab MSH, Hossain MA. Evaluation of antimicrobial and cytotoxic activities of polar solvents extracts of leaves of *Ammi majus* used by the Omanis. Pacific Science Review A: Natural Science and Engineering, 2016; 18: 62-65.
82. Kubas J. Investigations on known or potential antitumar plants by means of microbiological tests. Part III. Biological activity of some cultivated plant species in Neurospora crassa test. Act Biologica Cracoviensa, 1972; 15: 87-100.
83. El-Sharkawy E, Selim Y. Three new coumarin types from aerial parts of *Ammi majus* L. and their cytotoxic activity, Z Naturforsch C J Biosci. 2018; 73(1-2):1-7.
84. Akhtar MS, Ahmed M, Gulzar K, Adnan H. Hypoglycemic activity of *Ammi majus* leaves in normal and alloxane-induced diabetic rabbits. Diabetologia Croatica, 2011; 40(3): 71-79.
85. Bartnik M, Slawinska-Brych A, Zurek A, Kandefer-Szerszen M, Zdzisinska B. 8-methoxypsoralen reduces AKT phosphorylation, induces intrinsic and extrinsic apoptotic pathways, and suppresses cell growth of SK-N-AS neuroblastoma and SW620 metastatic colon cancer cells, J Ethnopharmacol. 2017; 207:19-29
86. Mohammed MM, El-Sharkawy ER. Cytotoxic new furoquinoline alkaloid isolated from *Ammi majus* L. growing in Egypt. Nat Prod Res. 2017; 31(6): 645-652.
87. Dou C, Chen Y, Ding N, Li N, Jiang H, Zhao C, Kang F, Cao Z, Quan H, Luo F, Xu J, Dong S. Xanthotoxin prevents bone loss in ovariectomized mice through the inhibition of RANKL-induced osteoclastogenesis, Osteoporos Int. 2016; 27(7): 2335-2344.
88. Al Akeel R, Al-Sheikh Y, Mateen A, Syed R, Janardhan K, Gupta VC. Evaluation of antibacterial activity of crude protein extracts from seeds of six different medical plants against standard bacterial strains, Saudi J Biol Sci. 2014; 21(2): 147-51.
89. Koriem KM, Asaad GF, Megahed HA, Zahran H, Arbid MS. Evaluation of the antihyperlipidemic, anti-inflammatory, analgesic, and antipyretic activities of ethanolic extract of *Ammi majus* seeds in albino rats and mice, Int J Toxicol., 2012; 31(3): 294-300.
90. Kiistala R, Makinen-Kiljunen S, Heikkinen K, Rinne J, Haahtela T. Occupational allergic rhinitis and contact urticaria caused by bishop's weed (*Ammi majus*). Allergy,1999; 54(6): 635-9.
91. Shlosberg A, Egyed MN. Examples of poisonous plants in Israel of importance to animals and man. Arch Toxicol Suppl. 1983; 6:194-6.
92. Lacy C. Drug information handbook, Lexicomp, Hudson, OH:, 2006; 6.

93. Ossenkoppele PM,Van der Slui WG,Van Vloten WA. Fototoxische dermatitis door het gebruik van de *Ammi majus* Linn. Vrucht bij Vitilogo. [Phototoxic dermatitis following the use of *Ammi majus* Linn. fruit for vitiligo], Nederlands Tijdschrift voor Geneeskunde, 1991; 135: 487-480.
94. Sheerazi MHA. *Majmaul Jawamein* (Qarabadeen-e-Kabir), 1856; 154.
95. Khan HS. *Ilaj ul Amraz* (urdu translation by M Hadi Hasan Khan) 2nd Reprint, Central Council for Research in Unani Medicine Publication, New Delhi, 2005; 822-823.
96. Khan MA.*Qarabadeen Azam-o-Akmal* (Urdu translation), Reprint, Central Council for Research in Unani Medicine Publication, New Delhi, 2005; 474-475.
97. Khan MA. *Qarabadeen-e-Azam*, Matba Nizami Kanpur, 1893; 257.
98. Husain N, Uddin Q, Kazmi MH. Clinical studies on the treatment of Baras (vitiligo) in unani system of medicine-a systematic review, European Journal of Biomedical and Pharmaceutical sciences, 2018; 5(5): 1088-1094.
99. Waheed MA, Ahmad M.Study of Vitiligo Repigmentation with Systemic and Topical Unani Formulations – An Open Label Clinical Study, Planta Med, 2012; 78:-115.
100. Shareef MA, Hussain SJ, Parveen S, Lateef A, Zaidi ST, Ahmed Z, et. al. Clinical screening of Atrilal and Sadab on Bars (Vitiligo) cases - A comparative study, Cureall J Unani Med., 2003; 1(3 & 4): 28–31.
101. Hussain SJ, Taiyab M, Zakiuddin. Effect of Atrilal on biochemical changes in cases of vitiligo. Indian J Unani Med., 1991; 1(1): 18–28.
102. Verma RS, Khan P, Mohammad N, Khan LA. A clinical study of Unani formulation UNIM-045 for Anti-Vitiligo (Bars) effect. Hippocratic Journal of Unani Medicine 2012; 7(2): 31-40.
103. Islam N, Ara I, Siddiqui MK. Breakthrough in the etiopathogenesis of bars (vitiligo)- a preliminary clinical study by DA_6+BSL_6 therapy, Hippocratic Journal of Unani Medicine, 2010; 5(1): 1-8.
104. Rehman S, Verma RS, Khan SA, Khan LA. The efficacy and safety of Unani coded drug UNIM-046 in cases of Bars (Vitiligo)- A preliminary clinical trial. Hippocratic Journal of Unani Medicine 2012; 7(4): 11-21.
105. Verma RS, Abbas A, Abbas S, Khan LA. Efficacy of Unani Coded drug UNIM-044 in Vitiligo (Bars) patients-A clinical study. Hippocratic Journal of Unani Medicine 2011; 6(2): 23-31.
106. Khan P, Verma RS, Ayub S, Afza S, Akhtar J, Khan AA. Comparative study of efficacy and safety of coded Unani formulations-UNIM-001+UNIM-003 with methoxsalen in cases of bars (vitiligo), Journal of Advanced Research in Ayurveda, Yoga, Unani, Sidhha & Homeopathy, 2020; 7(3&4): 16-26.