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Review Article

Habb-e-Azaraqi, A Potent Unani Pharmacopoeial preparation used in Neurological disorder: A review

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Abstract

Unani medicine relies on drugs of natural origin for the treatment of various medical conditions. It is practised throughout Asia and particularly in India. The rich natural drug asset of Unani medicine includes both single and compound drugs. *Habb-e-Azaraqi* is a polyherbal Unani formulation used clinically since decades for the management of various neurological disorders like facial palsy, paralysis, gout and arthritis. The explicit nature of *Habb-e-Azaraqi* rationalizes its use in nervine disorders. The main ingredient of *Habb-e-Azaraqi* is *Azaraqi mudabbar* (detoxified *Strychnos nux-vomica* L.) which is known for its diverse medicinal uses. This review highlights the traditional uses of *Habb-e-Azaraqi*, phytochemistry and pharmacological properties of its ingredient.

Keyword: *Habb-e-Azaraqi;* Facial palsy; Paralysis; Strychnos nux-vomica; Unani medicine

1. Introduction

Unani medicine is an ancient medicine system that involves a combination of therapies through the medication resources of plants, minerals and animals. *Unani* physicians follow two types of treatment regimens, which are based on *Mufrad* (single drug) and *Murakkab* (compound formulations). Compound formulations may include classical, Pharmacopoeial and proprietary/patent preparations. The selection of the drug for any ailment depends upon the choice of physicians. The *Hippocratic* theory of the humours-based *Unani* System of Medicine is well established in India [1,2]. It is thought that dosage forms of *Unani* are safe and do not have any harmful effects on the body. It is true up to some extent, but not at all. *Unani* drugs sometimes produce adverse effects, if not prepared as per their methods of preparation or if not detoxified before adding in a dosage form as needed [1,3]. There are four basic dosage forms of compound formulations in Unani medicine; solid, semisolid, liquid and gaseous form. *Habb* (Arabic: *Habb*; Urdu: *Goli*; Hindi: *Goli*; English: *Pill*; Latin: *Pilula* or *pilioli*) is one of the types of solid dosage forms and it has many advantages [4]. *Habb* is prepared by powdering the dried drug and mixed with water or a liquid to form a proper dough-like mass and from it, the spherical-shaped unit dosage form is prepared, which may be of different sizes, e.g., pea, gram, black pepper; and weight vary from 0.1-1 g. *Habb* was invented by *Hakeem Seelon* [4,5].

The drug *Habb-e-Azaraqi* is one of the classical Unani poly-herbal compound formulations cited in several classical books and Unani pharmacopoeias like *Qarabadeen Azam* [6], *Bayaz Kabeer* [7], *Qarabadeen-e-Majeedi* [8], *National formulary of Unani medicine* [9] etc. The formulation *Habb-e-Azaraqi* possesses *Muqawwi- ī -Dimāgh* (Brain tonic) *Muqawwi-ī-ʻasāb* (Nerve tonic), *Muharrik-ī-aʻsāb* (Nervine stimulant) properties and therapeutically useful for various ailments of the human body like as *Sara* (Epilepsy), *Fālij* (Hemiplegia), *Laqwa* (Facial palsy), *Raʻsha* (Tremor), *Niqras* (Gout), *Waja' al-Mafāṣil* (Polyarthritis) [8–11]. *Habb-e-Azaraqi* is a brownish-black coloured pill with a disagreeable odour and bitter taste [12]. It contains *Azaraqi mudabbar* (detoxified *Strychnos nux-vomica* L.), *Filfil siyah* (*Piper nigrum* L.), *Filfil daraz* (*Piper longum* L.) and *Arq-e-Ajwain* (Distillate of *Trachyspermum ammi* L.) [7,9]. All the individual drugs in the compound mixture contain some biologically important chemical constituents like phenolic compounds, flavonoids, tannins, alkaloids, Strychnine, Brucine [13]; Piperine, Piperamine [14]; Beta-sitosterol, Daucosterol, Thymol, carvacrol p-cymene, γ-terpinene, α- & β-pinenes [15] and possesses Immunomodulatory, Anticonvulsant, Neuroprotective, Antidepressant, Analgesic, Anti-inflammatory, Anti-arthritis, Antioxidant, and Anticancer properties [16–20]

2. Ingredients of *Habb-e-Azaraqi* as per NFUM

Habb-e-Azaraqi is a tablet dosage form compound formulation[9], which is made with the following ingredients in the composition as given in Table 1.

Table 1

Drug name	Scientific name	Family	Form of drug	Quantity
Azaraqi Mudabbar	*Strychnos nux-vomica*	Loganiaceae	Seed powder	20 g
Filfil Siyah	*Piper nigrum* L.	Piperaceae	Fruit powder	10 g
Filfil Daraz	*Piper longum* L.	Piperaceae	Fruit powder	10 g
Arq-e-Ajwain	*Trachyspermum ammi*	Apiaceae	Distillate of fruit	Q.S.

3. Important Points Regarding Preparation of *Habb-e-Azaraqi* [8–10]

- *Azaraqi Mudabbar*: 700 mg of *Azaraqi* is buried in yellow clay and water is poured over it daily for ten days. Then, it is removed and cleaned. The outer coating (Testa) is peeled off with the knife and the cotyledons are separated after the embryo portion (pitta) is removed. It is then washed with hot water and tied in a clean cloth bag. In a vessel containing two litres of milk, the bag is immersed. The milk is then heated until it has evaporated; care is taken to ensure that the bag does not touch the vessel's base. Thereafter, it is removed from the bag and washed with water to obtain *Azaraqi Mudabbar*.
- Poisonous or toxic drugs are first purified or detoxicated (*mudabbar*) and then ground to a fine powder. Besides being toxic (poisonous), *Kuchla* (nux-vomica) is very hard and difficult to powder. It is, therefore, immediately grounded when it is soft. In case it gets hard on drying, it is powdered by frying in *Roghan Zard* or any other suitable oil by which the drug is crisped.
- *Arq-e-Ajwain*: It is a liquid preparation obtained by steam distillation of *Ajwain* (Fruits).
- The pills should neither be very hard nor very soft.
- The *huboob* are preserved in well-dried clean glass jars, stoppered bottles etc. and stored in a cool and dry place to avoid contamination.

4. Method of preparation

Take all the ingredients of *pharmacopoeial* quality. Clean, dry and grind the whole ingredient separately and sieve through mesh number 100. The powder is then mixed with *Arq-e-Ajwain* to make a semi-solid mass and granulated by passing through No. 20 mesh sieve. The obtained granules are dried and kept in cooling pans and rotated. To make the pills, little water is spread over the granules to keep them moist. After that, these granules are coated with a fine powder of a mixture of all three drugs by rotating the pan with an interval of one minute to ensure the uniform and smooth coating of the granules and lastly passed through different sizes of sieves. This procedure is repeated until the pills of the appropriate size have been collected [7–9].

5. Dose

200-500 mg

6. Pharmacological Action

Muqawwi- ī -Dimāgh (Brain tonic), *Muqawwi-ī-'asāb* (Nerve tonic), *Muharrik-ī-a'sāb* (Nervine stimulant) [7,10].

7. Therapeutic uses

Sara (Epilepsy), *Fālij* (Hemiplegia), *Laqwa* (Facial palsy), *Ra'sha* (Tremor), *Niqras* (Gout), *Waja' al-Mafāṣil* (Polyarthritis) [9,12]

8. *Mizāj* of *Habb-e-Azaraqi*

Compound preparations are made to cure a particular disease, therefore the literature of *Murakkabāt* does not mention their *Mizāj*. Many other writers of Unani Medicine, such as *Al-Kindi, Ibn Rushd* and *Najmul Ghani*, have claimed that the compound formulations inherit *Mizāj* from their ingredients. So, a rule was established to test the *Mizāj* of the *Murakkab* drug. Following the same, *Habb-e-Azaraqi* is as follows (Table 2)

Table 2: *Mizāj* Assessment of *Habb-e-Azaraqi*

Ingredients	*Darjāt-i-Mizāj*	Dosage as *Mufrad* Drug *Hārr*	Dosage as *Mufrad* Drug *Yābis*	Product of *Hārr* Drugs and Dosage	Product of *Yābis* Drugs and Dosage
Azaraqi mudabbar (detoxified *Strychnos nux-vomica* L.)	Hot 4^0 and Dry 4^0	0.05g	0.05g	0.20g	0.20g
Filfil siyah (*Piper nigrum* L.)	Hot 3^0 and Dry 3^0	3g	3g	9g	9g
Filfil daraz (*Piper longum* L.)	Hot 2^0 and Dry 2^0	5g	5g	10g	10g
Calculation	dH=3, dB=nil dY=3, dR= nil	Σ DH= 8.05 Σ DB= nil	Σ DY= 8.05 Σ DR= nil	Σ DH × dH= 24.15 Σ DB × dB= nil	ΣDY× dY= 24.15 Σ DR × dR= nil

Note: d: *Darjāt* (Degree); D: dose; H: *Har* (Hot); B: *Barid* (Cold); Y: *Yabis* (Dry); R: *Ratab* (Moist)

- *Darjāt* and *Kayfiyāt Fā'ila* = {ΣDH ×dH – ΣDB ×dB}/ΣDH – ΣDB = 39/12=3.25
- *Darjāt* and *Kayfiyāt Munfa'ila* = {ΣDR ×dR – ΣDY ×Dy}/ΣDR – ΣDY =36/12=3
- Therefore, *Mizāj* of *Habb-e-Azaraqi* is *Hārr Yābis* of degree 3 (Hot and Dry in 3^0)

Table 3: Physicochemical standards of *Habb-e-Azaraqi* [12,21]

Appearance	Tablet
Colour	Brownish black
Smell	Disagreeable
Taste	Bitter
Alcohol soluble matter *(%w/w)*	15.84 -17.55%
Water soluble matter*(%w/w)*	34.07- 35.44%
Successive extractives	
Pet. ether (60-80")	7.07- 8.63%
Chloroform	1.11-1.12%
Ethyl alcohol	21.54 - 24.92%
pH of 1% aq. Solution	4.37
pH of 10% aq. solution	5.20
Loss in wt. on drying at 105°	6.60 - 7.62%
Total ash *(%w/w)*	4.95 - 5.29%
Water soluble ash *(%w/w)*	0.60 - 0.70%
Acid insoluble ash *(%w/w)*	2.70%

Table 4: Description of ingredients of *Habb-e-Azaraqi* in Unani medicine

Drug	Parts Used	Dosage	Pharmacological Action	Therapeutic Uses
Strychnos- nux-vomica L. [22–24]	Seed	5-60 mg	*Muqawwi-ī-'asāb* (nerve tonic), *Muharrik-ī-a'sāb* (nervine stimulant), *Muharrik-ī-qalb* (cardiac stimulant), *Muqawwi-ī-bāh* (aphrodisiac), *Mushtahi* (appetizer), *Munaffis-ī-balgham* (expectorant), *Muṣaffi-ī-dam* (blood purifier), *Muhallil-ī-warm* (anti-inflammatory).	*Fālij* (Hemiplegia), *Laqwa* (Facial palsy), *Ra'sha* (Tremor), *Waja' al-Mafāṣil* (Polyarthritis), *Waja' al-Qutn*, *Zo'f-ī-Qalb* (Weakness of heart), *Su'āl* (Cough), *Zo'f-ī-mi'da* (Weakness of stomach)
Piper nigrum L. [23,25,26]	Fruit	1-3 g	*Muqawwi-ī-'asāb* (nerve tonic), *Muqawwi-ī-bāh* (aphrodisiac), *Muqawwi-ī-mi'da* (stomachic), *Hāzim* (digestive), *Mushtahi* (appetizer), *Munaffis-ī-balgham* (expectorant), *Kasrat-i Luaab* (Excessive salivation), *Muhallil-ī-warm* (anti-inflammatory)	*Warm halaq* (Pharyngitis), *Waja ul asnan* (Toothache), *Balghami Amraz* (Phlegmatic diseases), *Su'āl-e-Balghami* (Phlegmatic cough), *Zo'f-ī-Ishtihā* (Anorexia), *Zo'f-ī-hazm* (Delayed digestion), *Nafakh-ī-Shikam* (Flatulence), *Zo'f-ī-'asāb* (Weakness of nerve), *Zo'f-ī-Bāh* (Sexual debility).
Piper longum L. [23,25,26]	Fruit	3-5 g	*Mushtahi* (appetizer), *Hāzim* (digestive), *Muqawwi-ī-mi'da* (stomachic), *Kāsir-ī-reyāh* (carminative), *Muhallil-ī-warm* (anti-inflammatory), *Muqawwi-ī-bāh* (aphrodisiac), *Jāli* (detergent)	*Zo'f-ī-mi'da* (Stomach weakness), *Nafakh-ī-Shikam* (flatulence), *Zo'f-ī-hazm* (Delayed digestion), *Zo'f-ī-Bāh* (Sexual debility), *Waja' al-Mafāṣil* (Polyarthritis), *'Irq al-Nisā* (Sciatica), *Niqras* (Gout).

Table 5: Important Isolated Chemical constituent and Scientific studies of ingredients of *Habb-e-Azaraqi*

Drug	Chemical constituent	Scientific Studies
Strychnos-nux-vomica L.	Strychnine, Brucine, Beta-colubrine, Isobrucine, Loganic acid, Caffeic acid, p-hydroxybenzoic acid, Vomicine, Novacine, Strychnine N-oxide [13,27]	Anti-cancerous [16], Anti-tumour [28], Antioxidant [29], Anticonvulsant [30], Antiallergic, Immunomodulatory [31], Anti-diarrhoeal [32], Antipyretic, Analgesic, Anti-inflammatory [33], Hepatoprotective [34], Anti-diabetic [35].
Piper nigrum L.	Piperine, Piperamine, Piperamide, α- and β-pinene, myrcene, Brachyamide B, α-phellandrene, limonene, linalool, methylpropanal, 2- and 3-methylbutanal, butyric acid and 3-methylbutyric acid [14,36,37]	Antimicrobial [17], Antioxidant [38], Anticancer [39], Analgesic [40], Anticonvulsant [41], Neuroprotective [18], Anti-inflammatory [42], Antidepressant [43].
Piper longum L.	Dehydropipernonaline, Piperine, Beta-sitosterol, Daucosterol, Tetrahydropiperine, Pipercide, Pellitorin, Pipyahyine, α -Pinene, Sabinene, Myrcene [15,44]	Analgesic [45], Anti-inflammatory, Anti-microbial [46], Anti-arthritis [47], Anti-diabetic [48], Anti-oxidant [19], Anthelmintic [49], Hepatoprotective [50], Anti-ulcer [51], Anti-asthmatic [52], Anti-fertility [53], Anti-convulsant, Anti-stress, Nootropic [20], Anti-parkinsonian [54], Anti-cancer [55], Antihyperlipidemic [56]

9. Clinical study on *Habb-e-Azaraqi*

Fathima et al. evaluated the efficacy and safety of *Habb-e-Azaraqi* in the management of diabetic peripheral neuropathy in patients with type 2 diabetes mellitus. A randomized single-blind standard controlled trial was carried out on 22 patients. Patients in the test group received *Habb-e-Azaraqi*, at a dose of 500 mg, twice a day, whereas the control group received Methylcarbylamine, 500 µg once a day for 45 days. The result revealed that the test drug is effective and safe in the management of diabetic peripheral neuropathy and no side effects or toxicity was observed during and after trial [57].

10. Toxicity

Ara et al., evaluate the acute toxicity of *Habb-e-Azaraqi* in rats as per OECD Guideline 425. At a dose of 2000 mg/kg bw no mortality was observed and therefore, the LD-50 of *Habb-e-Azaraqi* is considered > 2000 mg/kg in rats [58].

11. Conclusion

Herbs are used therapeutically all over the world to cure various types of diseases. Polyherbal formulations dominate as the largest segment, capturing a significant share of the overall herbal supplements and remedies worldwide. *Habb-e-Azaraqi* is considered a potent *Unani* formulation and is used in this system of medicine for several decades for various clinical pathologies, especially nervine and musculoskeletal disorders. In the compound formulation of *Habb-e-Azaraqi,* all three ingredients are *Muqawwi-ī-ʻasāb* (nerve tonic), *Muharrik-ī-aʻsāb* (nervine stimulant), *Munaffis-ī-balgham* (expectorant) and *Dāf-ī-tashannuj* (antispasmodic); can be used in neuromuscular disorders. However, preclinical and clinical studies are required by using different protocols to gather extensive knowledge of the formulation, especially to assure its use and effectiveness in *Fālij* (Hemiplegia), *Laqwa* (Facial palsy), *Raʻsha* (Tremor), *Waja' al-Mafāṣil* (Polyarthritis) as mentioned in classical Unani literature.

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References

1. Azhar M. Adverse Effect of Unani Pharmacopeial Formulation Habb-E-Shifa. J Pharmacovigil [Internet]. 2018;06(04):5-7. Available from: https://www.omicsonline.org/open-access/adverse-effect-of-unani-pharmacopeial-formulation-habbeshifa-2329-6887-1000269-107449.html https://doi.org/10.4172/2329-6887.1000269

2. Aleem M, Imran Khan M, Islam Usmani Q, Ahmad A. Review on Darunaj-aqrabi (Doronicum hookeri C.B. Clarke): an Unexplored Medicinal Plant of Unani System of Medicine. J AYUSH Ayurveda, Yoga, Unani, Siddha Homeopath [Internet]. 2020 Aug 2; 9(2):41-52. Available from: http://medicaljournals.stmjournals.in/index.php/JoAYUSH/article/view/2108 https://doi.org/10.37591/joayush.v9i2.2108

3. Rahman S, Jahan N, Makbul SAA, Ahmad M, Gani MA. Scientific appraisal of Unani concept of islah-e-advia (rectification/purification of drugs) and its importance. J Ethnopharmacol [Internet]. 2020 Aug https://doi.org/10.1016/j.jep.2020.112880

258(October 2019):112-880. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0378874119341170

4. Suhail S, Jamil SS, Jilani S, Jahangir U, Qamar MW. Habb-e-Suranjaan: A classical analgesic Unani formulation. Int J Adv Pharm Med Bioallied Sci. 2017; 2017:1-6.

5. Akhtar O, Rani S, Shamsi S. Need of Standardization of Habb: A Unani Medicine. J AYUSH Ayurveda, Yoga, Unani, Siddha Homeopath [Internet]. 2017 [cited 2021 Jan 10]; 6(2):37-44. Available from: www.stmjournals.com

6. Khan A. Qarabadeen E Azam (Urdu translation). New Delhi (India): Central Council for Research in Unani Medicine, Ministry of Health and Family Welfare, Govt. of India; 1996.

7. Kabiruddin M. Bayaz-e-Kabeer, Part II. New Delhi: Idara Kitabu-us-Shifa; 2010.

8. Anonymous. Qarabadeen Majeedi. 9th ed. New Delhi (India): (Waqf Hamdard) All India Unani Tibbi Confrence; 1986.

9. Anonymous. National Formulary of Unani Medicine part 1. first. New Delhi (India): Central Council for Research in Unani Medicine, Ministry of Health and Family Welfare, Govt. of India; 2006. 1-337 p.

10. Kabiruddin M. Al-Qarabadeen. New Delhi: CCRUM, Department of AYUSH. Ministry of Health and Family Welfare, Government of India; 2006.

11. Khan MS. Bayaz E Khas (Urdu Translation). New Delhi (India): Ejaz publishing house; 2006.

12. Anonymous. Physicochemical Standards of Unani Formulation, Part 2. New Delhi (India): Central Council for Research in Unani Medicine, Ministry of Health and Family Welfare, Govt. of India; 1987.

13. Behera MC, Mohanty TL, Paramanik BK. Silvics , phytochemistry and ethnopharmacy of endangered poison nut tree (Strychnos

nux - vomica L .) : A review. J Pharmacogn Phytochem. 2017; 6(5):1207-16.

14. Ahmad N, Fazal H, Abbasi BH, Farooq S, Ali M, Khan MA. Biological role of Piper nigrum L. (Black pepper): A review. Asian Pac J Trop Biomed. 2012; 2(3 SUPPL.):1-10. https://doi.org/10.1016/S2221-1691(12)60524-3

15. Yadav V, Krishnan A, Vohora D. A systematic review on Piper longum L.: Bridging traditional knowledge and pharmacological evidence for future translational research. J Ethnopharmacol [Internet]. 2020 Jan; 247:112255. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0378874119326443 https://doi.org/10.1016/j.jep.2019.112255

16. Shu G, Mi X, Cai J, Zhang X, Yin W, Yang X, et al. Brucine, an alkaloid from seeds of Strychnos nux-vomica Linn., represses hepatocellular carcinoma cell migration and metastasis: The role of hypoxia inducible factor 1 pathway. Toxicol Lett. 2013; https://doi.org/10.1016/j.toxlet.2013.07.024

17. Khan M, Siddiqui M. Antimicrobial activity of piper fruits. Indian J Nat Prod Resour. 2007;

18. AO C, AAP C, ATRD A, JRG D, KBF S, PIM C, et al. Neuroprotective effects of piperine, an alkaloid from the Piper genus, on the Parkinson's disease model in rats. J Neurol Ther [Internet]. 2015 Nov 2; 1(1):1-8. Available from: http://nobleresearch.org/Doi/10.14312/2397-1304.2015-1 https://doi.org/10.14312/2397-1304.2015-1

19. Chaudhary SK, Mukherjee PK, Maiti N, De Kumar A, Bhadra S, Saha BP. Evaluation of angiotensin converting enzyme inhibition and anti-oxidant activity of Piper longum L. Indian J Tradit Knowl. 2013; 12(3):478-82.

20. Juvekar M, Kulkarni M, Juvekar A. Anti-stress, nootropic and anticonvulsant potential of fruit extracts of Piper longum L. Planta Med. 2008; 74(09). https://doi.org/10.1055/s-0028-1084242

21. Yaqub S, Aftab M, Asif M, Yousuf PY. QUALITY ASSESSMENT OF UNANI POLYHERBAL FORMULATION "HABB-E-AZARAQI" BY CONTEMPORARY SCIENTIFIC PARAMETERS. Int J Pharm Sci Res. 2013; 4(9):3569-74.

22. Khan A. Muheet-i Azam, Vol 1. New Delhi (India): Central Council for Research in Unani Medicine, Ministry of Health and Family Welfare, Govt. of India; 2011.

23. Ghani M. Khazainul Advia (Urdu). New Delhi (India): Idara Kitab al Shifa; 2011.

24. Kabeeruddin M. Makhzanul Mufradat. New Delhi: Aijaz Publication; 2014. 392 p.

25. Khan A. Muheet-e-Azam, Vol 3. New Delhi (India): Central Council for Research in Unani Medicine, Ministry of Health and Family Welfare, Govt. of India; 2014.

26. Haleem A. Mufradat Azizi. New Delhi (India): Central Council for Research in Unani Medicine (CCRUM); 2009.

27. Patel K, Laloo D, Singh GK, Gadewar M, Patel DK. A review on medicinal uses, analytical techniques and pharmacological activities of Strychnos nux-vomica Linn.: A concise report. Chin J Integr Med. 2017; (221005):1-13. https://doi.org/10.1007/s11655-016-2514-1

28. Prakash O, Kumar A, Kumar P, Ajeet A. Anticancer Potential of Plants and Natural Products: A Review. Am J Pharmacol Sci. 2013; https://doi.org/10.12691/ajps-1-6-1

29. Abirami A, Sinsinwar S, Rajalakshmi P, Brindha P, Rajesh YBRD, Vadivel V. Antioxidant and cytoprotective properties of loganic acid isolated from seeds of Strychnos potatorum L. against heavy metal induced toxicity in PBMC model. Drug Chem Toxicol [Internet]. 2019 Oct 23; 1-11. Available from: https://www.tandfonline.com/doi/full/10.1080/01480545.2019.1681445 https://doi.org/10.1080/01480545.2019.1681445

30. Parida N. K., Sahu M. R., Debata P.C., Panda PK. Analgesic and anticonvulsant effects of extracts from the leaves of strychnos nux vomica Linn. | | Virtual Health Sciences Library. Hamdard Med [Internet]. 2011 [cited 2021 Jan 10];54(3):9-18. Available from: https://vlibrary.emro.who.int/imemr/analgesic-and-anticonvulsant-effects-of-extracts-from-the-leaves-of-strychnos-nux-vomica-linn-2/

31. Duddukuri GR, Brahmam AN, Rao DN. Suppressive effect of strychnos nux-vomica on induction of ovalbumin-specific IgE antibody response in mice. Indian J Biochem Biophys. 2008;

32. Shoba FG, Thomas M. Study of antidiarrhoeal activity of four medicinal plants in castor-oil induced diarrhoea. J Ethnopharmacol. 2001; https://doi.org/10.1016/S0378-8741(00)00379-2

33. Eldahshan OA, Abdel-Daim MM. Phytochemical study, cytotoxic, analgesic, antipyretic and anti-inflammatory activities of Strychnos nux-vomica. Cytotechnology. 2015; https://doi.org/10.1007/s10616-014-9723-2

34. Sanmugapriya E, Venkataraman S. Studies on hepatoprotective and antioxidant actions of Strychnos potatorum Linn. seeds on CCl4-induced acute hepatic injury in experimental rats. J Ethnopharmacol [Internet]. 2006 Apr; 105(1-2):154-60. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0378874105007440 https://doi.org/10.1016/j.jep.2005.10.028

35. Chitra V, Varma P VKRCH, Raju MVRK, Prakash KJ. Study of antidiabetic and free radical scavenging activity of the seed extract of Strychnos nuxvomica. Int J Pharm Pharm Sci. 2010;

36. Takooree H, Aumeeruddy MZ, Rengasamy KRR, Venugopala KN, Jeewon R, Zengin G, et al. A systematic review on black pepper (Piper nigrum L.): from folk uses to pharmacological applications. Crit Rev Food Sci Nutr. 2019; 59:S210-43. https://doi.org/10.1080/10408398.2019.1565489

37. Damanhouri ZA. A Review on Therapeutic Potential of Piper nigrum L. (Black Pepper): The King of Spices. Med Aromat Plants. 2014; 03(03).

https://doi.org/10.4172/2167-0412.1000161

38. Ahmad N, Fazal H, Abbasi BH, Rashid M, Mahmood T, Fatima N. Efficient regeneration and antioxidant potential in regenerated tissues of Piper nigrum L. Plant Cell, Tissue Organ Cult [Internet]. 2010 Jul 6; 102(1):129-34. Available from: http://link.springer.com/10.1007/s11240-010-9712-x https://doi.org/10.1007/s11240-010-9712-x

39. Samykutty A, Shetty AV, Dakshinamoorthy G, Bartik MM, Johnson GL, Webb B, et al. Piperine, a Bioactive Component of Pepper Spice Exerts Therapeutic Effects on Androgen Dependent and Androgen Independent Prostate Cancer Cells. Williams BO, editor. PLoS One [Internet]. 2013 Jun 18; 8(6):e65889. Available from: https://dx.plos.org/10.1371/journal.pone.0065889 https://doi.org/10.1371/journal.pone.0065889

40. Tasleem F, Azhar I, Ali SN, Perveen S, Mahmood ZA. Analgesic and anti-inflammatory activities of Piper nigrum L. Asian Pac J Trop Med. 2014; 7(S1):S461-8. https://doi.org/10.1016/S1995-7645(14)60275-3

41. Bukhari IA, Alhumayyd MS, Mahesar AL, Gilani AH. The analgesic and anticonvulsant effects of piperine in mice. J Physiol Pharmacol. 2013; 64(6). https://doi.org/10.1096/fasebj.27.1_supplement.660.5

42. Jeena K, Liju VB, Umadevi NP, Kuttan R. Antioxidant, Anti-inflammatory and Antinociceptive Properties of Black Pepper Essential Oil (Piper nigrum Linn). J Essent Oil Bear Plants [Internet]. 2014 Jan 2; 17(1):1-12. Available from: http://www.tandfonline.com/doi/abs/10.1080/0972060X.2013.831562 https://doi.org/10.1080/0972060X.2013.831562

43. Hritcu L, Noumedem JA, Cioanca O, Hancianu M, Postu P, Mihasan M. Anxiolytic and antidepressant profile of the methanolic extract of Piper nigrum fruits in beta-amyloid (1-42) rat model of Alzheimer's disease. Behav Brain Funct [Internet]. 2015 Dec 29; 11(1):13. Available from: http://behavioralandbrainfunctions.biomedcentral.com/articles/10.1186/s12993-015-0059-7 https://doi.org/10.1186/s12993-015-0059-7

44. Kumar S, Kamboj J, Suman, Sharma S. Overview for Various Aspects of the Health Benefits of Piper Longum Linn. Fruit. JAMS J

Acupunct Meridian Stud. 2011; 4(2):134-40. https://doi.org/10.1016/S2005-2901(11)60020-4

45. Vedhanayaki G, Shastri G V., Kuruvilla A. Analgesic activity of Piper longum Linn. root. Indian J Exp Biol. 2003; 41(6):649-51.

46. Vaghasiya Y, Nair R, Chanda S. Investigation of Some Piper Species for Anti-Bacterial and Anti-Inflammatory Property. Int J Pharmacol [Internet]. 2007 Aug 15; 3(5):400-5. Available from: https://www.scialert.net/abstract/?doi=ijp.2007.400.405 https://doi.org/10.3923/ijp.2007.400.405

47. Yende SR, Vrushali D. Sannapuri, Niraj S. Vyawahare, Uday N. Harle. Anti-rheumatoid activity of aqueous extract of Piper longum on Freunds Adjuvant-induced arthritis in rats' Evaluation of Polyhebal formulation for Rheumatoid Arthritis View project. Int J Pharm Sci Res [Internet]. 2010 [cited 2021 Jan 10]; 1(9):129-33. Available from: www.ijpsr.com

48. Nabi SA, Kasetti RB, Sirasanagandla S, Tilak TK, Kumar MVJ, Rao CA. Antidiabetic and antihyperlipidemic activity of Piper longum root aqueous extract in STZ induced diabetic rats. BMC Complement Altern Med. 2013; 13. https://doi.org/10.1186/1472-6882-13-37

49. Chaudhari GN, Kokate CK, Nimbkar AY. SEARCH FOR ANTHELMINTICS OF PLANT ORIGIN: ACTIVITIES OF VOLATILE PRINCIPLES OF ACORUS CALAMUS against ASCARIS LUMBRICOIDES. Anc Sci Life. 1981;

50. Sharma AK, Kumar S, Chashoo G, Saxena AK, Pandey AK. Cell cycle inhibitory activity of Piper longum against A549 cell line and its protective effect against metal-induced toxicity in rats. Indian J Geo-Marine Sci. 2014; 51(5):358-64.

51. Agrawal AK, Rao C V., Sairam K, Joshi VK, Goel RK. Effect of Piper longum Linn, Zingiber officianalis Linn and Ferula species on gastric ulceration and secretion in rats. Indian J Exp Biol. 2000; 38(10):994-8.

52. Manoj P, Soniya E, Banerjee N, Ravichandran P. Recent studies on well-known spice, Piper longum Linn. Indian J Nat Prod Resour. 2004;

53. Lakshmi V, Kumar R, Agarwal SK, Dhar JD. Antifertility activity of Piper longum Linn. in female rats. Nat Prod Res. 2006; 20(3):235-9. https://doi.org/10.1080/14786410500045465

54. Bi Y, Qu PC, Wang QS, Zheng L, Liu HL, Luo R, et al. Neuroprotective effects of alkaloids from Piper longum in a MPTP-induced mouse model of Parkinson's disease. Pharm Biol. 2015; 53(10):1516-24. https://doi.org/10.3109/13880209.2014.991835

55. Ovadje P, Ma D, Tremblay P, Roma A, Steckle M, Guerrero J-A, et al. Evaluation of the Efficacy & Biochemical Mechanism of Cell Death Induction by Piper longum Extract Selectively in In-Vitro and In-Vivo Models of Human Cancer Cells. Filleur S, editor. PLoS One [Internet]. 2014 Nov 17; 9(11):e113250. Available from: https://dx.plos.org/10.1371/journal.pone.0113250 https://doi.org/10.1371/journal.pone.0113250

56. Kumar S, Sharma S, Vasudeva N. Screening of antidiabetic and antihyperlipidemic potential of oil from Piper longum and piperine with their possible mechanism. Expert Opin Pharmacother [Internet]. 2013 Sep 23; 14(13):1723-36. Available from: http://www.tandfonline.com/doi/full/10.1517/14656566.2013.815725 https://doi.org/10.1517/14656566.2013.815725

57. Fathima N, Anwar M, Farooque M, Ahmed T. Evaluation of a Unani formulation, in diabetic peripheral neuropathy: A randomized single blind standard controlled study. Asian J Med Clin Sci. 2012; 1(3).

58. Ara SA, Viquar U, Zakir M, Urooj M, Kazmi MH, Husain GM. Preclinical toxicity evaluation of Habb-e-Azaraqi : A nux-vomica-based traditional Unani polyherbal formulation in rats . Tradit Kampo Med. 2020; 1-13. https://doi.org/10.1002/tkm2.1263