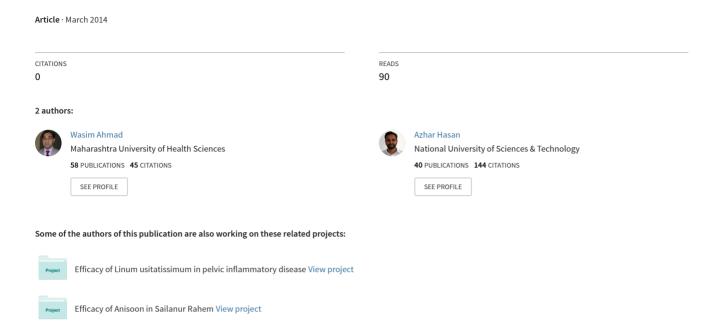
Azadirachta indica Linn. - An Overview



Azadirachta indica Linn. - An Overview

Wasim Ahmad¹, Azhar Hasan² and Tahera Tarannum²

1 Department of Ilmul Advia; 2 Department of Ilmul Qabalat wa Amraze Niswan, Mohammadia Tibbia College and Assayer Hospital, Mansoora, Malegaon, Nashik (MS) E-mail: drwasim@gmail.com

Neem (Azadirachta indica) is a tropical, large size, evergreen tree. The tree is regarded as the Village Dispensary in India because of the use of all its parts for various ailments in the indigenous systems of medicine. It has shown diverse biological and pharmacological activities. Keeping in view the medicinal important of the tree in Tibb-e-Unani (Unani Medicine), an attempt has been made to review the available literature on its medicinal uses and scientific studies

Keywords: Azadirachta indica; Neem; Unani Medicine

Introduction

Neem (Azadirachta indica A. Juss. Family-Meliaceae) is a large size tree¹. It is a tropical evergreen tree that grows up to 25 m high² with almost straight trunk. The tree is regarded as the Village Dispensary in India because of the use of all its parts for various ailments in the indigenous systems of medicine³. The tree has rough dark brown bark with wide longitudinal fissures separated by flat ridges. The leaves are compound, imperipinnate, each comprising 5-15 leaflets that are arranged in alternate pairs with terminal leaflets. The compound leaves are themselves alternating with one another. The thin, lanceolate leaflets measure about 6 cm long and 2 cm broad². The leaves are crowded near the end of branches. They are acuminate, serrate, glabrous, dark green above and pale beneath with the characteristic odour and very bitter taste. The plant bears many flower panicles, mostly in the leaf axils. The sepals are ovate and about 1 cm long with sweet scented, white, oblanceolate petals2. They are hermaphrodite. Calyx is 5 lobed. Petals 5, much exceeding the calyx, free, imbricate. Stamina tube a little shorter than the petals, cylindric, widening abive, 9-10 lobed at the apex. The lobes are truncated, against slightly toothed. Anthers are within the tube opposite to and shorter than the lobes. Ovary is 3 celled. Style is elongate and slender. Stigma is shortly cylindric, 3 lobed. Ovules are 2 in each cell and collateral⁴. The tree produces yellow drupes that are ellipsoid and glabrous, 12-20 cm long². Flowers are numerous, white and honey scented. The tree has 1-seeded, ovoid oblong and smooth fruit that becomes yellow when ripe^{1,3}. The seed is ellipsoid, cotyldones are thick, flashy and cordate at base. Radical is superior⁴. Every part of the tree is bitter in taste but pulp of ripe fruit is sweet. The tree also yields a gum which is soluble in water. The gum and stem bark are used as colouring agent. The tree may survive up to thousand of years. The wood of that tree gives aromatic odour like wood of sandal⁵. The gum has resemblance with acacia gum but less mucilaginous⁶. Various parts of the tree such as flowers, fruits, leaves, bark, seeds, latex and twigs are commonly being used for the treatment of various diseases in the traditional system of medicine^{1,3,7,8}.

Vernaculars

The tree is known by different vernacular names: Neeb, Neem (Arabic); Nimba, Nimbaka (Ayurvedic); Nim gachh (Bengali); Balnimb, Nim (Bombay); Margosa tree, Indian lilac, Nim tree, Indian Azadirech, Coral tree (English); Malba, Limba (Gujrati); Nim, Nimb

(Hindi); Limba (Maharashtra); Arytikta, (Malyalam); Neem, (Nepali); Neeb, Neem, Azad darachte hindi, Neeb (Persian); Namb, Arishta (Sanskrit); Vembu (Siddha); Aazaad–darakht–ul–hindi (Unani) and Neem (Urdu) 1-5,9-15.

Distribution

It is native to India and commonly cultivated throughout the country¹. It grows wild in sub-Himalayan Tract and forests of other areas³. This tree is found elsewhere in hot climate¹⁶, such as Indonesia and Australia⁸. It grows in much of Southeast Asia and West Africa and more recently the Caribbean and South and Central America².

It is estimated that India has about 1,38,00,000 neem trees with the potential to produce over 83,000 tonnes of neem oil and 4,13,000 tonnes neem seeds. Single neem tree yield 37-50 kg fruits per year. Fourty kilograms of fresh fruits yield nearly 24 kg of dry fruits (60%). It has been reported that a 50 year old tree yields 51 kg fuel wood in aride areas of Rajasthan. The neem wood is generally considered to be highly resistant to fungi and insect attack and is durable even when used outdoors¹⁷.

Actions

The drug Neem (Azadirachta indica) is described in detail in ethnobotanical and classical Unani literature and various actions of the flower, fruit, leaf, bark, seed and latex of the tree have been reported such as abortificient, antioestrogenic, antiascariasis, analgesic. antibacterial. antitussive. antifertility. antifilarial, anthelminthic, antiinflammatory, antimalarial, antimycobacterial, antinematodal, antipyorrhoea, antipyretic, antiparasite, antiseptic, antispasmodic, antispermatogenic, antitrichomonal, antitumour, antiulcer, antiviral, antibilious, antidiabetic, antidote, antiemetic, antimicrobial, antiphlegmatic, antifungal, antiprotozoal, antiseptic, antiperiodic, aphrodisiac, astringent, blood purifier, CNS depressant. carminative, concoctive, demulscent, diuretic, emmenogouge, emollient, expectorant, hypocholestrolemic, hypoglycaemic, hypotensive, insecticidal, larvicidal, laxative, liver tonic, pesticidal, purgative, resolvent, sedative, spermicidal and stomachic 1-15,17-22.

Medicinal Uses It is therapeutically used in various diseases such as acne, amenorrhoea, ascites, atonic dyspepsia, bad smell of vulva, biliousness, bleeding and itching of piles, burning of the body, chlamydia trachomatus infection, chronic fever, chronic malaria, conjunctivitis, contraceptive, diabetes, earache, eczema, erysipelas, fatigue, gastric ulcer, helminthiasis, heart burn. gingivitis, hemiplegia, human papilloma virus-16, infection of female genital tract, intermittent fever, internal parasite, internal tumour, itching, jaundice, leprosy, leucoderma, leucorrhoea, liver disorder, long standing ulcers, loss of appetite, oedema, paralysis, periodic fever, piles, rheumatism, scabies, skin diseases, skin ulcer, snake bite and scorpion sting, syphilis, thirst, toothache, urinary discharge and vomiting. There is no side effect or health hazards are known in conjunction with administration of designated therapeutic dosage1-8,11-14,17,18,20,22,23

Phytochemistry

mostly 100 compounds, About protolimonoids triterpenoids of (protolimonoids (or meliacins or meliacins). tetranortriterpenoid-ytetranortriterpenoids), C butenolides. ring secohvdroxy secotetranortriterpenoids and ring C tetranortriterpenoid-y- hydroxy butenolides, pentanortriterpenoids, a hexanortriterpenoid apart from a few nontriterpenoid constituents have been reported from various parts as detailed below:

Azadirachtin, azadirachtol, azadirachnol, deacetyl-azadirachtinol (≡3-tigloylazadirachtol), azadiradione, an isomer of epoxyazadiradione, 17-epi and 17β-hydroxyazadiradione, azadirone, gedunin, 7-hydroxygedunin, melianone, nimbiol, nimboeinol (7-acetoxy-7-hydroxyazadiradione), nimocin, 7-deacetoxynimolicinol, nimolinone; nimbochalcin and nimbocetin; 21,23:24,25-diepoxytirucall-7-en-21-ol salannin (fruits). Kernels yield about 40.0-

48.9% of the oil (Oil of Margosa) and contain high amount of tocopherol, arachidic, linoleic, margosic, myristic, oleic, palmitic and stearic azadirone, acids. azadiradione. epoxyazadiradione (nimbinin) although their specific rotations differ widely), gedunin, desacetyl gedunin, meldenin, meliatriol, nimbin, nimbinene, 6-desacetyl nimbinene, nimbidin, nimbidiol, 6-O-acetylnimbandiol, nimbidic acid. salannin, 3-desacetylsalannin, salannol and its acetate, salannolide, vepinine, vilasinin, 1,3diacetylvilasinin, 1-tigloyl-3-acetyl-vilasinin and tiglic acid (seed oil); in addition, azadirachtin. 22,23-dihydro-23-β-methoxyazadirachtin (vepaol) and its C-23 epimer (isovepaol), 7-desacetyl-7-benzoyl derivatives of azadirone, azadiradione, epoxyazadiradione, 2-dihydroepoxyazadiradione, 18. diepoxyazadiradione, 7-desacetyl-7-benzoylgedunin, acetylneotrichilenone, nimbidinin, nimbidin, salannic (nimbidic) acid(seeds); benzyl alcohol, β-sistosterol; thioamyl alcohol; arachidic, behenic, linoleic, oleic, palmitic and stearic acids; kaemferol and its 3-glucoside, quercetin-3-galactoside myricetin-3-Land arabinoside; azadirachtin and margosene (flowers): azadirachtin, azadirachtanin, azadirone, azadiradione and epoxyazadiradione. isoazadirolide, nimbandiol, nimbinene, desacetylnimbinene, nimbin, nimbocinolide, isonimbocinolide, nimbolide. nimocinolide. isonimocinolide. nimocinone, dehydrosalannol, kaempferol-3-O-β-glucoside, myricetin and its 3'-L-arabinoside (melictrin), 3-O-α-L-rhamnoside and 3-O-rutinoside. quercetin, its 3-galactoside, 3-O-L-rhamnoside and 3-O-rutinoside, nimbaflavones, scopoletin, β -sitosterol and its β -D-glucoside, amino acids, B-carotene. carbohydrates, n-hexacosanol. nonacosanol, protein and vitamins (leaves); tannin, bakalactone, β-sitosterol and glucoside, 24-methylene-cycloartenol, 4, 14-αdimethyl-5- α -ergosta-8,24 (28)-dien-3 β -ol, 4 α methyl-5α-ergosta-8,24(28)-dien-3β-ol. nimatone, nimbinene, 6-desacetyl nimbinene, nimbolins A and B (heartwood); vanillic acid, catechol, campesterol, stigmasterol, sitosterol, β-amyrin, lupeol, nimbin, nimbidin, nimbinin, sugiol, kulinone, kulactone, kulolactone, methyl

kulonate, 6β-hydroxy-4-stigmasten-3-one and 6β-hydroxy-4-campesten-3-one (stem bark): gedunin, 7-deacetoxy-7-oxogedunin, fraxinellone, nimbolin A and cycloeucalenone, melianin A and melianin B (wood); margosinolide, isomargosinolide, desacetylnimbinolide desacetvl isonimbinolide (twigs): cycloeucalenol, 24methylene cycloartenol and β-sitosterol (wood oil); nimbiol, sugiol and nimbosterol (trunk bark); nimbolins A and B (trunk wood); 24-methylene-cycloartenol, 24methylene cycloartenone. cycloeucalenol, cycloeucalenone, 4-campesten-3-one. stigmasten-3-one, trans-cinnamic and vanillic acids (root); nimbin and nimbidin (root bark); besides aesculetin, campesterol, 6-hydroxy-7methoxy-coumarin, 4α,6α-dihydroxy-A-homoazadirone, isomeldenin, meldenindiol, acetoxy-meliacin, 6-O-acetylnimbandiol, desacetylnimbin, nimocinol, isonimolicinolide and nimolinolic acid have been isolated from various parts of the tree³.

Pharmacological Studies

A number of studies have been carried out on various parts of Neem (*Azadirachta indica*) in recent years showing the diverse pharmacological effect. These are mentioned as follows:

Analgesic

Antinociceptive effects of Neem leaf extract and its interaction with morphine and to delineate the probable site of action of Neem leaf extract using an opioid antagonist, naloxone has been investigated. The results of the present study revealed the antinociceptive effect of neem leaf extract in the pain model of the tail-flick test due to thermal stimulation²⁴.

Antibacterial

Neem oil was evaluated as a preventive against leptospiral infection (Leptospiricidal activity) through skin. Neem oil was found as an effective, antibacterial film on skin that prevents the portal entry of bacteria²⁵.

Anticancer

A study reported that an ethanolic extract of *Azadirachta indica* has been shown to cause cell death of prostate cancer cells (PC-3) by inducing apoptosis as evidenced by a dose-

dependent increase in DNA fragmentation and a decrease in cell viability²⁶.

Antioxidant

Leaves, fruits, flowers and stem bark extract from the Siamese Neem tree (Azadirachta indica var. siamensis) have been demonstrated to possess antioxidant activity in vitro. The results showed that aqueous extract of leaf, ethanolic extract of flower and stem bark exhibited higher free radical scavenging effect on the DPPH assay with 50 percent scavenging activity at 26.5, 27.9 and 30.6 microg/ml, respectively²⁷.

80% ethanolic extract of the leaves of Azadirachta indica were examined on drug metabolizing Phase-1 and Phase-2 enzymes, antioxidant enzymes, glutathione content, lactate dehydrogenase, and lipid peroxidation in the liver of 7 week old Swiss albino mice. Anticarcinogenic potential of Azadirachta indica leaf extract was also studied. The primary findings revealed its potential to induce only the Phase-2 enzyme activity associated mainly with carcinogen detoxification in liver of mice²⁸.

Antispermatogenicity | Antifertility

A study reported the antispermatogenicity of leaves of *Azadirachta indica* in seminiferous epithelium of rats. Damaged seminiferous tubules and abundance of vacuoles of varying size were observed in leaf treated rats. Total count of spermatocytes, spermatids and Leydig cells were reduced²⁹.

Effect of aqueous leaf extract of neem on the male reproductive organs of the Parkes (P) strain mice was investigated. The results revealed that treatment with neem leaf extract caused reversible alterations in the male reproductive organs of P mice³⁰.

Effect on ovary and uterus

Bhargava et al., (2005) reported that 50% ethanolic extract of stem bark of Azadirachta indica caused remarkable changes in biochemical constituents in ovary and uterus of cyclic rats³¹.

Gastric Ulcer healing

A study reported the ulcer healing activity of *Azadirachta indica* in gastric ulcers induced by acetic acid and HCL. The results clearly revealed that in both, normal and

NIDDM rats, *Azadirachta indica* significantly decreased blood glucose level. However, AIE (500 mg/kg) showed significant anti-ulcer and ulcer-healing activities in normal and NIDDM rats³².

Ulcer protective/healing actions of Azadirachta indica leaves was studied on various parameters of offensive acid-pepsin sectreation in 4 hr pylorus ligation, pentagastrin stimulated acid secretion and gastric mucosal proton pump activity and defensive mucin secretion including life span of gastric mucosal cells in rats. The results suggest that the ulcer protective activity of AIE may be due to its anti-secretary and proton pump inhibitory activity rather than on defensive mucin secretion³³.

Hepatoprotective

Koul et al., (2007) evaluated preventive effect of Azadirachta indica against diethylnitrosamine induced hepatotoxicity in male Balb/c mice. Aqueous leaf extract pretreatment showed protective effects against NDEA induced toxicity³⁴.

Hypocholestrolemic

Total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), triglyceride (TG) and C-reactive protein (CRP) were evaluated at week 0, 2, 4, 6 and 8 in animals. The control group (C) cholesterol control group (CC), cholesterol-fed groups treated with Neem (Azadirachta indica) leaf extract at doses of 50 and 300 mg/kg/day orally (N1 & N2), respectively. Neem extract treated TC. LDL and TG levels remained within the normal range similar to group C and CRP concentrations were lowered but HDL levels were not. Association between CRP and serum lipid concentrations is directly proportionate. The result clearly reveals that it has significant lipid lowering activity³⁵.

Hypoglycaemic

A study reported that the extract from *Azadirachta indica* was investigated as a potential hypoglycaemic effect. The extract exhibited hypoglycaemic activity without altering the serum cortisol concentration. It was apparently safe for therapeutic use, as lipid-peroxidation was not enhanced in liver, the primary target organ of a drug metabolism³⁶.

A study reported the protective role of extracts of Neem seeds in diabetes caused by streptozotocin in rats. Effect of petroleum ether extracts of kernel and husk of neem (Azadirachta indica) seeds were investigated on the prevention of oxidative stress caused by streptozotocin (STZ). Results suggest that husk and kernel prevent oxidative stress caused by STZ in heart and erythrocytes³⁷.

Conclusion

Neem (Azadirachta indica) has been in use since times immemorial to treat wide range of indications. It has been subjected to quite extensive phytochemical, experimental and clinical investigations. Experimental studies have demonstrated its gastric ulcer, analgesic, antifungal, antifertility, antibacterial, antioxidant, hypoglycemic, hypocholestrolemic and hepatoprotective effects. The scientific studies have proved the claims of traditional systems of medicine. However, further, detailed clinical research appears worthwhile to explore the full therapeutic potential of this plant in order to establish it as a standard drug.

Looking upon wide prospects and potential of Neem tree for various purposes, it is worthwhile to cultivate the tree at large scale especially on unproductive and wasteland.

Acknowledgement

The authors are thankful to Dr. Ghufran Ahmad, Department of Ilmul Advia, A.K. Tibbiya College, Faculty of Unani Medicine, AMU, Aligarh for moral encouragement and support.

References

- Anonymous. (1992). Standardisation of Single Drugs of Unani Medicine, Part-II, CCRUM, New Delhi, pp. 79-83.
- Ross, A.I. (2001). Medicinal Plants of the world, Vol. II, Humana Press, Totowa, New Jersey, pp. 81-82, 86-97.
- 3. Chatterjee, A. & Pakrashi, S.C. (1994). The Treatise on Indian Medicinal Plants, Vol. III, CSIR, New Delhi, pp. 76-79.
- Kirtikar, K.R. & Basu, B.D. (1991). Indian Medicinal Plants, Vol. I, Connaught palace, Dehradun, pp. 536-541.

- 5. Ghani, M.N. (YNM). Khazainul Advia, Idara Kitab al Shifa, Dariya Ganj, New Delhi, pp. 1330-1334.
- 6. Khan, M.A. (1313H). Moheet-e-Azam, Vol. II, Nizami Press, Kanpur, pp. 176-179.
- 7. Evans, W.C. (2002). Trease and Evans Pharmacognosy, 15th Edn, Harcourt Publishers Limited, Edinburgh, pp. 412, 470, 476, 491.
- 8. Thomas, F. (2000). PDR for Herbal Medicine, Medical Economic Comp, New Jersey, p. 539.
- Aawan, M.H. (1984). Kitabul Mufradat Al-Maroof Ba Khawasul Advia Batarz-e-Jadeed, published by Shaikh Ghulam Ali and Sons (Pvt.) Ltd., Lahore, pp. 510-511.
- 10. Ahmad, S. (1314H). Khazainul Malook, Vol. I, Matba Nizami, p. 255.
- 11. Chopra, R.N. Nayer, S.L. & Chopra, I.C. (1956). Glossary of Indian Medicinal Plants, CSIR, New Delhi, pp. 31-32.
- 12. Khare, C.P. (2004). Encyclopaedia of Indian Medicinal Plants, Springer Berlin, Heideberg, New York, pp. 86-88.
- Nabi, M.G. (1920). Makhzan Mufradat wa Murakkabat maroof ba Khawasul Advia, Matba Iftekhar, Delhi, p. 228.
- 14. Nadkarni, A.K. (1982). Indian Materia Medica, Vol. I, Bombay Popular Prakashan, Mumbai, pp. 776-783.
- 15. Prajapati, Prohit, Sharma and Kumar, (2003). Handbook of Medicinal Plants, published by Agrobois, p. 79.
- Hooker, J.D. (1990). Flora of British India, Vol. I, Connaught palace, Dehradun, p. 544.
- Anonymous. (2004). The Wealth of India A Dictionary of Indian Raw Materials and Industrial Products, First Supplement Series, Vol. I; A-Ci, CSIR, New Delhi, pp. 107-111.
- Dey, A.C. (1988). Indian Medicinal Plants Used in Ayurvedic Preparations, New Connaught palace, Dehradun, pp. 165-166.
- 19. Dutt, N.B. (1979). Commercial drugs of India, Bishen Singh Mahendra Pal Singh, Dehradun, pp. 166-167.
- 20. Husain, M.M. (1285H). Makhzanul Advia maa Tohfatul Momineen, Matba Mohammadi, Delhi, pp. 632-633.
- 21. Rastogi, R.P. & Mehrotra, B.N. (1999). Compendium of Indian Medicinal Plants, Vol. II, CDRI, Lucknow, pp. 87-90.
- 22. Waring, E.J. (1982). Remarks on the uses of some of the bazaar medicines and common

- medicinal plants of India, Bishen singh Mahindra Pal Singh, Dehradun, pp. 105-107.
- 23. Takmili, I.H. (YNM). Advia Unani, Nizami Press, Lucknow, p. 79.
- Patel, J.P. Hemavati, K.G. & Bhatt, J.D. (2005). Study of the antinociceptive effect of Neem leaf extract and its interaction with morphine in mice, *Indian J Pharmacol*, 37(1), 37-38.
- Kurian, P. & Thomas, M. (2004). Neem oil-A preventive against leptospiral infection in man, *Aryavaidyan*, 18(1), 41-44.
- Kumar, S. Suresh, P.K. Vijayababu, M.R. Arunkumar, A. & Arunakaran, J. (2006). Anticancer effects of ethanolic Neem leaf extract on prostate cancer cell line (PC-3), J Ethnopharmacol, 105(1-2), 246-250.
- Sithisarn, P. Supabphol, R. & Gritsanapan, W. (2005). Antioxidant activity of Siamese Neem tree, *J Ethnopharmacol*, 99(1), 109-112.
- 28. Dasgupta, T. Banerjee, S. Yadava, P.K. & Rao, A.R. (2004). Chemopreventive potential of *Azadirachta indica* (Neem) leaf extract in murine carcinogenesis model systems, *J Ethnopharmacol*, 92(1), 23-36.
- Aladakatti, R.H. & Ahmed, R.N. (2006). *Azadirachta indica* A. juss induced changes in spermatogenic pattern in albino rats, *J Nat Rem*, 6(1), 62-67.
- Mishra, R.K. & Singh, S.K. (2005). Effect of aqueous leaf extract of *Azadirachta* indica on the reproductive organs in male mice, *Indian J Exp Biol*, 43(11), 1093-1103.
- 31. Bhargava, V. & Jain, S.M. (2005). Effect of bark extract of *Azadirachta indica* on biochemical constituents in ovary and uterus of cyclic rats, *Flora and Fauna*, 11(2), 203-207.

- Dorababu, M. Prabha, T. Priyambada, S. Agrawal, V.K. Aryya, N.C. & Goel, R.K. (2004). Effect of *Bacopa monniera* and *Azadirachta indica* on gastric ulceration and healing in experimental NIDDM rats, *Indian J Exp Biol*, 42(4), 389-397.
- 33. Dorababu, M. Joshi, M.C. Bhawani, G. Mohan Kumar, M. Chaturvedi, A. & Goel, R.K. (2006). Effect of aqueous extract Neem (*Azadirachta indica*) leaves on offensive and diffensive gastric mucosal factors in rats, *Indian J Physiol and Pharmacol*, 50(2), 241-249.
- 34. Koul, A. Binepal, G. & Gangar, S.C. (2007). Impediment of diethylnitrosamine induced hepatotoxicity in male Balb/c mice by preatment with aqueous *Azadirachta indica* leaf extract, *Indian J Exp Biol*, 45(4), 359-366.
- 35. Zuraini, A. Vadiveloo, T. Taufik Hidayat, M. Arifah, A.K. Sulaiman, M.R. & Somchit, M.N. (2007). Effects of Neem (*Azadirachta indica*) leaf extracts on lipid and C-reactive protein concentration in cholesterol-fed rats, *J Nat Rem*, 6(2), 109-114.
- 36. Gholap, S. & Kar, A. (2005). Regulation of cortisol and glucose concentration of some plant extracts in mice, *J Med Arom Plant Sci*, 27(3), 478-482.
- 37. Gupta, S. Kataria, M. Gupta, P.K. Murganadan, S. & Yashroy, R.C. (2004). Protective role of extracts of Neem seeds in diabetes caused by streptozotocin in rats, *J Ethnopharmacol*, 90(2-3), 185-189.