Melia azedarach L.
(Meliaceae)

(**Syns.**: *M. japonica* G. Don.; *M. sempevirens* Swartz; *M. toosendan* Sieb. et Zucc.)

Abstract

It is an ornamental deciduous tree often found on street sides in warmer countries, such as India, China, Indonesia, Iran, Syria, Guiana, Madagascar, and Antilles. It is one of the most commonly used plants for various diseases, especially skin diseases, by tribal people throughout the world. Fresh leaves boiled in water are used by women to grow and strengthen their hair. The plant has deobstruent, resolvent and alexipharmic properties. Flowers and leaves are applied as poultice to relieve nervous headaches, and internally, the leaves' juice is administered as anthelmintic, antilithic, diuretic and emmenagogue, and is thought to resolve cold swellings, and expel the humours which give rise to them. The bark and leaves are used externally and internally in leprosy and scrofula. A poultice of flowers kills lice and cures eruptions of the scalp. The fruit is poisonous, but nevertheless is prescribed in leprosy and scrofula, and is worn as a necklace to avert contagious diseases. The root bark was in the secondary list of United States Pharmacopoeia as anthelmintic. The flowers, leaves and fruits are recommended in Iranian traditional medicine as a remedy to normalize temperament in elderly, for brain obstruction, intestinal worms, kidney stones, leprosy, vitiligo, purulent sores, as an antidote to toxins, diuretic, emmenagogue, hair growth inducer and to kill lice. A series of limonoids, triterpenes, steroids and flavonoids and limonoid glycosides, including salannin, meldenin, melianoninol, melianol, meliandiol, vanillin, vanillic acid, ring C-seco limonoids, lignanes, and tirucallane triterpenoids have been isolated from the fruits. Methanol flower extract healed *S. aureus* caused skin infection in rabbits, an effect that was comparable to neomycin. The fruit extract showed higher antibacterial effect against Gram-negative bacteria, while the leaf extract was more effective on *C. albicans*. Various bark extracts have shown significant *in vitro* antibacterial activities against a number of pathogenic bacteria. Fresh green leaves extracts contain an antiviral factor that inhibits replication of several

S. Akbar, *Handbook of 200 Medicinal Plants*,
https://doi.org/10.1007/978-3-030-16807-0_124

animal viruses, protects neonatal mice against Tacaribe virus inoculation-induced lethal encephalitis, and protects offspring of nursing mothers from developing viral encephalitis.

Keywords
Agrión · Azédarach · Azufeifo · Bakayen · Chinaberry · Dharek · Haralshajr · Liàn · Mahanimba · Tespih ağacı

Vernaculars: **Urd.**: Bakayen; **Hin.**: Bakayen, Dharek, Ghora neem; **San.**: Arishta, Himadruma, Mahanimba, Parvatanimba vraksha; **Ben.**: Bakarjam, Ghora-nim, Hebbevu, Maha-nimb; **Mal.**: Malaivembu, Malai-veppam; **Mar.**: Bakana-nimb, Goru-nima, Vilayati-nimb; **Tam.**: Kattu vembhu, Malaivembu, Malai-veppam; **Tel.**: Konda-vepa, Nimbarun, Turukavepa, Vepa-manu; **Ara.**: Habb-ul-ban, Haralshajr, Harbeet, Shajratal-harra; **Chi.**: 楝树, Chuan lian, Chuan liang zi, Ku-lian, Kulianpi, Liàn, Tz'u-hua shu; **Cze.**: Zederach hladký; **Dan.**: Paternostertræ; **Dut.**: Galbessen, Kralenboom, Paternosterboom; **Eng.**: Cape syringa, Chinaberry tree, Chinese um árbol de los rosarios brella tree, Persian lilac, Pride of India; **Fre.**: Acacie d'Égypte, Arbre à chapelets, Azédarach, Cornier des Indes, Faux sycomore, Laurier grec, Lilas de Perse, Lilas des Antilles, Lilas des Indes, Margousier, Patenôtre; **Ger.**: Indischer zedrachbaum, Paternosterbaum, Persischer flieder, Zedarachbaum; **Ita.**: Albero da rosari, Albero dei paternostri, Albero della pazienza, Perlaro, Sicomoro falso; **Jap.**: Sendan; **Kor.**: Meol gu seul na mu; **Maly.**: Mullayvempu; **Nep.**: Bakenu, Khaibasi; **Per.**: Aaraatos takhak, Azad derakht, Taghak, Tak, Zanzalakht; **Pol.**: Miotla; **Por.**: Agrião, Amargoseira, Amargoseira-bastarda, Amargoseira-do-himaláia, Azufeifo, Árvore-santa, Árvore-dos-rosários, Azedarague, Cinamomo, Falso-sicómoro, Jazmim-de-caiena (Br.), Lilás-das-índias, Méliados-himaláias, Sicómoro-bastardo; **Spa.**: Agriaz, Agrión, Árbol de cuentas, Árbol del paraíso, Árbol de los rosarios, Bolillero, Canelo, Cinamomo, Falso sicomoro, Jaboncillo, Lilo de China, Lilo de Persia, Jacinta; **Swe.**: Zedrak; **Tag.**: Bagalunga, Balgango, Paraiso; **Tha.**: Hian, Lian, Lian bai yai; **Tur.**: Tesbih ağacı, Tespih ağacı; **Vie.**: Cây xoan, Sâ dông.

Description: It is an ornamental deciduous tree often found on street sides in warmer countries, such as India, China, Indonesia, Iran, Syria, Guiana, Madagascar, and Antilles. It grows up to 20 m tall; leaves are long-petioled, two or three-times compound alternate, pinnate, leaflets are dark green above and lighter green below, opposite, glabrous when mature, oval-lanceolate, acuminate, margin irregularly dentate. Flowers grow in clusters, are small, odoriferous, elongate, purple, 1 cm long with five pale purple or liliac petals (April–May); fruit a glabrous drupe, marble-sized, light-yellow at maturity and gradually becoming wrinkled and almost white (September to October).[LXXIX] Fresh root-bark is thick and rather spongy, the

Fig. 1 *Melia azedarach*, Leaves, Flowers and Berries, Anna Anichkova, WikimediaCommons; Share Alike 3.0 Unported CC BY-SA 3.0, https://commons.wikimedia.org/wiki/File:Melia_azedarach_01434.jpg; https://creativecommons.org/licenses/by-sa/3.0/deed.en

Fig. 2 *Melia azedarach*, Berries, J.M. Garg, WikimediaCommons; ShareAlike 3.0 Unported CC BY-SA 3.0, https://commons.wikimedia.org/wiki/File:Indian_Grey_Hornbill_(Ocyceros_birostris)_eating_Bakain_(Melia_Azadirachta)_berries_at_Roorkee,_Uttarakhand_W_IMG_9016.jpg; https://creativecommons.org/licenses/by-sa/3.0/deed.en

external surface scabrous and warty, of a dark-brown color with irregular ridges; the inner surface is white, taste acrid, nauseous, astringent and slightly bitter.[XL] It is very similar to neem (*Azadirachta indica*) except that its fruit pulp is not bitter like that of neem[1] (Figs. 1 and 2).

Actions and Uses: It is one of the most commonly used plants for various diseases, especially skin diseases, by tribal people throughout the world [1, 7, 35, 46]. Fresh leaves boiled in water are used by women to grow and strengthen their hair.[LXIX] The plant has deobstruent, resolvent and alexipharmic properties. Flowers and

[1]Tayyab M: Personal Communication.

leaves are applied as poultice to relieve nervous headaches, and internally, the leaves' juice is administered as anthelmintic, antilithic, diuretic and emmenagogue, and is thought to resolve cold swellings, and expel the humours which give rise to them. The bark and leaves are used externally and internally in leprosy and scrofula.[XXI,LXXXI,CV] A poultice of flowers kills lice and cures eruptions of the scalp. The fruit is poisonous, but nevertheless is prescribed in leprosy and scrofula, and is worn as a necklace to avert contagious diseases. The root bark has a bitter, nauseous taste and yields its virtues to boiling water. One hundred ten (110 g) of fresh bark boiled in about a liter of water until the volume was reduced to half; the dose for a child was one tablespoonful every three hours until the bowel and stomach were cleared, or twice daily for several days followed by a cathartic.[XL] *Unani* physicians describe it as blood purifier, analgesic, antihemorrhoidal, wound healer, anthelmintic, antipyretic for chronic fevers and antiperiodic; and use the leaves and bark in diseases like leprosy and leucoderma, and externally the leaves decoction for fomentation and poultice for boils and sores. Bark decoction is used to kill and expel intestinal worms.[LXXVII] Externally, the seed oil is used as an antiseptic for indolent sores and ulcers, for rheumatism and skin diseases such as ringworm and scabies, and internally, the oil is used in malaria fever and leprosy [28], as antidiabetic, spermicidal, and antifertility agent [44]. Leaves juice is also used in the Philippines as anthelmintic, antilithic, diuretic and emmenagogue.[CXVII] The flowers, leaves and fruits are recommended in Iranian traditional medicine as a remedy to normalize temperament in elderly, for brain obstruction, intestinal worms, kidney stones, leprosy, vitiligo, purulent sores, as an antidote to toxins, diuretic, emmenagogue, hair growth inducer and to kill lice [25]. Fruit powder is insecticide against flies,[LXXXVIII] and the root is considered anthelmintic by Ethiopians [31],[LXXIX] while the bark was considered vermifuge in the Philippines.[LVI] In Indo-China, seeds were recommended for typhoid fever and retention of urine [17]. The root bark was included in the official Pharmacopoeias of the United States and Mexico.[XV] In traditional Chinese medicine, it is used orally and topically as an antiparasitic and antifungal agent [40]; the roots and barks of *M. azedarach* and *M. toosendan* are known as *Kulianpi*; and are described as bitter, 'cold' and slightly toxic. They are indicated for the treatment of ascariasis, oxyuriasis, erysipelas, rubella, scabies and *tinea favosa.* Powdered *Kulianpi*, mixed with vinegar is used externally for scabies.[XVIII]

Phytoconstituents: A series of limonoids, triterpenes, steroids and flavonoids and limonoid glycosides, including salannin, meldenin [49, 50], melianoninol, melianol, melianone, meliandiol, vanillin, vanillic acid [22, 32, 48], 3-deacetyl-4′-demethyl-salannin, 3-deacetyl-28-oxosalannin, and 1-detigloylohchinolal [38], ring C-seco limonoids [63, 64], lignanes: pinoresinol, bis-epi-pinoresinol, hemicetal and diacid [11], and tirucallane triterpenoids [2, 62] have been isolated from the fruits. Steroids [56], triterpenoids and sterol [61], and flavonoid glycosides, including quercetin 3-O-rutinoside, kaempferol 3-O-robinobioside and kaempferol 3-O-rutinoside [30] have been isolated from the leaves. Triterpenoids, steroids [21, 57]; limonoids, and sesquiterpenoid [58] have also been isolated from the bark. Azadirachtin-type

limonoids, meliacarpinin D, melianin B, highly cytotoxic sendanin-type limonoids [19, 20, 24, 52], and trichilin-type limonoids, including meliatoxin B1, trichilin H, trichilin D and 1,12-diacetyltrichilin B [53] have been reported from the root bark. Chemical constituents of the seeds include β-sitosterol, vanillin, benzoic acid, vanillic acid, daucosterol, α-D-glucopyranose, limonoid glycosides: 6,11-diacetoxy-7-oxo-14β,15β-epoxymeliacin (1,5-diene-3-O-β-D-glucopyranoside) and scopoletin, melianol, meliacin, meliacarpin, meliartenin hydroxyl-3-methoxcinnamaldehyde and (+-) pinoresinol [12, 13]. *Kulianpi* is reported to contain toosendanin, margoside, kaempferol, resin, tannin, *n*-triacontane, β-sitosterol, and the triterpene kulinone. Seeds yield 60% of a fatty oil comprising stearic, palmitic, lauric, valerianic, and butyric acids, and traces of a sulfurated essential oil.[XVIII]

Pharmacology: Methanol flower extract healed *S. aureus* caused skin infection in rabbits, an effect that was comparable to neomycin [47]. The fruit extract showed higher antibacterial effect against Gram-negative bacteria, while the leaf extract was more effective on *C. albicans* [37]. Various bark extracts have shown significant antibacterial activities against a number of pathogenic bacteria [59]. Fresh green leaves extracts contain an antiviral factor that inhibits replication of several animal viruses [5, 18, 54, 55], protects neonatal mice against Tacaribe virus inoculation-induced lethal encephalitis, and protects offspring of nursing mothers from developing viral encephalitis [6]. Meliacine is identified as the compound possessing antiviral activity that inhibits HSV-1 replication [3], exerts a strong antiviral action on corneal HSV-1 inoculation in mice [4, 10, 41], and has a protective effect against genital herpetic infection in mice [39]. Hydroethanol leaf extract showed pediculicidal activity, killing all lice faster than 1% permethrin [45]. Ethanol leaf extract also possesses significant *in vitro* radical scavenging activity, and protects cells against oxidative damage [34]. Hexane leaf and seed extracts exhibited significant antipyretic activity in rabbits, comparable to aspirin [23, 29].

Ethanol leaf extract in a dose of 100 mg/kg daily for 21-days caused complete loss of libido in male rats [14], and ethanol root extract and its chloroform fraction interrupted pregnancy in 75% of female rats [26, 27]. Seed extract also increases preimplantation, post-implantation and total prenatal mortalities during early and late stages of gestation in rats [33]. However, 50% ethanol and acetone extracts of leaf showed no anti-implantation activity in rats [42]. The fruit extracts showed activity against tapeworms and hookworms better than piperazine phosphate and hexylresorcinol, respectively [51]. Methanol extracts of leaves and seeds are strong larvicidal, pupicidal, adulticidal, and repellent to mosquito [15, 36], so is the hydroalcohol extract of the leaves [43]. Aqueous leaf extract showed strong anti-complementary activity, but did not affect phagocytic activity of PMNL [9]. Treatment of mice with the aqueous extract diminished production of antibodies and inhibited graft vs host and delayed type hypersensitivity reactions [16].

Human A/Es, Allergy and Toxicity: *Melia azedarach* pollens have been reported to cause respiratory allergy [8]. Eating fruits is described as a fatal poison; causes vomiting, asphyxation, dizziness, coma and death. Consumption of six to nine

fruits, 30–40 seeds, or 400 g of the bark are considered toxic to human in Chinese medicine. Poisoning may cause gastrointestinal, cardiovascular, respiratory, or neurological effects; general weakness, myalgia, numbness, and ptosis are the presenting symptoms, which may occur within 4–6 h after ingestion [40]. Children have died from eating berries and adults from making a brew out of leaves. A resinous poison is in the fruit-pulp, but the amount varies with the strain and growing conditions. Irritant activity of the plant is evident in causing vomiting and constipation or diarrhea. Difficulty in breathing, weakening heart activity, and nervous depression or excitement and paralysis may develop. Symptoms may occur for several hours and death may take place within a few days.[CXXXV] The epiderm of the bark is more toxic and should be discarded.

Animal Toxicity: Oral administration of aqueous and alcoholic extracts of flowers and berries caused mild CNS depression but were nontoxic up to a dose of 1,500 mg/kg in mice and rats. Intravenously, LD50 of aqueous extract of berries in mice and rats were 700 and 925 mg/kg, respectively; and of flowers extract 395 and 580 mg/kg, respectively [60].

Commentary: Despite many clinical uses in traditional medicines, no RCTs are reported in the published literature, except from China on fresh *Kulianpi* decoction being very effective against ascariasis infestation in both adults and children.[XVIII]

References

1. Abbasi AM, Khan MA, Ahmad M, et al. Ethnopharmacological application of medicinal plants to cure skin diseases and in folk cosmetics among the tribal communities of North-West Frontier Province, Pakistan. J Ethnopharmacol. 2010;128:322–35.
2. Akihisa T, Pan X, Nakamura Y, et al. Limonoids from the fruits of *Melia azedarach* and their cytotoxic activities. Phytochemistry. 2013;89:59–70.
3. Alché LE, Barquero AA, Sanjuan NA, Coto CE. An antiviral principle present in a purified fraction from *Melia azedarach* L. leaf aqueous extract restrains herpes simplex virus type 1 propagation. Phytother Res. 2002; 16:348–52.
4. Alché LE, Berra A, Veloso MJ, Coto CE. Treatment with meliacine, a plant derived antiviral, prevents the development of herpetic stromal keratitis in mice. J Med Virol. 2000;61:474–80.
5. Andrei GM, Coto CE, de Torres RA. Assays of cytotoxicity and antiviral activity of crude and semipurified extracts of green leaves of *Melia azedarach* L. Rev Argent Microbiol. 1985;17:187–94 (Spanish).
6. Andrei GM, Lampuri JS, Coto CE, de Torres RA. An antiviral factor from *Melia azedarach* L. prevents Tacaribe virus encephalitis in mice. Experientia. 1986;42:843–5.

7. Ayyanar M, Ignacimuthu S. Ethnobotanical survey of medicinal plants commonly used by Kani tribals in Tirunelveli hills of Western Ghats. India. J Ethnopharmacol. 2011;134:851–64.
8. Baena-Cagnani CE, Patiño CM, Cáceres MS. Pollinosis: some immunologic and regional considerations and the description of *Melia azedarach* respiratory allergy. Allergol Immunopathol (Madr). 1987;15:393–7.
9. Benencia F, Courrèges MC, Massouh EJ, Coulombié FC. Effect of *Melia azedarach* L. leaf extracts on human complement and polymorphonuclear leukocytes. J Ethnopharmacol. 1994;41:53–7.
10. Bueno CA, Lombardi MG, Sales ME, Alché LE. A natural antiviral and immunomodulatory compound with antiangiogenic properties. Microvasc Res. 2012;84:235–41.
11. Cabral MM, Garcia ES, Kelecom A. Lignanes from the Brazilian *Melia azedarach*, and their activity in *Rhodnius prolixus* (Hemiptera, Reduviidae). Mem Inst Oswaldo Cruz. 1995;90:759–63.
12. Carpinella MC, Ferrayoli CG, Palacios SM. Antifungal synergistic effect of scopoletin, a hydroxycoumarin isolated from *Melia azedarach* L. fruits. J Agric Food Chem. 2005;53:2922–7.
13. Chong XT, Tian GZ, Cheng ZL, Yao QQ. Study on chemical constituents of the seed of *Melia azedarach* L. Food Drug. 2009;11:30–1.
14. Choudhary DN, Singh JN, Verma SK, Singh BP. Antifertility effects of leaf extracts of some plants in male rats. Indian J Exp Biol. 1990;28:714–6.
15. Coria C, Almiron W, Valladares G, et al. Larvicide and oviposition deterrent effects of fruit and leaf extracts from *Melia azedarach* L. on *Aedes aegypti* (L.) (Diptera: Culicidae). Bioresour Technol. 2008;99:3066–70.
16. Courrèges MC, Benencia F, Coulombié FC, Coto CE. *In vitro* and *in vivo* activities of *Melia azedarach* L. aqueous leaf extracts on murine lymphocytes. Phytomedicine. 1998;5:47–53.
17. Crevost CH, Petelot A. Catalogue des Produits de l'indo-Chine (Plantas Medicinales). Bull Econ IndoChine. 1934;37.
18. Descalzo AM, Coto C. Inhibition of the pseudorabies virus (Suis herpesvirus 1) by an antiviral agent isolated from the leaves of *Melia azedarach*. Rev Argent Microbiol. 1989;21:133–40 (Spanish).
19. Fukuyama Y, Nakaoka M, Yamamoto T, Takahashi H, Minami H. Degraded and oxetane-bearing limonoids from the roots of *Melia azedarach*. Chem Pharm Bull. 2006;54:1219–22.
20. Fukuyama Y, Ogawa M, Takahashi H, Minami H. Two new meliacarpinins from the roots of *Melia azedarach*. Chem Pharm Bull (Tokyo). 2000;48:301–3.
21. Ge JJ, Wang LT, Chen P, et al. Two new tetracyclic triterpenoids from the barks of *Melia azedarach*. J Asian Nat Prod Res. 2016;18:20–5.
22. Han J, Lin WH, Xu RS, et al. Studies on the chemical constituents of *Melia azedarach* L. Yao Xue Xue Bao. 1991;26:426–9 (Chinese).
23. Ikram M, Khattak SG, Gilani SN. Antipyretic studies on some indigenous Pakistani medicinal plants: II. J Ethnopharmacol. 1987;19:185–92.

24. Itokawa H, Qiao ZS, Hirobe C, Takeya K. Cytotoxic limonoids and tetranortriterpenoids from *Melia azedarach*. Chem Pharm Bull (Tokyo). 1995;43:1171–5.
25. Jafari S, Saeidnia S, Hajimehdipoor H, et al. Cytotoxic evaluation of *Melia azedarach* in comparison with, *Azadirachta indica* and its phytochemical investigation. Daru. 2013;21:37.
26. Keshri G, Bajpai M, Lakshmi V, et al. Role of energy metabolism in the pregnancy interceptive action of *Ferula assafoetida* and *Melia azedarach* extracts in rat. Contraception. 2004;70:429–32.
27. Keshri G, Lakshmi V, Singh MM. Pregnancy interceptive activity of *Melia azedarach* Linn. in adult female Sprague-Dawley rats. Contraception. 2003;68:303–6.
28. Khan AV, Ahmed QU, Mir MR, et al. Antibacterial efficacy of the seed extracts of *Melia azedarach* against some hospital isolated human pathogenic bacterial strains. Asian Pac J Trop Biomed. 2011;1:452–5.
29. Khattak SG, Gilani SN, Ikram M. Antipyretic studies on some indigenous Pakistani medicinal plants. J Ethnopharmacol. 1985;14:45–51.
30. Kumazawa S, Kubota S, Yamamoto H, et al. Antiangiogenic activity of flavonoids from *Melia azedarach*. Nat Prod Commun. 2013;12:1719–20.
31. Lemordant D. Contribution a l'ethnobotanique Ethiopienne. J Agric Trop Bot Appl. 1971;18:1–35; 18:142–79.
32. Liu HB, Zhang CR, Dong SH, et al. Limonoids and triterpenoids from the seeds of *Melia azedarach*. Chem Pharm Bull (Tokyo). 2011;59:1003–7.
33. Mandal R, Dhaliwal PK. Antifertility effect of *Melia azedarach* Linn. (dharek) seed extract in female albino rats. Indian J Exp Biol. 2007;45: 853–60.
34. Marimuthu S, Balakrishnan P, Nair S. Phytochemical investigation and radical scavenging activities of *Melia azedarach* and its DNA protective effect in cultured lymphocytes. Pharm Biol. 2013;51:1331–40.
35. Mavundza EJ, Maharaj R, Finnie JF, et al. An ethnobotanical survey of mosquito repellent plants in uMkhanyakude district, KwaZulu-Natal province, South Africa. J Ethnopharmacol. 2011;137:1516–20.
36. Nathan SS, Savitha G, George DK, et al. Efficacy of *Melia azedarach* L. extract on the malarial vector *Anopheles stephensi* Liston (Diptera: Culicidae). Bioresour Technol. 2006;97:1316–23.
37. Orhan IE, Guner E, Ozcelik B, et al. Assessment of antimicrobial, insecticidal and genotoxic effects of *Melia azedarach* L. (chinaberry) naturalized in Anatolia. Int J Food Sci Nutr. 2012;63:560–5.
38. Pan X, Matsumoto M, Nakamura Y, et al. Three new and other limonoids from the hexane extract of *Melia azedarach* fruits and their cytotoxic activities. Chem Biodivers. 2014;11:987–1000.
39. Petrera E, Coto CE. Therapeutic effect of meliacine, an antiviral derived from *Melia azedarach* L., in mice genital herpetic infection. Phytother Res. 2009;23:1771–7.

40. Phua DH, Tsai WJ, Ger J, et al. Human *Melia azedarach* poisoning. Clin Toxicol (Phila). 2008;46:1067–70.
41. Pifarré MP, Berra A, Coto CE, Alché LE. Therapeutic action of meliacine, a plant-derived antiviral, on HSV-induced ocular disease in mice. Exp Eye Res. 2002;75:327–34.
42. Prakash AO. Potentialities of some indigenous plants for antifertility activity. Int J Crude Drug Res. 1986;24:19–24.
43. Prophiro JS, Rossi JC, Pedroso MF, et al. Leaf extracts of *Melia azedarach* Linnaeus (Sapindales: Meliaceae) act as larvicide against *Aedes aegypti* (Linnaeus, 1762) (Diptera: Culicidae). Rev Soc Bras Med Trop. 2008;41: 560–4.
44. Roop JK, Dhaliwal PK, Guraya SS. Extracts of *Azadirachta indica* and *Melia azedarach* seeds inhibit folliculogenesis in albino rats. Braz J Med Biol Res. 2005;38:943–7.
45. Rutkauskis JR, Jacomini D, Temponi LG, et al. Pediculicidal treatment using ethanol and *Melia azedarach* L. Parasitol Res. 2015;114:2085–91.
46. Saikia AP, Ryakala VK, Sharma P, et al. Ethnobotany of medicinal plants used by Assamese people for various skin ailments and cosmetics. J Ethnopharmacol. 2006;106:149–57.
47. Saleem R, Ahmed SI, Shamim SM, et al. Antibacterial effect of *Melia azedarach* flowers on rabbits. Phytother Res. 2002;16:762–4.
48. Shahwar D, Raza MA, Shafiq-Ur-Rehman, et al. An investigation of phenolic compounds from plant sources as trypsin inhibitors. Nat Prod Res. 2012;26:1087–93.
49. Srivastava SD. Further constituent from the seeds of *Melia azedarach*. Planta Med. 1987;53:100–1.
50. Srivastava SD. Limonoids from the seeds of *Melia azedarach*. J Nat Prod. 1986;49:56–61.
51. Szewczuk VD, Mongelli ER, Pomilio AB. *In vitro* anthelmintic activity of *Melia azedarach* naturalized in Argentina. Phytother Res. 2006;20:993–6.
52. Takeya K, Qiao ZS, Hirobe C, Itokawa H. Cytotoxic azadirachtin-type limonoids from *Melia azedarach*. Phytochemistry. 1996;42:709–12.
53. Takeya K, Quio ZS, Hirobe C, Itokawa H. Cytotoxic trichilin-type limonoids from *Melia azedarach*. Bioorg Med Chem. 1996;4:1355–9.
54. Wachsman MB, Coto CE. Susceptibility of picornaviruses^{++} to an antiviral of plant origin (meliacin). Rev Argent Microbiol. 1995;27:33–7 (Spanish).
55. Wachsman MB, Damonte EB, Coto CE, de Torres RA. Antiviral effects of *Melia azedarach* L. leaves extracts on Sindbis virus-infected cells. Antiviral Res. 1987;8:1–12.
56. Wu SB, Ji YP, Zhu JJ, et al. Steroids from the leaves of Chinese *Melia azedarach* and their cytotoxic effects on human cancer cell lines. Steroids. 2009;74:761–5.
57. Wu SB, Bao QY, Wang WX, et al. Cytotoxic triterpenoids and steroids from the bark of *Melia azedarach*. Planta Med. 2011;77:922–8.

58. Yuan CM, Zhang Y, Tang GH, et al. Cytotoxic limonoids from *Melia azedarach*. Planta Med. 2013;79:163–8.
59. Zahoor M, Ahmed M, Naz S, Ayaz M. Cytotoxic, antibacterial and antioxidant activities of extracts of the bark of *Melia azedarach* (China Berry). Nat Prod Res. 2015;29:1170–2.
60. Zakir-ur-Rahman, Ahmad S, Qureshi S, et al. Toxicological studies of *Melia azedarach* L. (flowers and berries). Pak J Pharm Sci. 1991;4:153–8.
61. Zhang WM, Liu JQ, Peng XR, et al. Triterpenoids and sterols from the leaves and twigs of *Melia azedarach*. Nat Prod Bioprospect. 2014;4:157–62.
62. Zhou F, Ma X, Li Z, et al. Four new tirucallane triterpenoids from the fruits of *Melia azedarach* and their cytotoxic activities. Chem Biodivers. 2016;13:1738–46.
63. Zhou H, Hamazaki A, Fontana JD, et al. Cytotoxic limonoids from Brazilian *Melia azedarach*. Chem Pharm Bull (Tokyo). 2005;53:1362–5.
64. Zhou H, Hamazaki A, Fontana JD, et al. New ring C-seco limonoids from Brazilian *Melia azedarach* and their cytotoxic activity. J Nat Prod. 2004;67:1544–7.