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## Therapeutic, phytochemistry and pharmacology of *Azadirachta indica*: A review

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### Abstract

*Azadirachta indica* (Neem), a tropical, large size, evergreen plant, has been known as the wonder tree for centuries in the Indian subcontinent. It is considered as the 'Village dispensary' in India because of the use of all its parts for various ailments in the indigenous system of medicine. It has an ancient history about its medicinal properties as per the classical medical literatures. Each and every part has been used in the Indian systems of medicines. It has become important in the global context today for its variety of medicinal uses. Neem is used in various diseases like dermatitis eczema, acne, bacterial and fungal infections and other skin disorders. It is now being used in the manufacture of modern day medicinal, cosmetics, toiletries and pharmaceuticals. Various parts of the tree have shown diverse biological and pharmacological activities. Keeping in view the medicinal importance of the tree in Unani Medicine (*Tibb-e-Unani*) and other traditional systems of medicine, an attempt has been made to review the available literature on therapeutic uses, phytochemical and ethno-pharmacological properties of its different parts.

**Keywords:** *Azadirachta indica*, Neem, Unani medicine

### Introduction

Neem or Margosa is a botanical cousin of mahogany. It belongs to the family Meliaceae. The Latinized name of Neem is *Azadirachta indica*. It is derived from the Persian word 'Azad Darakht-e-Hindi' (Azad = Free, darakht = Tree, Hindi = of Indian origin). This literally means 'The Free Tree of India' (Anand *et al.*, 2010) [4]. The plant is considered as the 'Village dispensary' in India because of the use of all its parts for various ailments in the indigenous system of medicine (Chatterjee and Pakrashi, 1991). The Neem tree has an ancient history about its medicinal properties as per the classical medical literatures. Each and every part has been used in the Indian Ayurvedic and Unani systems of medicines, and is now being used in the manufacture of modern day medicinal, cosmetics, toiletries and pharmaceuticals.



The Neem tree has been known as the wonder tree for centuries in the Indian subcontinent. Neem has become important in the global context today for its variety of medicinal uses. Neem is used in various diseases like dermatitis eczema, acne, bacterial, fungal infections and other skin disorders. Different types of extracts of different parts of the tree shows activities like hypoglycemic, anti-bacterial, anti-fungal, anti-viral (Bhowmik *et al.*, 2010) [13] etc. The tree is supposed to reduce chemical pollutants from atmosphere and also particulate pollutants (Agarwal, 1986) [1]. It is estimated that India has about 1,38,00,000 neem trees with the potential to produce over 83,000 tons of neem oil and 3,30,000 tons of neem cake from 4,13,000 tons neem seeds.

The neem wood is generally considered to be highly resistant to fungi and insect attack and is durable even used outdoors (Anonymous, 2004) <sup>[10]</sup>. Neem grows in tropical arid regions with high temperatures, altitudes between 50m and 1000m, as little rainfall as 130mm/yr and long stretches of drought. Ideal places are well drained sunny hills. It grows on most kinds of soils including dry, stony, shallow, nutrient deficient soils with scanty vegetation, moderately saline and alkali soils, black cotton, compact clays and laterite crusts (Anonymous, 1998) <sup>[9]</sup>.

### Distribution

The tree is indigenous to India (Nadkarni, 1982; Anonymous, 2000) <sup>[10, 36]</sup>, Burma (Khare, 2007) <sup>[27]</sup> and Sri Lanka (Anonymous, 2000) <sup>[10]</sup>; and cultivated nearly all over India (Agarwal, 1986; Khare, 2007; Nadkarni, 1982; Prajapati *et al.*, 2003) <sup>[1, 27, 36]</sup> and in Burma (Nadkarni, 1982) <sup>[36]</sup>, including village shrubberies. It also grows wild in sub-Himalayan tract and forests of other areas (Chatterjee and Pakrashi, 1991). The tree is wild in the dry regions of the Irawadi valley. It is also cultivated and naturalized in the Punjab to the Jhelum, and rare in the west of the Sutlej (Kirtikar and Basu, 1991) <sup>[28]</sup>. The tree is also found today in other tropical regions such as Indonesia, Australia, western Africa (Anonymous, 2000) <sup>[10]</sup>, South and Central America, southern Florida, California and USA (Anonymous, 2007) <sup>[7]</sup>, the Carribeans, Puerto Rico and Haiti. The largest known plantation of nearly 50,000 trees is at Arafat plains on the way to Mecca in Saudi Arabia for providing shade to Haj pilgrims (Ahmed, 1988) <sup>[2]</sup>.

### Vernaculars

The plant is known by different vernacular names in different language, areas and traditions: *Nimba, Nimbaka, Arishta, Arishtaphala, Pichumarda, Pichumanda, Pichumandaka, Tiktaka, Sutiktak, Paaribhadra* (Ayurveda); *Nim, Nimb, Nimgachh* (Bengali); *Nim, Balnimb* (Bombay); *Tamabin, Ta-mar bin, Kamakha, Bawtamaka, Kamaka, Thamaka, Thin, Thinborotamakha* (Burma); *Bevina-mara, Kahibevu, Bemu, Bevina, Bevu, Kaybevu, Kaypebevu, Nimba, Ollebevu* (Canarese); *Nim* (Deccan); *Neem* or *Margosa tree*, *Indian Lilac* (English); *Agem Lilas, Azadirae d'Inde, Margousier, Arbre saint, Azadirac de l'Inde, Lilas de chine, Margosier* (French); *Indiseher Zedrach, Gemeiner, Grossblaettiger Zedrach* (German); *Limba, Danujhada, Kohumba, Limbado, Limbra* (Gujrati); *Nim, Nimb, Nimgachh, Balnimb, Ninb* (Hindi); *Bevu, Turakabevu, Huccabevu, Cikkabevu* (Kannada); *Nim, Beva-rooku* (Konkani); *Vepa, Veppu, Aryaveppu, Arytikta, Nimbam, Rajaveppu* (Malayalam); *Balantanimba, Kadukhajur, Limbachajhada, Nimbay, Limba* (Marathi); *Azaddarachtehindi, Neeb, Neem* (Persian); *Bakam, Nim, Bukhain, Drekh, Mahanim* (Punjab); *Arishta, Ravipriya, Vranashodhakari, Nimba, Prabhadra, Arkapadapa, Chhardana, Kitaka, Malaka, Shita, Subhadra, Yavaneshtha* (Sanskrit); *Nim* (Santal); *Nimuri* (Sindh); *Kohumba, Nimbu, Nimbagaha* (Sinhalese); *Vepa, Veppu, Vembu, Veppan, Arulundi, Vempu* (Tamil); *Vepa, Kondavepa, Turakavepa, Nimbamu, Vemu, Yapa* (Telugu); *Azaad-Darakht-e-Hindi* (Unani) and *Neem* (Urdu) (Chatterjee and Pakrashi, 1991; Khare, 2007; Kirtikar and Basu, 1991; Kurian, 1998; Nadkarni, 1982; Prajapati *et al.*, 2003) <sup>[27, 36, 28]</sup>.

### Unani Description

The tree is described in detail in classical Unani literatures. Neem is a very common tree found in India. It's all parts are bitter in taste. It is cultivated in various parts of India and also grown itself. The height of the tree is 40-50 feet or more. Its trunk is small and straight having 6-9 feet diameter. Its small braches bear 9-15 inches long petioles. The petioles bear 9-13 pairs of leaves (Ghani, 2011). Its leaves are thin, delicate with serrated margins slightly larger than leaves of pomegranate but more serrated. The flowers are fragrant having a yellow, small and round somewhat elongated fruits. The fruits are bitter with somewhat sweet taste. The tree is known as 'Sanjad Karkhi' in Isfahan and 'Darakht-e-Toz' in some other cities (Kareem, YNM).

### Ethnobotanical Description

The tree of *Azadirachta indica* is a deciduous (Anonymous, 2000) <sup>[10]</sup>, medium to large sized having a height of 15-20m with a clear bole of 7m long (Prajapati *et al.*, 2003) and mostly evergreen having wide spreading branches and glabrous twigs forming a round to oval crown (Anonymous, 1998) <sup>[9]</sup>. The bark is grayish-brown, externally fissured, and has a buff inner surface and fibrous fracture (Anonymous, 2000; Anonymous, 2007) <sup>[10, 9]</sup>.

The leaves are alternately arranged, pinnately compound, up to 40 cm long, composed of 8-18 short-petiolate narrow-ovate, pointed, curved toothed leaflets (Anonymous, 2007) <sup>[10]</sup>. The leaflets are 5-15 in number, opposite, subopposite or alternately arranged; lanceolate, serrate or dentate (Chatterjee and Pakrashi, 1991), 3.5- 8cm long, dark green above and paler beneath (Anonymous, 1992), serrate, acuminate and glabrous (Anonymous, 1992; Chatterjee and Pakrashi, 1991).

The flowers are numerous, white in color, honey-scented (Chatterjee and Pakrashi, 1991), hermaphrodite and in axillary panicles. The calyx is 5-lobed; petals are 5, much exceeding the calyx, free and imbricate; disk 0. Staminal tube is little shorter than the petals, cylindrical, widening above, 9-10-lobed apex, the lobes truncate, again slightly toothed; anthers are within the tube opposite to and shorter than the lobes. Ovary is 3-celled, style is elongated and slender, stigma is shortly cylindrical, 3-lobed, ovules are 2 in each cell and collateral (Kirtikar and Basu, 1991) <sup>[28]</sup>.

The fruit is 1-seeded drupe (Anonymous, 1998; Chatterjee and Pakrashi, 1991; Kirtikar and Basu, 1991; Prajapati *et al.*, 2003) <sup>[28]</sup> with woody endocarp (Anonymous, 1998; Kirtikar and Basu, 1991; Prajapati *et al.*, 2003) <sup>[28]</sup>, about 1.5 cm long, containing thin pulp surrounding the seed (Anonymous, 2007), ovoid-oblong, smooth (Anonymous, 1992) and yellow when ripe (Anonymous, 1992; Chatterjee and Pakrashi, 1991).

The seeds are ellipsoid having thick fleshy (Anonymous, 1998; Kirtikar and Basu, 1991; Prajapati *et al.*, 2003) <sup>[28]</sup> and oily cotyledons (Anonymous, 1998; Prajapati *et al.*, 2003) <sup>[10, 7]</sup>, cordate at base and superior radicle (Kirtikar and Basu, 1991) <sup>[28]</sup>.

### Mizaj (Temperament)

All parts of the tree have Hot and Dry in first degree (Ghani, 2011; Kabiruddin, YNM).

### Afa'al (Action)

In classical Unani literature, various actions of the plant *Neem (Azadirachta indica)* have been described in details.

All parts of Neem are mohallil (resolvent) (Ghani, 2011; Kareem, YNM; Kabiruddin, YNM; Khan, 1313H); mulattif (demulcent), muqatte, mulaiyin (laxative) (Kabiruddin, YNM; Khan, 1313H); munzij (concoctive) (Ghani, 2011; Kabiruddin, YNM; Khan, 1313H); daf safra wa bad wa balgham, daf fasad chahar khilt, qabiz (astringent), rade (repellent) (Khan, 1313H); hazim (Digestive) (Ghani, 2011); munzij-e-aaza-ur-ras (Kareem, YNM); musaffi-e-khoon (blood purifier), daf-e-bukhar (antipyretic), daf-e-taffun (antiseptic), qatil-e-jaraseem, qatil-e-kirm-e-shikam (anthelmintic) and munaqqi-e-qurooh (Kabiruddin, YNM). Decoction of its flower is muqawwi-e-dandan wa lissah. The flowers are daf-e-safra (Antibilious) often used with Tamarind and red sugar. The flowers oil is muqavvi, daf-e-zaher (Antidote), muqavvi-e-baah (Aphrodisiac) and mushtahi (Appetizer) (Ghani, 2011).

The fruit also possess daf-e-juzam (Kareem, YNM), mulaiyin-e-shikam and habis-e-ishal [in a dose of 1 misqal (4.5g)] properties (Kareem, YNM; Khan, 1313H).

The leaves act as munzij, mufajjir-e-awram and mumbit-e-lahm when locally applied in the form of paste. Decoction of leaves is musakkin-e-dard-e-gosh. Sheera-e-barg neem is nafe amraz-e-jild and qatil-e-kirm. Fresh leaves water with or without honey is musakkin and musleh jarahat (Khan, 1313H). Barg-e-neem also possess musaffi-e-dam (blood purifier), daf taffun (antiseptic) (Anonymous, 1992)<sup>[10]</sup> and mohallil (resolvent) properties (Anonymous, 1992; Khan, 1313H)<sup>[8]</sup>.

Its fruit (Kareem, YNM) and leaves (Khan, 1313H) both act as munaqqi-e-qurooh-e-khabisa and akkal on local application in the form of paste along with NaCl and, as akkal-e-jurooh wa qurooh along with Gud (Jaggery).

The decoction of post-e-beekh (neem root bark) in a dose of 2-10 misqal (9-45g) is mudir-e-haiz. Bar-e-kham (immature root) is mushily. Maghz-e-tukhm-e-neem is qabiz and daf tap. Its roghan (oil) is qatil-e-kirm-e-shikam, munaqqi-e-qurooh, mufatteh sudad-e-jigar wa tehal and daf dard (Khan, 1313H). Its gum is muharrik-e-daurane khoon and muqawwi (Ghani, 2011). Tila of Chob-e-neem (neem wood) is rade (Khan, 1313H).

### **Istemaal (Uses)**

Whole tree is useful in amraz-e-badi wa balghami wa khooni wa safravi, basoor (pustules), jarab, fasad-e-chahar khilt, quba, sozish, damameel, tapha-e-sammiya, qai, zaher, amraz-e-saudavi, bahaque safeed wa siyah, kalaf wa namash and jamee amraz-e-jildiya wa ghair jildiya. The Indian people believe that its shade prevents diseases. It is also beneficial for treating tap-e-garm, zyadti-e-abe dahan, tishnagi, mandgi, jarahat, fasad-e-khoon and kharish. Neem is the best remedy for the treatment of qurooh-e-usrul indemal (Khan, 1313H; Ghani, 2011). It resolves riyah from all organs (Nabi, 1920), cures juzam (leprosy) and bars (vitiligo) (Khan, 1313H; Ghani, 2011; Nabi, 1920).

Decoction and paste of leaves are useful in awram (inflammations) (Shamsuddin, 1314H), damameel, riyah, qarha-e-majari-e-bol. The decoction of leaves is beneficial in dard-e-gosh, qurooh, zarba, saqta and bawaseer-e-raddiya. Water extracted from barg-e-narm called as konpal is useful in ramad. Barg-e-neem is efficacious in jarab, qooba and amraz-e-damvi and its sheera cures kharish, josh-e-khoon, basoor and bars internally. Burnt leaves ground with lemon water is applied in eyes for jarab, kharish and bayaz. Hot leaves application below the umbilicus reduces

pain of menstruation or intercourse or puerperium. The powder of leaves with its branches is taken with water for hook or dard-e-pehlu. Gargle of water of ground leaves with honey for three days relieves dard-e-gelo (throat pain). Local application of dry leaves powder and lime with green leaves juice is found efficacious in nasoor, qurooh-e-khabeesa, afoonat and ghosht-e-fasid, and regenerates ghosht-e-swaleh in few days. Fresh leaves water with or without honey is useful in suda and jarahat. The application (zimad) of leaves with or without salt is efficacious in khanazeer and surkhbada. Steam of leaves is efficacious in waja-ul-mafasil. Leaf juice is instilled in nose for dard-e-sar and kirm-e-demagh, in eyes is for shabkori and in ears for samam (deafness). It is not only beneficial for chechak (small pox) in children but also for scars and marks of pox lesions. Shoots are used in amraz-e-chashm. The paste of leaves applied on abdomen and sitting near fire kills worms. The leaves mixed with Zeera safed are given in suzak and jiryan. Abe barge neem made from ground 3-6 masha (3-6g) leaves in water or rose or sandal water is useful in qai, dast and shiddat-e-tishnagi of haiza (cholera). Arque barge neem is efficacious in istisqa. It is used for ishal-e-shikam, khasoor-e-masana (Ghani, 2011; Khan, 1313H) and amraz-e-jild (skin diseases) (Anonymous, 1992).

Leaves, flowers, seed kernel (maghz-e-tukhm) and gum are useful in damameel, basoor, kirm-e-shikam (Ghani, 2011; Khan, 1313H); leaves, seed kernel, gum and tree water (Aab-e-darakht) are efficacious in amraz-e-jild (Anonymous, 1992; Ghani, 2011; Khan, 1313H; Nabi, 1920). Flowers are useful in fasad-e-khoon, juzam (Khan, 1313H; Ghani, 2011), kirm-e-shikam, dhund, zaher, beragbati-e-taam, basoor, damameel, tap-e-safravi, zyabitus and sugar in urine (Ghani, 2011). The fruit known as Niboli is useful in juzam and bawaseer (Khan, 1313H). Tukhm (seed) is useful in bawaseer khooni wa badi (Shamsuddin, 1314H). Maghz-e-tukhm-e-neem is used in fever and its oil is useful in damameel, basoor, kharish (itching from foot to neck), amraze jildiya, bawaseer, kirm-e-shikam, nawaseer, qurooh-e-gosh, dard-e-mafasil and sudad-e-jigar wa tehal (Khan, 1313H).

Post-e-darakht-e-neeb (bark) is efficacious in juzam, bars and aatishak (Shamsuddin, 1314H). Arq-e-chhal in a dose of 2-4 tola (is beneficial for laqwah, istarkha (paralysis), dard-e-mafasil, istisqa, daad, bad wounds and wet itching. The thin bark inner to thick bark is useful in purane bukhar, tishnagi and yarqan; its hamool (pessary) removes badbu-e-farfj. Steam inhalation of bark and mako resolves warm-e-khunaque. Decoction of bark in a dose of 8-10 g is useful in continuous and intermittent fevers and also for debility after fever, amraz-e-lissah and boils. It kills stomach worms (Ghani, 2011).

Application of oil on wounds removes kirm (worms) (Nabi, 1920). Samag-e-neem is used in fever and its oil is useful in damameel, basoor, kharish, amraz-e-jildiya, bawaseer, kirm-e-shikam, nawaseer, qurooh-e-gosh, dard-e-mafasil and sudad-e-jigar wa tehal (Khan, 1313H). Aab-e-darakht-e-neem is useful in juzam, atishak (Khan, 1313H; Ghani, 2011; Nabi, 1920) and amraz-e-jild (skin diseases) (Nabi, 1920). Tila (application) of Chob-e-neem (wood) ground in water on basoor poshishe badan and miswak (tooth brush of tree branch) of neem is useful in amraz-e-dahan (Ghani, 2011). The powder of fruit, flower, bark and leaves all taken in equal part and mixed when given internally in a dose of 2

to 6 masha (g) is beneficial in bars and bahaque. Different parts of the tree used in different forms are efficacious in amraz-e-barida, qurooh, qurooh usr-ul-indemal and nawaseer-e-raddiya (Khan, 1313H).

#### **Muzir (Adverse Effect)**

The Neem has adverse effect for the recipient having Yabis Mizaj (dry temperament) (Kabiruddin, YNM). it also increases yaboosat (dryness) (Hakeem, 2011).

#### **Musleh (Corrective)**

Pure Honey, Fihil Siyah (*Piper nigrum*) and Roghanyat are being used as Musleh (corrective) for adverse effect (Kabiruddin, YNM; Hakeem, 2011).

#### **Pharmacological Actions**

(As described in Ethnobotanical and traditional literature)

The plant *Azadirachta indica* is described in detail in ethnobotanical and scientific literature and various actions have been reported to possess by it. Some pharmacological actions and therapeutic uses are as follows:

The tree *Azadirachta indica* has anti-inflammatory and antipyretic properties (Anonymous, 2000). In Unani medicine, it is munzij (concoctive), resolvent and blood purifier (Nadkarni, 1982)<sup>[36]</sup>.

The leaves are antifungal, Antiviral, antiperiodic, anodyne (Chatterjee and Pakrashi, 1991); antiseptic (Agarwal, 1986; Chatterjee and Pakrashi, 1991; Nadkarni, 1982)<sup>[1, 36]</sup>; antimicrobial, antipyretic, antimalarial, mosquito larvicidal, anti-inflammatory, antifertility, spermicidal, hypoglycaemic (Khare, 2007)<sup>[27]</sup>; bitter, acrid, astringent, depurative, ophthalmic, appetizer, demulcent, refrigerant (Prajapati *et al.*, 2003), alexeteric (Kirtikar and Basu, 1991; Prajapati *et al.*, 2003); anthelmintic, insecticidal (Khare, 2007; Kirtikar and Basu, 1991; Nadkarni, 1982; Prajapati *et al.*, 2003)<sup>[27, 36, 28]</sup>; carminative, expectorant, aphrodisiac, maturant and resolvent. The tender young leaves are astringent (Kirtikar and Basu, 1991; Prajapati *et al.*, 2003)<sup>[28]</sup>; oil from leaves is local stimulant and emmenagogue (Nadkarni, 1982)<sup>[36]</sup>.

The young branches are anthelmintic (Kirtikar and Basu, 1991)<sup>[28]</sup>. The twigs are antipyorrhoeal, carminative and digestive (Chatterjee and Pakrashi, 1991). Flowers are stimulant (Kirtikar and Basu, 1991; Nadkarni, 1982)<sup>[36, 28]</sup>, tonic (Nadkarni, 1982; Chatterjee and Pakrashi, 1991)<sup>[36]</sup>, stomachic (Kirtikar and Basu, 1991; Nadkarni, 1982; Chatterjee and Pakrashi, 1991; Agarwal, 1986)<sup>[1, 36, 28]</sup>, antiseptic (Agarwal, 1986)<sup>[1]</sup>, bitter and anthelmintic (Kirtikar and Basu, 1991)<sup>[28]</sup>.

Oil from nuts is local stimulant (Agarwal, 1986; Nadkarni, 1982)<sup>[1, 36]</sup>; antiseptic (Agarwal, 1986; Chatterjee and Pakrashi, 1991; Nadkarni, 1982)<sup>[1, 36]</sup>; insecticide (Nadkarni, 1982)<sup>[36]</sup>; anthelmintic and alterative (Kirtikar and Basu, 1991)<sup>[28]</sup>. Oil known as oil of Margosa or Neem oil possess antifertility, antifungal, antimicrobial and antiseptic properties (Chatterjee and Pakrashi, 1991).

Root-bark is astringent, tonic, antiperiodic (Chatterjee and Pakrashi, 1991; Nadkarni, 1982)<sup>[36]</sup> and alterative (Agarwal, 1986)<sup>[1]</sup>. Bark is antimicrobial, antifungal, antiviral, antipyretic, antimalarial, mosquito larvicidal, anti-inflammatory, antifertility, spermicidal, insecticidal (Khare, 2007; Prajapati *et al.*, 2003)<sup>[27]</sup>, bitter (Agarwal, 1986; Kirtikar and Basu, 1991; Nadkarni, 1982; Prajapati *et al.*, 2003)<sup>[36, 1, 28]</sup>, vermifuge (Nadkarni, 1982)<sup>[36]</sup>, acrid, depurative, vulnerary, demulcent, liver tonic, expectorant,

urinary astringent (Prajapati *et al.*, 2003), refrigerant (Prajapati *et al.*, 2003; Kirtikar and Basu, 1991)<sup>[28]</sup>, astringent (Agarwal, 1986; Kirtikar and Basu, 1991; Chatterjee and Pakrashi, 1991; Nadkarni, 1982; Prajapati *et al.*, 2003)<sup>[1, 36, 28]</sup>, anthelmintic (Chatterjee and Pakrashi, 1991; Khare, 2007; Kirtikar and Basu, 1991; Prajapati *et al.*, 2003)<sup>[27, 28]</sup>, antiperiodic (Agarwal, 1986; Kirtikar and Basu, 1991; Nadkarni, 1982; Prajapati *et al.*, 2003; Chatterjee and Pakrashi, 1991; Khare, 2007)<sup>[1, 36]</sup>, pectoral, maturant, aphrodisiac, resolvent (Kirtikar and Basu, 1991)<sup>[28]</sup>, hypoglycaemic (Chatterjee and Pakrashi, 1991; Khare, 2007)<sup>[27]</sup> and tonic (Agarwal, 1986; Chatterjee and Pakrashi, 1991; Kirtikar and Basu, 1991; Nadkarni, 1982; Prajapati *et al.*, 2003)<sup>[1, 36, 28]</sup>. Gum from the bark is stimulant (Chatterjee and Pakrashi, 1991; Nadkarni, 1982)<sup>[36]</sup>, demulcent and tonic (Chatterjee and Pakrashi, 1991; Nadkarni, 1982; Agarwal, 1986)<sup>[1, 36]</sup>.

The fruit is emollient (Agarwal, 1986; Chatterjee and Pakrashi, 1991; Nadkarni, 1982)<sup>[1, 36]</sup>; purgative, anthelmintic (Agarwal, 1986; Chatterjee and Pakrashi, 1991; Nadkarni, 1982; Kirtikar and Basu, 1991)<sup>[1, 36, 28]</sup>; the young fruit is astringent (Chatterjee and Pakrashi, 1991; Nadkarni, 1982)<sup>[36]</sup>, tonic and antiperiodic (Chatterjee and Pakrashi, 1991; Kirtikar and Basu, 1991; Nadkarni, 1982)<sup>[36, 28]</sup>.

The toddy (a drink made of spirits with hot water and sugar) is refrigerant, nutrient, alterative tonic, antiprotozoal and emmenagogue (Nadkarni, 1982)<sup>[36]</sup>. Sap (from the stem tip) is refrigerant, tonic and nutritive (Chatterjee and Pakrashi, 1991). Bark, fruits, flowers, leaves, root, gum and oil are anthelmintic, stomachic, blood purifier, febrifuge, antiseptic, healer and antidote (Anonymous, 1984).

#### **Therapeutic Uses**

The drug Neem (*Azadirachta indica*) was used in folk medicine for the treatment of many complains and described in details in ethno-botanical literature and various uses have been reported as useful in inflammatory and febrile diseases including malaria, although unconfirmed (Anonymous, 2000). When planted the tree is beneficial to health as a prophylactic against malaria. Tender twigs of the tree are used as tooth-brushes, which will keep the system healthy and the breath and mouth clean and sweet (Nadkarni, 1982)<sup>[36]</sup>. An ointment is prepared from neem for dermatological use. Another neem cream is a fly or mosquito repellent (Anonymous, 2004).

The leaves are used in gingivitis, periodontitis, sores, enlargement of spleen, fever during childbirth, measles, head scald, cutaneous affections (Khare, 2007)<sup>[27]</sup>; boils (Khare, 2007; Nadkarni, 1982; Agarwal, 1986; Prajapati *et al.*, 2003; Chatterjee and Pakrashi, 1991)<sup>[1, 27]</sup>; malarial fever (Khare, 2007; Prajapati *et al.*, 2003; Anonymous, 2004)<sup>[27]</sup>; smallpox (Khare, 2007; Nadkarni, 1982)<sup>[27, 36]</sup>; swollen glands, bruises, sprains (Nadkarni, 1982; Chatterjee and Pakrashi, 1991)<sup>[36]</sup>; ulcers, skin diseases (Nadkarni, 1982; Chatterjee and Pakrashi, 1991; Prajapati *et al.*, 2003; Kirtikar and Basu, 1991)<sup>[36, 28]</sup>; piles (Nadkarni, 1982; Kirtikar and Basu, 1991)<sup>[36, 28]</sup>; leucoderma, ophthalmopathy, leprosy (Prajapati *et al.*, 2003; Kirtikar and Basu, 1991)<sup>[28]</sup>; intermittent fevers (Nadkarni, 1982; Prajapati *et al.*, 2003)<sup>[36]</sup>; eczema (Prajapati *et al.*, 2003; Chatterjee and Pakrashi, 1991); burning sensation, pruritus, intestinal worms, dyspepsia, tuberculosis (Prajapati *et al.*, 2003); biliousness, lumbago, inflammations, earache,

rheumatism, syphilitic sores, blood impurities (Kirtikar and Basu, 1991) <sup>[28]</sup>. Leaves heated over boiling water or in the form of pulp or paste (ointment and liniment) or poultice or ground with honey into a lep form antiseptic applications to unhealthy pustules. A pill made of leaves 1 tola in weight, camphor and asafetida 2 grains each, given mixed with 3 drachm of jiggery at bed time is said to act as prophylactic against epidemics. Leaf juice is given in worms with sweet oil, in jaundice with honey and in skin diseases like prurigo, eczema, urticaria etc with chebulic myrabolan. Paste of leaves is used externally in small pox and spread on the bed of patients of small pox and its fans are used. A soup made of neem leaves is administered in convalescence after diarrhea. Decoction of leaves is beneficial in complicated with congestion of liver (Nadkarni, 1982) <sup>[36]</sup> and also used as a galactagogue for initiating milk secretion in nursing mothers, and also recommended for diabetes mellitus in adults, nonketonic diabetes as well as in cases of insulin sensitivity. Tablets and injections are being formulated for chronic malaria. A neem leaf preparation is also recommended as a local sedative for external application (Anonymous, 2004). The leaves are applied in the form of poultice in abscess, adenitis and also beneficial for all types of anorexia (Chatterjee and Pakrashi, 1991). A decoction as an errhine relieves nose troubles, heals wounds, good as a gargle in stomatitis and for bad gums (Kirtikar and Basu, 1991) <sup>[28]</sup>.

Dried flowers are used as a tonic also after fevers (Nadkarni, 1982). The flowers remove 'kapha' and biliousness (Kirtikar and Basu, 1991) <sup>[28]</sup>; useful in some cases of atonic dyspepsia and general debility (Kirtikar and Basu, 1991; Nadkarni, 1982) <sup>[28]</sup>. The fruit is useful in chronic fevers, bronchitis, leprosy, intestinal worms (Nadkarni, 1982); piles, urinary diseases (Kirtikar and Basu, 1991; Chatterjee and Pakrashi, 1991; Nadkarni, 1982) <sup>[28]</sup>; skin diseases (Kirtikar and Basu, 1991; Chatterjee and Pakrashi, 1991) <sup>[28]</sup>; abdominal lump, worms, polyuria (Chatterjee and Pakrashi, 1991); tumours, some cases of intermittent fevers and general debility (Kirtikar and Basu, 1991) <sup>[28]</sup>. The seeds are used for killing pediculi and the powdered kernel for washing hairs. Dry seeds possess the same properties as the oil when bruised and mixed with water and some other fluid and applied to itch etc (Nadkarni, 1982). The seeds are good for leprosy and oil is for skin diseases (Kirtikar and Basu, 1991) <sup>[28]</sup>.

The bark is used in the form of powder or fluid extract or decoction in cases of vomiting, intermittent fevers, lumbago (Nadkarni, 1982; Prajapati *et al.*, 2003; Kirtikar and Basu, 1991) <sup>[28]</sup>; general debility, thirst (Nadkarni, 1982; Kirtikar and Basu, 1991) <sup>[28]</sup>, malarial fevers, anorexia (Nadkarni, 1982; Prajapati *et al.*, 2003; Chatterjee and Pakrashi, 1991), skin diseases (Nadkarni, 1982; Prajapati *et al.*, 2003; Anonymous, 1984); cough, inflammations, leprosy, otalgia, ulcers, wounds, syphilis, haemorrhoids, fatigue, leucoderma, amenorrhoea (Prajapati *et al.*, 2003; Kirtikar and Basu, 1991) <sup>[28]</sup>; hepatopathy (Prajapati *et al.*, 2003; Chatterjee and Pakrashi, 1991); other paroxysmal fevers and nausea. A decoction made of 1 drachm of bark and 2 drachm of long pepper is used for rheumatism. A decoction of neem and babula barks in equal parts is efficacious in leucorrhoea (Nadkarni, 1982). The bark tincture is used in fevers in the form of infusion (Agarwal, 1986; Nadkarni, 1982) <sup>[1]</sup>. It is useful in vitiated conditions of pitta, hyperdipsia, eczema, pruritus, burning sensation, tumour, tubercular glands,

dyspepsia, intestinal worms, bronchitis, urorrhoea, diabetes (Prajapati *et al.*, 2003); colic, sprue, pyresis (Chatterjee and Pakrashi, 1991); burning sensation near the heart, bad taste in the mouth, blood complaints, urinary discharges and syphilis (Kirtikar and Basu, 1991) <sup>[28]</sup>. The gum is useful in catarrh (Agarwal, 1986; Chatterjee and Pakrashi, 1991; Kirtikar and Basu, 1991; Nadkarni, 1982) <sup>[28, 1]</sup>, other affections (Agarwal, 1986; Kirtikar and Basu, 1991; Nadkarni, 1982) <sup>[1, 28]</sup>, great debility (Kirtikar and Basu, 1991) <sup>[28]</sup> and splenic enlargement (Chatterjee and Pakrashi, 1991).

The oil known as "Margosa oil" is useful in skin diseases, leprosy, ulcers and rheumatism (Chatterjee and Pakrashi, 1991; Nadkarni, 1982) <sup>[36]</sup> headache. Its application is favourite in tetanus, urticaria, eczema, erysipelas, scrofula and skin diseases like ringworm, scabies, pemphigus etc. Sodium and potassium margosates derived from the margosic acid of oil are useful for disinfecting many forms of skin affections. It is applied as an insecticide for the destruction of lice and in chronic malaria, syphilis, etc requiring an alternative remedy. As anthelmintic it is given in doses of ½-1 drachm (Nadkarni, 1982) <sup>[36]</sup>. Oil is used as a contraceptive for intravaginal use, for the treatment of vaginal infections, and as a mosquito repellent (Khare, 2007) <sup>[27]</sup>. It is useful in sprains common as external application. Warm oil relieves dental, ear and gum troubles. Hair oil containing Neem oil prevents baldness and greying of hair (Chatterjee and Pakrashi, 1991). The toddy or fermented sap of the tree is valuable in consumption, atonic dyspepsia, general debility, chronic leprosy and other skin diseases (Nadkarni, 1982) <sup>[36]</sup>. Bark, fruits, flowers, leaves, root, gum and oil are used as healer and antidote to poisons (Anonymous, 1984).

### Phyto-Chemistry

About 100 compounds, mostly triterpenoids of protolimonoids (proto-meliacins), limonoids (or meliacins or tetranortriterpenoids), tetranortriterpenoid- $\alpha$ -hydroxy butenolides, ring C seco-tetranortriterpenoids and ring C seco-tetranortriterpenoid- $\beta$ -hydroxy butenolides, pentanortriterpenoids, a hexanortriterpenoids apart from a few nontriterpenoids constituents have been reported from various parts of the tree (Chatterjee and Pakrashi, 1991). The diterpenoids, margolone, nimbonone, nimbolone and nimbolinin have been isolated from the plant (Anonymous, 2004).

The fruits contain azadirachtin, an isomer of epoxyazadiradione (Chatterjee and Pakrashi, 1991; Rastogi and Mehrotra, 1991), azadirachtol, azadirachnol, deacetyl-azadirachtinol, azadiradione, 17-epi- and 17 $\beta$ -hydroxyazadiradione, azadirone, gedunin, 7-hydroxygedunin, melianone, nimbiol, nimboeinol (7-acetoxy-7-hydroxy-azadiradione), nimocin, 7-deacetoxy-nimolicinol, nimolinone; nimbochalcin and nimboctin; 21,23:24,25-diepoxytirucall-7-en-21-ol salannin (Chatterjee and Pakrashi, 1991). Nimolicinol isolated from fresh, ripe fruit (Rastogi and Mehrotra, 1993).

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 acids, azadirone, azadiradione, epoxyazadiradione (nimbinin) although their specific rotation differ widely, gedunin, desacetyl gedunin, meldonin, meliatriol, nimbin, nimbidin, nimbiol, nimbidic acid, salannin, 3-desacetylsalannin,

salannol and its acetate, salannolide, vepinine, vilasinin, 1,3-diacetylvilasinin, 1-tigloyl-3-acetyl-vilasinin and tiglic acid (Chatterjee and Pakrashi, 1991), nimbinene, 6-desacetyl nimbinene, nimbandiol and 6-O-acetyl nimbandiol (seed oil) (Chatterjee and Pakrashi, 1991; Rastogi and Mehrotra, 1993). Neem seed oil contains Triterpenes and tetranortriterpenes (limonoids and protolimonoids of the gedunin-group): for example nimbolin A and B, nimbin, gedunin (Anonymous, 2000); in addition, azadirachtin, 22,23-dihydro-23- $\beta$ -methoxy-azadirachtin (vepaol) and its C-23 epimer (isovepaol), 7-desacetyl-7-benzoyl derivatives of azadirone, azadiradione, epoxyazadiradione, 2-dihydroepoxyazadiradione, 1 $\beta$ , 2 $\beta$ -diepoxyazadiradione, 7-desacetyl-7-benzoyl-gedunin, acetylneotrichilenone, nimbidinin, nimbidin, salanic (nimbidic) acid (seeds) (Chatterjee and Pakrashi, 1991). A new tetranortriterpene-nimbidinin- isolated from amorphous bitter principle (nimbin) of seeds and characterized (Rastogi and Mehrotra, 1991). Six new tetranortriterpenoids- 1 $\alpha$ -methoxy-1,2-dihydro-epoxyazadiradione, 1 $\beta$ , 2 $\beta$ : 14 $\beta$ , 15 $\beta$ -diepoxyazadiradione, 7-acetylneotrichilenone and three C-7 benzoates of tetranortriterpenoids (I, II, III)- isolated from seeds (Rastogi and Mehrotra, 1993).

The flowers contain benzoyl alcohol,  $\beta$ -sitosterol; thioamyl alcohol; arachidic, behenic, linoleic, oleic, palmitic and stearic acids; azadirachtin and margosene (Chatterjee and Pakrashi, 1991); kaempferol and its 3-glucoside, quercetin-3-galactoside and myricetin-3-L-arabinoside (Chatterjee and Pakrashi, 1991; Rastogi and Mehrotra, 1991).

The leaves contain azadirachtin, azadirachtanin, azadirone, azadiradione and epoxyazadiradione, isoazadirolide, nimbin, nimboicinolide, isonimboicinolide, nimbolide, nimboicinolide, isonimocinolide, nimocinone, 2',3'-dehydrosalannol, kaempferol-3-O- $\beta$ -glucoside, myricetin and its 3'-L-arabinoside (melictrin), 3-O- $\alpha$ -L-rhamnoside and 3-O-rutinoside, quercetin, its 3-galactoside, 3-O-L-rhamnoside and 3-O-rutinoside, nimbaflavones, scopoletin, amino acids, carbohydrates, nonacosanol, protein and vitamins (Chatterjee and Pakrashi, 1991),  $\beta$ -sitosterol and its  $\beta$ -D-glucoside,  $\beta$ -carotene, n-hexacosanol (Chatterjee and Pakrashi, 1991; Rastogi and Mehrotra, 1991), nimbandiol, nimbinene and 6-desacetylnimbinene (Chatterjee and Pakrashi, 1991; Rastogi and Mehrotra, 1993). Hyperoside, quercitrin and rutin are identified in leaves; meldonindiol isolated from green leaves; meldenin and isomeldenin isolated from fallen yellow leaves and quercetin as aglycon isolated from the glycosides of either type of leaves. A new tetranortriterpene - 4 $\alpha$ , 6 $\alpha$ -dihydroxy-A-homoazadirone (IV) is also isolated (Rastogi and Mehrotra, 1993). The leaves also contain tannins and a volatile oil (Anonymous, 2000).

The heartwood contains tannin, bakalactone, 4, 14- $\alpha$ -dimethyl-5- $\alpha$ -ergosta-8,24(28)-dien-3 $\beta$ -ol, 4 $\alpha$ -methyl-5- $\alpha$ -ergosta-8,24(28)-dien-3 $\beta$ -ol, nimatone, nimbinene, 6-desacetyl nimbinene, nimbolins A and B (Chatterjee and Pakrashi, 1991),  $\beta$ -sitosterol and its glucoside, 24-methylene-cycloartenol (Chatterjee and Pakrashi, 1991; Rastogi and Mehrotra, 1991).

The stem bark contains vanillic acid, catechol, campesterol, stigmasterol, sitosterol,  $\beta$ -amyrin, lupeol, nimbin, nimbidin, nimbinin, sugiol (Chatterjee and Pakrashi, 1991), 6 $\beta$ -hydroxy-4-stigmasten-3-one, 6 $\beta$ -hydroxy-4-campesten-3-one, kulinone, kulactone, kulolactone and methyl kulonate (Chatterjee and Pakrashi, 1991; Rastogi and Mehrotra,

1991). Two related arabinofucoglucans Gla and Glb isolated from bark; both composed of main chain of repeating (1 $\rightarrow$ 4) linked glucopyranosyl units with side chains of  $\alpha$ -L-arabinofuranosyl units. A process of extracting an anti-inflammatory polysaccharide consisting of glucose, arabinose and fucose in molar ratio of 1:1:1 from bark (Rastogi and Mehrotra, 1993). The ethanolic extract of the stem bark contains two isomeric diterpenoids, nimbonone and nimbonolone and methylgrevillate; three new tricyclic diterpenoids, nimbosodione, nimbisonol and methylnimbonol; phenols, nimbone (C<sub>18</sub>H<sub>22</sub>O<sub>3</sub>, m p 102-03o); nimbinone (C<sub>10</sub>H<sub>9</sub>O<sub>2</sub>, m p 124-25o); nimbinone (C<sub>18</sub>H<sub>24</sub>O<sub>4</sub>, m p 78-79o); and nimbionol (C<sub>18</sub>H<sub>24</sub>O<sub>4</sub>, m p 127-29o) and c-seco-tetranortriterpenoid, isonimbinolide (C<sub>30</sub>H<sub>36</sub>O<sub>11</sub>, m p 172-73o) and two fatty acid derivatives (polyacetates), margosinone and margosinolone. The pentacyclic nortriterpenoids, 6-desacetylnimbinen, nimbiol, nimbinen have also been isolated from the stem bark. The methanolic extract of the bark also contains gedunin (Anonymous, 2004). The bark also contains tannins and a volatile oil (Anonymous, 2000).

A glycoprotein containing carbohydrate and protein in ratio of 19:81 isolated from neem gum containing mannose, glucosamine, arabinose, galactose, fucose, xylose and glucose in molar ratio of 4:3:3:2:2:1:1 (Rastogi and Mehrotra, 1993).

The twigs contain margosinolide, isomargosinolide, desacetylnimbinolide and desacetyl isonimbinolide (Chatterjee and Pakrashi, 1991).

The wood contains gedunin, 7-deacetoxy-7-oxogedunin, fraxinellone, nimbolin A and cycloeucaleanone, melianin A and melianin B. the wood oil contains cycloeucaleanol, 24-methylene cycloartenol,  $\beta$ -sitosterol (Chatterjee and Pakrashi, 1991; Rastogi and Mehrotra, 1991) and azadarcic acid (Rastogi and Mehrotra, 1991).

The trunk bark contains nimbiol, sugiol and nimboosterol; trunk wood contains nimbolins A and B (Chatterjee and Pakrashi, 1991).

The root contains 24-methylene-cycloartenol, 24-methylene-cycloartenone, cycloeucaleanol, cycloeucaleanone, 4-campesten-3-one, 4-stigmasten-3-one, trans-cinnamic and vanillic acids; root bark contains nimbin and nimbidin (Chatterjee and Pakrashi, 1991). The diterpenoid nimbidiol (C<sub>17</sub>H<sub>22</sub>O<sub>3</sub>) has been isolated from root bark. The tricyclic diterpenoids, margosin, margocinin, margocillin and nimolinin and a tetranortriterpenoid, nimbinin have been isolated from the root bark (Anonymous, 2004).

Various parts of the tree contains aesculetin, campesterol, 6-hydroxy-7-methoxy-coumarin, 4 $\alpha$ ,6 $\alpha$ -dihydroxy-A-homoazadirone, isomeldenin, meldonindiol, 17-acetoxymeliacin, 6-O-acetylnimbandiol, desacetylnimbin, nimocinol, isonimolicinolide and nimolinolic acid (Chatterjee and Pakrashi, 1991).

### Pharmacological Studies

A number of studies have been carried out on *Azadirachta indica* in recent years showing that it possesses diverse pharmacological effects. Some of the important pharmacological actions are as follows:

#### Analgesic

The analgesic effect of an extract of the leaves was assessed in mice using the acetic acid writhing test and the tail flick test. Intragastric administration of 10–100mg/kg body

weight of the extract reduced the incidence of writhing and enhanced tail-withdrawal latencies (Khanna *et al.*, 1995).

#### **Antiandrogenic**

Histological and biochemical changes were observed in the caput and cauda epididymis of rats treated orally with 20, 40 and 60 mg doses of the dry powdered leaves given daily for 24 days. The height of the epithelium and the diameter of the nucleus in both regions were reduced. Serum testosterone concentrations were also reduced significantly in animals receiving the highest dose (Kasturi *et al.*, 1995) [24].

#### **Antianxiety/ Anxiolytic**

The freshly prepared leaf extract at low doses (10, 20, 50, 100 and 200mg/kg) produced significant antianxiety effect whereas at high doses (400 and 800mg/ kg) it did not show the activity (Anonymous, 2004).

Intragastric administration of 10–200 mg/kg body weight (bw) of an aqueous extract of *Azadirachta indica* leaf produced anxiolytic effects similar to those of 1 mg/kg bw of diazepam in rats in the elevated-plus-maze and open-field behaviour tests (Jaiswal *et al.*, 1994) [21].

#### **Anti-atherosclerotic**

The ethanol extract of *Azadirachta indica* leaves have been shown to reverse the diabetes-associated increase in circulating immune cells and hence may play a significant role in the control of atherosclerosis and management of diabetic vascular complications in alloxan-induced diabetic rats (Itemobong *et al.*, 2010) [20].

#### **Anti-bacterial**

The ethanolic extract of stem bark of *Azadirachta indica* exhibited antibacterial activity against *Bacillus megaterium* (Anonymous, 2004).

#### **Anticandidal**

The hexane, methanol, chloroform, water, petroleum ether, dichloromethane, acetone and absolute alcohol extracts of *Azadirachta indica* seed kernels were used for evaluating anticandidal effect on *Candida* species using broth dilution method at concentrations from 1 to 0.0625mg/ ml. The hexan extract, ethanol extract of commercial neem seed oil and ethanol extract of neem seed kernel showed promising anticandidal activity (Lloyd *et al.*, 2005) [32].

#### **Antifeedant**

The ethanolic extract (90%) of the heart wood containing 4 $\alpha$ -methyl-5- $\alpha$ -ergosta-8, 24(28)-dien-3 $\beta$ -ol (24-methylene lophenol) (C29H48O) sterol has shown antifeedant activity against *Diascisia oblique* (Anonymous, 2004).

#### **Anti-fungal**

The ethanolic extract of stem bark of *Azadirachta indica* exhibited antifungal activity against *Aspergillus niger* (Anonymous, 2004).

The 100% ethanolic extract of neem leaves inhibited the fungus *Pityrosporum ovale* causing the dandruff more widely than the lower concentration levels using agar cup method (Anand *et al.*, 2010) [4].

#### **Antihepatotoxic**

The effect of an aqueous extract of the leaves was evaluated in paracetamol induced hepatotoxicity in rats. Intragastric

administration of 500.0 mg/kg bw of the extract significantly ( $P < 0.01$ ) reduced elevated levels of serum 93 aspartate aminotransferase, alanine aminotransferase and  $\gamma$ -glutamyl transpeptidase (Bhanwra S. *et al.*, 2000) [12].

#### **Anti-inflammatory**

The aqueous extract of *Azadirachta indica* leaves exhibited anti-inflammatory activity (Anonymous, 2004; Khare, 2007) [27].

Aqueous and petroleum ether extracts of *Azadirachta indica* leaves reduced the inflammation caused by *S. typhimurium* and its OMPs as assessed by paw flicking response. Petroleum ether A. indica leaf extract was found to be more effective than aqueous extract may be due to presence of steroids and triterpenoids observed in petroleum ether extract (Koul *et al.*, 2009).

A comparative study of the anti-inflammatory effect of aqueous extract of neem leaf and dexamethasone was carried by administering 400mg/ kg body weight of neem extract and 0.75mg dexamethasone intraperitoneally and 1 hour before the formalin injection and once daily for 7 days in rats. The results showed significant reduction in the paw edema of rats (Mosaddek & Rashid, 2008).

#### **Antileishmanial**

The ethanolic extract of the leaves and dichloromethane and chloroform fractions have shown excellent anti-leishmanial activity based on bioactivity-guided fractionation of ethanolic extracts of leaves and seeds and *in vitro* activity against promastigotes and intracellular amastigotes of *Leishmania amazonensis* (Carneiro *et al.*, 2012).

#### **Antimalarial**

The methanolic extract of the bark of neem containing gedunin showed antimalarial activity against *Plasmodium falciparum* (Anonymous, 2004; Khare, 2007) [27].

#### **Antimicrobial**

The organic extracts of neem (petroleum ether, chloroform, ethanol and aqueous) were screened for its antimicrobial activity against *Streptococcus mutans*, *Streptococcus salivarius* and *Fusobacterium nucleatum* strains causing dental caries using disc diffusion method and showed that the chloroform extracts of neem has a strong antimicrobial activity (Lekshmi *et al.*, 2012).

#### **Antinociceptive**

A study revealed the antinociceptive effect of Neem leaf extract in the pain model of the tail-flick test due to thermal stimulation. Neem leaves have been reported to relieve pain by opioidergic as well as other mechanisms (Patel *et al.*, 2005) [38].

#### **Anti-plasmodial**

The concoction prepared from aqueous leaf extract of *Azadirachta indica* exhibited significant antiplasmodial activity against *Plasmodium berghei* infected BALB/c mice at 50 mg/kg and 100 mg/kg dosages when compared with the negative control (Oseni Lateef *et al.*, 2012) [37].

#### **Antipyretic**

The ethanol extract of the leaves of *A. indicia* showed appreciable antipyretic effect (up to 70%) on rats. This

effect might be due to inhibition of the synthesis of prostaglandin E2 which is described as key mediator of fever (Zaman *et al.*, 2009) [43].

#### **Antitumor**

The intraperitoneal injection of Neem Leaf Preparation (NLP) in 500 mg/ kg body weight dose for 20 days efficiently suppressed the growth of tumors which was associated with normalization of the LPx levels and augmentation of GSH contents. NLP enhanced the activity of the endogenous antioxidant scavenging enzymes, superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT) and glutathione-S-transferase (GST) in liver and tumor tissue. The effect of NLP was more pronounced when treated as early as day 5 of post-tumor cell inoculation (Metwally *et al.*, 2014).

#### **Antiulcer**

The aqueous extract of *Azadirachta indica* leaves exhibited antiulcer activity (Anonymous, 2004; Khare, 2007) [27].

#### **Antiviral**

The aqueous solution of seeds of *Azadirachta indica* showed antiviral activity against okra mosaic virus (Anonymous, 2004). Neem oil has been found to slow down the growth of HIV-virus (Anonymous, 2004; Khare, 2007) [27].

#### **CNS depressent**

The acetone extract of leaves exhibited CNS depression, reduction of blood pressure as well as heart rate without showing diuretic activity (Anonymous, 2004).

#### **Hepatoprotective**

The water soluble portion of alcoholic extract of the *Azadirachta indica* leaves was found to possess hepatoprotective activity in rats (Anonymous, 2004).

The extract of *A. indica* leaf was administered in rats with paracetamol induced hepatic damage and significantly enhanced the hepatic level of glutathione dependent enzymes and superoxide dismutase and catalase activity suggesting that the hepatoprotective effect of the extract on paracetamol induced hepatotoxicity may be due to its antioxidant activity (Chattopadhyay and Bandyopadhyay, 2005).

#### **Hypoglycemic**

The water soluble portion of alcoholic extract of the neem leaves was found to possess significant blood sugar lowering effect in glucose fed and adrenalin –induced hyperglycemic rats (Anonymous, 2004; Khare, 2007) [27].

#### **Hypolipidemic**

The leaf extract of *Azadirachta indica* exhibited significant hypolipidemic activity. The effect of leaf extract on serum and liver lipid parameters viz. cholesterol, total lipids, phospholipids and triglycerides was studied in rats fed on anthergenic diet for 4 weeks (Chattopadhyay, 1995).

#### **Larvicidal**

The aqueous extract of leaves of *Azadirachta indica* shows a slight larvicidal activity. In another study, a major volatile constituent (75.74%) di-n-propyl disulphide from the seed exhibited larvicidal activity against yellow fever mosquito

(*Aedes aegypti* Linn) (Anonymous, 2004).

The Azadirachtin, the *Azadirachta indica* tree extract exhibited significant larvicidal activity against *Culex pipiens* mosquito larvae and pupae in east of the Republic of Algeria under laboratory conditions. Mosquito adult fecundity were markedly decreased and sterility was increased by the Azadirachtin after treatment of the fourth instar and pupal stage. The treatment also prolonged the duration of the larval stage (Alouani *et al.*, 2009).

#### **Nimaticidal**

The ethanolic extract of the leaves of *Azadirachta indica* exhibited nimaticidal activity against *Cephalobus littoralis* (Anonymous, 2004).

#### **Spermicidal**

The powder of the Neem leaves at a dose of 20mg, 40mg and 60mg/rat/day for 24 days exhibited spermicidal activity (Anonymous, 2004). A volatile fraction of the Neem oil is reported to be responsible for spermicidal activity at a dose of 25 mg/ml for human sperm (Khare, 2007) [27].

#### **Conclusion**

*Azadirachta indica* (Neem) 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 analgesic, antiandrogenic, antianxiety/ anxiolytic, anti-atherosclerotic, anti-bacterial, anticandidal, antifeedant, anti-fungal, antihepatotoxic, anti-inflammatory, antileishmanial, antimalarial, antimicrobial, antinociceptive, anti-plasmodial, antipyretic, antitumor, antiulcer, antiviral, cns depressant, hepatoprotective, hypoglycemic, hypolipidemic, larvicidal, nimaticidal and spermicidal effects. The scientific studies have proved most of the claims of traditional medicines. However, further, detailed clinical research appears worthwhile to explore the full therapeutic potential of various parts of *Azadirachta indica* in order to establish it as a standard drug.

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