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Review Article

Comprehensive Review on Pharmacological Effect of Melia Azedarach

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ABSTRACT

Medicinal plants and its essential additives, beverages and medicine have been part of human culture since the dawn of time. Medicinal plant mainly consists of nutritional, biological, pharmacological and toxicological properties in numerous applications. Nowadays, most people depend on the alternative therapies to treat many types of illnesses derived from the natural sources. Melia azedarach is one of the plants in which belong to the family of meliaceae which mainly grown in Indian states. The parts of plant have medicinal properties and also use in a native and tribal people in various parts of India for very ancient time, this plant mainly traditionally been used to cure various diseases including piles, asthma, cough, vomiting, nausea, and itching. This study mainly includes a comprehensive analysis of systematic botanical description, phytochemistry, traditional uses, research on plants, pharmacological activity, and medicinal applications.

INTRODUCTION

From time immemorial, Herbs/herb product are being used for treatment of numbers of ailments by the people of India, Sri Lanka, Pakistan, China, Japan and other Asian countries and the system of treatment is known as Alternative system of medicine. In India the alternative system of medicine is known as Ayurveda. Apart from Ayurveda, there is Unani and Siddha system of medicine in India which also uses herb/herb product for treatment of ailments. Medicinal plant plays an important role in healthcare system, based on experimental theories on indigenous people, mainly it is concluded that the medicinal plant is not only used in disease treatment but it also been used in maintaining a good health.

Bakayan (*melia Azedarach)* is a popular unani plant which is belongs to the family of meliaceae. The bakayan tree also known as the bakain tree, mahanimb in Hindi, Persian lilac in English also in South Africa known as the Paradiso. The whole Bakayan parts have a specific medicinal property as specific used including (leaves, stem and roots). The Melia azedarach is having a small to big sizes and having shrub of 5-15 metre in height. It is known to the close relative of neem; it is mainly

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distributed in tropical and subtropical countries and it contains the phytochemical constituents which is used in pest control.

Melia Azedarach various parts i.e leaf, flower, seeds, fruits, root, root bark, stem has been used for the treatment of various disease malaria, diabetes, cough, skin diseases, bronchitis, leprosy, asthma [1,2]. It having various types of activities [3]. Various types of chemical constituent have been detected in *Melia Azedarach* leaf including kaempferol, quercetin, stigmasterol, B-sitosterol, B-carobene, tocopherol etc. [4]. In bark the compound 2, 3-dihydrobenzofuran is present in (0.22%) an essential oil is used in treatment of diabetes retinopathy and arthritis [5,6,7]

Taxonomic Classification

Kingdom:	Plantae
Order:	Sapindales
Family:	Meliaceae
Genus:	Melia
Species:	Melia Azedarach
Binomial name:	Melia Azedarach Linn
Class:	Magnoliopsida

Source and botanical description

Botanical source:	Melia Azedarach
Family:	Meliaceae
Synonyms:	Melia composita
Sanskrit synonyms:	Mahanimba, Himadruma, Paratanimba vraksha.

Regional names:

Language	Regional Names
English:	Persian lilac, Pride of India, common bead tree.
Hindi:	Bakayan, Bakain, Mahanimb
Bengali:	Ghora neem
Gujrati:	Bakan, limbodo
Telgu:	Taraka vepa
Kannada:	Bevu
French:	Fleurslilas
United State:	White Cedar
Malyalam;	Mullay vaempu
South America	Paradise or Paraiso

It is a large medium size tree which is losses its leaves in every autumn, its height is 9-12 metre, with a cylindrical bole and a dark grey bark having a longitudinal furrow. Leaves are compound and alternate, they are long, dark green with sparse hair along the veins and light green [8,9].

Pellets are pinkish lavender and fruits is drupe, one seeded, stalked greenish yellow to yellowish and 1-1.5 centimetre in diameter [10].

Vernacular names:

Chinaberry, Persian lilac, pride of India, China tree, Indian lilac and breed tree, Bakain, Bakayan, Mahanimb [11].

Microscopic examination:

- **Leaves:**

➢ **Rachis:**

The transverse section of the rachis epidermis reveals unicellular and multicellular trichomes, as well as multicellular glandular trichomes on unicellular stalks. It features a wide cortex, cells containing rosette crystals of calcium oxalate, and vascular tissue located nearly circularly in the middle region.

➢ **Midrib:**

Midrib mainly contains single layer epidermis and shows are ridge above and below, and also converted with cuticle on both surfaces. In that also cortex consists above 3 layers of collenchymatous cells on the both sides of thin wall parenchymatous cells.

➢ **Lamina**:

Lamina Mainly compose of single layer of epidermal cells, multicellular glandular. It is Isobilateral thick cuticle situated part. Cork cell are compressed and rectangular in shape as well as secondary phloem multilayered and compressed. The cork cambium and secondary cortex are absent. In that phloem parenchyma is irregular as well as thin walled, plates and composed of group of fibres [12,13,14].

Phyto-Chemical study:

Melia Azedarach contains various types of phytoconstituents, each with distinct pharmacological actions. Additionally, it includes a variety of organic compounds such as anthraquinones, flavonoids, acids, steroids, alkaloids, and tannins [15,16,17].

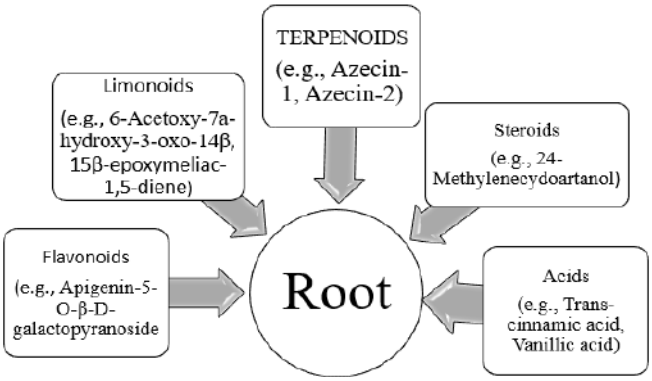

Fig. [1] Phyto constituent of root [18]

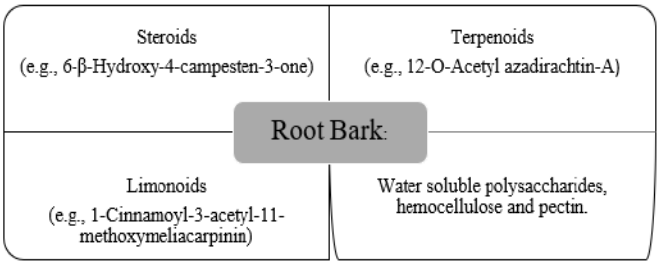

Fig. [2] Phyto constituent of root bark

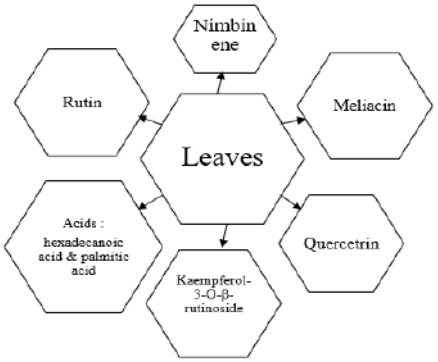

Fig. [3] Phyto constituent of Leaves [19,20]

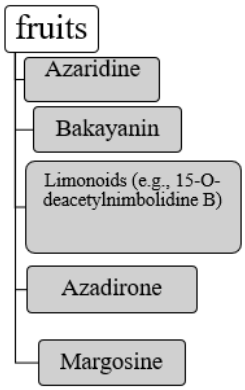

Fig. [4] Phyto constituent of fruit

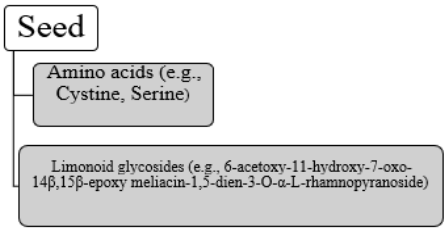

fig. [5] Phyto constituent of seed

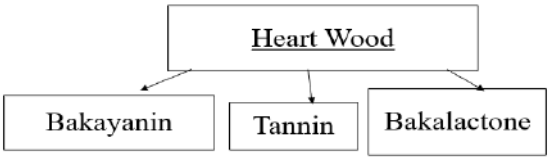

Fig. [6] Phyto constituent of Heart Wood

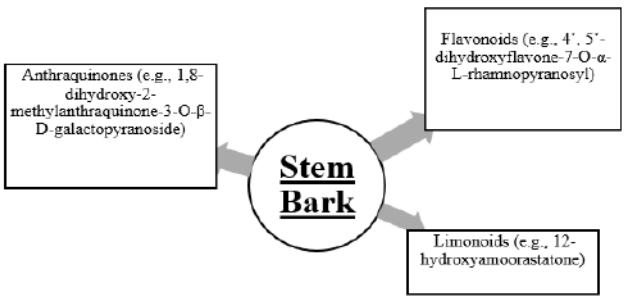

Fig. [7] Phyto constituent of Stem Bark

Traditional Uses:

Part of Plant	Uses
Stem 	The executed gum obtained from its trunk is useful product in spleen enlargement. It wood extract is mainly used in internally in asthma, decoction of bark generally used for the loss of appetite, skin diseases, paroxysmal fever to relieve thirst, nausea, and vomiting [22].
Leaves 	Leaves of *Melia azedarach* is used to relieve a nervous headache and to cure the eruption on the scalp. leaf juice is of *Melia azedarach* is used as an anti-helminthic, diuretic and emmenagogue, expectorant [22,28,29]. These have been significant advancements both internally and externally in the treatment of leprosy and other skin-related diseases, paving the way for effective cures and improved patient care.
Flower 	The flower of *Melia azedarach* is used in a various disease and its having a various medicinal properties, they are astringent and also applied to relieve nervous headache. The flowers are vermicides, stomatic and used for to kill the lice in head [22,29].
Fruit 	Fruits consist of various medicinal properties i.e. purgative, emollient and anthelmintic [21]. Fruits are regarded as tonics, and Sushruta recommended the internal use of mahanimb fruits for treating indigestion, colic, and intestinal catarrh [30].
Seed 	The seeds of *Melia azedarach* (Mahanimb) are useful in various health problem likes expectorant, anthelmintic, helminthiasis, typhoid fever, pain in the pelvic region uropathy [29]. They are generally bitter in taste called as (nimboni). They also used for rheumatism. For skin diseases oil obtained from the seed is use for treatment [28]. The seeds also used for a gout from ancient time, its also prescribed for urinary disorder, and pile 16th century [30].

Root 	The root of the mahanimb is conscious the traditional uses properties. They are generally bitter in taste; the roots are prescribed in the form of bitter tonic in low doses. They are astringent, mildly thermogenic, purgative, voluntary, antiseptic, anthelmintic constipating, expectorant, antiperiodic, urinary astringent use in the form of Tonic. They are useful in skin diseases, wounds, ulcer, piles, worm infection, cough, headache, leprosy, asthma, diabetes, abnormal urethral discharge, chronic and Intermittent fevers, vomiting, post labour pain in uterus [22,29].
Root Bark 	The root bark of *Melia azedarach* is useful as an anthelmintic and, in large doses, as a narcotic [31]. It helps remove obstructions in the body by opening ducts and acts as a resolvent and alexipharmic antidote for treating poisoning or infections.

4. Scientific validated Uses:

4.1 Analgesic activity:

Melia azedarach shows the narcotic analgesic activity/ mediated through opioid receptor [32].

4.2 Haematological activity:

The role of in haematological parameter was studied in mice the extract of leaves exhibited increase red blood cells volume and haemoglobin concentration and increases in neutrophile number an a decrease in lymphocyte number [33].

4.3 Immunomodulatory activity:

Melia azedarach leaves extract was found to inhibit phagocytosis and the respiratory burst in human monocytes that are triggered by the post-receptor stimulus phorbol 12-myristate 13-acetate [34].

4.4 Anti Feedant activity:

Melia azedarach powdered fruit gives effect as an extract in petroleum ether and acetone reduces F1 progeny and repellency to adult of Sitophilus oryzae at different concentration.

The results indicated that mortality rates following exposure to the powder were initially low during the first week of treatment, gradually increasing to moderate levels thereafter [35]. A water extract from the leaves and fruits of M. azedarach demonstrated a reduction in live larvae of B. fusca after 72 hours of treatment [36]. Systematic fractionation of a fruit extract from Argentine Melia azedarach, monitored through insect antifeedant bioassays, led to isolation of melia tanin a limonoid antifeedant composed of two interchangeable isomers. At concentrations of (4 µg/cm²,1 µg/cm²) this isomeric mixture exhibited antifeedant activity comparable to azadirachtin, effectively inhibition of larval feeding of Epilachna paenulata and the polyphagous pest Spodoptera eridania, respectively [37].

In laboratory bioassays, both choice and no-choice tests showed that treating elm leaves with extracts from unripe fruits and green or senescent leaves of Melia azedarach at concentrations ranges from 1% to 10% significantly deterred feeding by adult elm leaf beetles, Xanthogaleruca luteola. From various plant extract exhibited similar antifeedant effects, and the resulting starvation likely contributed to the high mortality rates observed [38].

Additionally, three new limonoid antifeedants meliacarpinins 1-3—were isolated from the root bark of Chinese Melia azedarach Linn (Meliaceae), along with fourteen known limonoids. The structures and antifeedant activities of these compounds were characterized. The isolated limonoids (1-17) were tested for antifeedant activity against the larvae of S. exigua Hubner and S. eridania (Boisduval) using the conventional leaf disk method. The most potent among these were meliacarpinins 1-4, which exhibited activity at a concentration of 50 pw, equivalent to 1 pg/cm². Although this potency may be lower than that of azadirachtins from the Indian neem tree, M. azadirachta indica, these limonoids belong to the top tier in terms of effectiveness [39].

4.5 Insecticidal Activity:

Insecticidal activity of methanolic extracts stems part of Melia azedarach with (acetone, benzene, and hexane) extracts, it has been tested against pests like Helicoverpa armigera, Earias vittella, and Plutella xylostella. A 7.5% concentration of the methanolic extract gives result in higher larval mortality, while a 10% concentration of methanolic extract mainly shows improved ovicidal activity against tested pest [40].

Various concentrations (2.5%, 5.0%, 7.5%, and 10%) of the methanolic extract from Melia azedarach roots and its acetone, benzene, and hexane constituent mainly (0.5% and 1.0%) were evaluated for their insecticidal effects on Earias vittella larvae. The 10% methanolic extract mainly yielded the good outcomes regarding to larval and pupal duration, pupation rates, adult emergence (both reduced), adult longevity, and minimal egg hatching. Among the fractions, the 1% acetone extract performed the best [41]. Aqueous extract of Melia azedarach was evaluated against the mosquito larvae (Anopheles stephensi Liston), with a particular focus on the seeds. These assessments involve measuring of larval mortality percentages at different concentrations [42].

Methanolic extracts from dried and crushed neem, Melia azedarach seeds were analysed for their affection on the food consumption indices of Earias vittella. When it compared to nimbecidine (300 ppm azadirachtin), the neem, and nimbecidine (0.5%) treatments negatively impact to several biological processes of the pest. Larvae that consumed fruits treated with higher concentrations of the extracts showed reduced weight, prolonged development times, and decreased pupation, adult emergence, and fecundity compared to those fed untreated food [43].

Extracts of the fruits and leaves of Melia azedarach were tested against the eggs and nymphs of Triatoma infestans for their repellent and insecticidal properties. The unripe fruit extract was highly repellent to first and fourth instar nymphs, while the ripe fruit had a milder effect, and the leaves showed no effectiveness. There is no significant affection on egg hatching, nymph survival, or development time, but first instar nymphs that were in contact with extract treated refuges were significantly smaller after moulting compared to controls [44]. Fazal's research mainly focused on non-toxic and eco-friendly plant-based repellents, highlighting the effect of Bambusa arundinaceae, Coriander sativum, Melia azedarach, Mentha spicata, Ocimum basilicum, Ricinus communis, Urtica dioica, Vitex nigundo, Withania somnifera, and Xanthium strumarium in insect control [45].

4.6 Antiviral activity:

A peptide extracted from the leaves of Melia azedarach (Meliacine), it has been evaluated effect against foot-and-mouth disease virus (FMDV) in BHK-21 cells as an antiviral activity [46]. By blocking the production of specific infected cell polypeptides and viral DNA synthesis it gets action as an inhibits herpes simplex virus type 1 (HSV-1), thereby limiting the spread of the virus [40]. In vitro studies have shown that MA prevents

HSV-1 replication and protects against herpetic stromal keratitis into mice [47]. In a murine model mice infected with HSV-1 showed significantly reduction in incidence and symptoms after receiving topical MA treatment three times a day for three days, starting 24- or 96-hours post-infection. Histological analysis analyses the no tissue damage in MA-treated mice, while untreated mice exhibited inflammation and necrosis. Notably, MA mainly treat initiated 96 hours post-infection still effectively prevented ocular disease, indicating potential immunomodulating properties of MA [48].

4.7 Antifungal activity:

Against aspergillus flavours and candida valbicans the ethanolic extract of ripe fruit of m. azedarach show fungistatic and fungicidal activity [49].

4.8 Antibacterial activity:

The antibacterial activity of Melia azedarach flowers evaluates potent effects against skin infections caused by Staphylococcus aureus in rabbits [50]. A methanolic extract of the flowers was used, with methanolic extract of leave, roots, and stem bark mainly shows the action. Melia azedarach show broad-spectrum antibacterial activity, which increased upon fractionation into petrol, dichloromethane, and ethyl acetate (51).

4.9 Cytotoxic activity:

There are various types of researchers who have reported the cytotoxic activity of Melia azedarach by study on it. One study mainly demonstrated that cytotoxic effects against to the P388 lymphocytic leukaemia cell is get by ethanolic extract of root bark of plant. Another study indicated that the strong cytotoxic potential effect against cultured human lung (A549) and colon (Col2) cancer cells by the ethanolic extract of M. azedarach [52]. Additionally, the effects of meliacine (MAS) and two fractions, Mab 1 and Mab 2, derived from it were examined on the in vitro production of TNF-alpha in murine macrophages it mainly induced by bacterial lipopolysaccharide (LPS) from E. coli. When these fractions were administered simultaneously to macrophage cultures, they significantly increased the release of TNF-alpha 24 hours after induction in a dose-dependent manner. Meliacine alone, at concentration of 56 microg/ml, was found to be a weak inducer of TNF-alpha production [53]. Furthermore, a methanolic extract of ripe Melia azedarach fruits yielded seven new ring C-Seco limonoids, which exhibited inhibitory activity against the HeLa S3 cancer cells [54].

4.10 Antimalarial activity:

The antimalarial activity of M. azedarach leaf extracts was tested against laboratory adapted isolates of Plasmodium falciparum by the use of an in vitro radio isotopic uptake techniques. Chloroquine mainly defined as the standard antimalarial drug for comparison [55].

4.11 Anthelmintic activity:

The anthelmintic efficacy of Melia azedarach seeds mainly tested against gastrointestinal part of sheep by counting the number of eggs per gram of faeces (EPG) before and after treatment. The results mainly evaluated that Melia azedarach does not have anthelmintic activity against Trichostrongylus infections in sheep [56].

4.12 Antilithic activity:

Lithiasis was induced in rats by providing them with 0.75% ethylene glycol in their drinking water for 28 days. Concurrently, an oral administration of an aqueous extract of Melia azedarach at a dose of 250 mg/kg for the same duration resulted in a reduction of urinary levels of calcium, oxalate, and phosphate, while increasing urinary magnesium levels. This suggests that Melia azedarach has an antilithiatic effect on ethylene glycol-induced nephrolithiasis in rats [57].

4.13 Antifertility activity:

The ethanolic leaf extract of plant Melia azedarach as an antifertility activity was studied in male rats, where a daily oral dose of 100 mg/kg for 21 days resulted in a complete termination of libido in all

treated males [58]. In other study, the ethanolic extract of Melia azedarach roots when administered at daily doses of 250 mg/kg as well as 500 mg/kg, respectively, during days 1-10 post-coitum it mainly prevents pregnancy in adult female rats about 60-75%. Upon fractionation, the potent activity was localized in the chloroform fraction of the extract, which exhibited 80-100% effect at a daily dose of 250 mg/kg in repeated tests [59]. Additionally, oral administration of polar and nonpolar fractions of Melia azedarach seed extract at 24 mg/kg for 18 days significantly decreased it mainly decrease ovarian follicles in rats [60]. To evaluate the potent role of energy metabolism in the antifertility action, researchers mainly measured changes in the action of key carbohydrate metabolism enzymes in the uterus on the 7th day of pregnancy. They found that the enzyme phosphofructokinase, a critical component of the glycolytic pathway, it mainly reduced in the uteri of treated rats compared to controls. The hexose monophosphate pathway also appeared sensitive to the treatment of, exhibition of inhibitory effects on glucose-6-phosphate dehydrogenase activity [61]. Furthermore, various concentrations of petroleum ether fractions from Melia azedarach seeds inhibited the motility in rat and mouse spermatozoa over time intervals ranging from 20 to 240 seconds compared to controls. This action was dose-dependent, with complete immobilization observed at potent concentrations of 10 mg and 25 mg tested over 240 as well as 20 seconds, respectively [62].

4.14 Antiulcer activity:

In a study conducted by Moursi in 1984 [63], the lipoidal fraction of Melia azedarach extracts was tested on rats subjected to Gipsing restrain stress to induce ulcers. The results determined that the lipid components, particularly the phytosterol fraction, effectively reduced both free and total hydrochloric acid levels while decrease in the overall acidity. Additionally, the study found increase in the volume of gastric juice, suggesting the antiulcer potential action of Melia azedarach.

4.15 Antipyretic activity:

Sultana et al. (2014) [64] this study evaluates the antipyretic effect of a hydro-methanolic extract of Melia azedarach leaves, the extract demonstrated significant antipyretic activity at a dose of 500 mg/kg. The effectively reducing yeast-induced elevated temperatures compared to the standard drug, paracetamol.

4.16 Antiprotozoal activity:

Lee et al. (2007) [65] reported antiprotozoal effects on Trichomonas vaginalis cells by inhibiting cell multiplication and impairing protein synthesis by Melia azedarach extract.

4.17 Wound healing activity:

Vidya et al. (2012) [66] it mainly reported that the wound healing effect of Melia azedarach leaves in alloxan-induced diabetic rats. Their results indicated that the topical application of methanol leaf extract significantly promoted wound healing, comparable to the standard treatment with povidone-iodine. The increasing in wound healing mainly observed with Melia azedarach leaf extract by its antimicrobial properties.

4.18 Antinephrolithiasis:

Christina et al. (2006) [67] in that in vivo study conducted on rats to determine the effects of aqueous extract of Melia azedarach on induced ethylene glycol nephrolithiasis. The results showed that the extract reduced urinary calcium, oxalate, and phosphate levels, indicating its potential to inhibit nephrolithiasis, as judged by serum as well as urine creatinine levels.

4.19 Anticancerous activity:

Jafari et al. (2013) [68] studied the anticancer activity of Melia azedarach extracts on various cancer cell lines and evaluate their safety on normal cells. They found that the seed kernel extract mainly exhibited the potent cytotoxicity and selectivity against cancer cells IC50 range of (8.18-60.10 µg/mL), while the methanol leaf

fraction show greater safety. The presence of flavonol in the leaves mainly contribute to the medicinal effect noted in traditional uses.

4.20 Antioxidant activity:

Ahmed et al. (2012) [69] concluded that phenolic compounds in Melia azedarach contribute to its antioxidant activity, with high DPPH causing attributed to hydroxyl groups get inactivate the lipid free radicals. Polyphenols, a large group of antioxidant compounds, mainly play a role as an antioxidant effect. Munir et al. (2012) [70] further evaluated that the antioxidant activity of Melia azedarach, demonstrating that the total phenolic content [TPC] and total flavonoid content [TFC] in sun dried extracts mainly ranged 74.43-112.10 mg and 13.32-28.11 mg, respectively. In that ambient-dried extract mainly consists of TPC (total phenolic content) and TFC (total flavonoid content) values ranges of 66.89-103.34mg 10.67-23.45mg respectively. The DPPH activity of sun-dried extract ranged from 55.43-63.86%, for ambient dried extract mainly range from 48.54-61%. For sun dried extract (0.727-1.211) compared with ambient dried (0.601-0.890). Overall, the study indicated that sun-dried extracts of Melia azedarach exhibited least antioxidant activity, with the stem bark showing the best results.

4.21 Hepatoprotective activity:

In these study by Ahmed et al. (2012) [69], the hepatoprotective effects of Melia azedarach is investigate against the liver injury induced by carbon tetrachloride (CCl4). Researcher mainly measures parameters such as ALP, SGPT, SGOT, and serum bilirubin, and conducted pathological evaluations. They found that the biochemical markers improved after treatment and the histological changes, like change in fatty in liver cells and fibrosis in the CCl4-treated group, get returned to normal levels. This research is underway for identification of the specific compounds responsible for the hepatoprotective effects.

DISCUSSION & CONCLUSION

In this review mainly contains the information about the M. Azedarach plant with their pharmacological activities in various types of the disease treatment. The main approach of this review is to determine the beneficial traditional uses of the M. Azedarach with their research studies, theories as well as non-research studies. The major objective of the selected plant i.e. it mainly gives various types of therapeutic action onto the biological system as listed in scientific validated uses. It mainly composed of anticancerous, antioxidant, insecticidal, antipyretic, antibacterial, antiulcer and etc. activities. Around the world, there are various type of medicinal plants are recognized for their beneficial effects on different health conditions. However, the therapeutic potency of herbal remedies is often limited by challenges into standardization, pharmacodynamics, as well as pharmacokinetics due to their complex mixtures. This review mainly focuses on the pharmacological activities of the Melia azedarach plant, aiming to provide valuable information to the health professionals, scientists, and scholars in pharmacology and therapeutics. By doing so, it seeks to support the development of evidence based alternative medicines for treatment of various diseases. This review is particularly beneficial for researchers aiming to cover the scientifically unverified and verified aspects of this plant's efficacy. Recently, there has been a growing interest in exploring the pharmacological properties of herbal medicines from diverse sources. Given the characteristics of Melia azedarach, a thorough and systematic investigation is necessary for the identification, cataloguing, and documentation of plants. This approach could significantly increase the preservation of traditional knowledge surrounding herbal

medicine. Future research, especially involving human subjects, could lead to the development of a versatile drug that meets market needs

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