

A Review on Pharmacological Activities, and Bioactive Compounds of *Mangifera indica* (Mango) *Saraca indica*

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ABSTRACT

Mangifera indica (family Anacardiaceae), commonly known as mango, is a pharmacologically, ethnomedically, and phytochemically diverse plant. Various parts of *M. indica* s. *indica* tree have been used in traditional medicine for the treatment of different ailments, and a number of bioactive phytochemical constituents of *M. indica* have been reported, namely, polyphenols, terpenes, sterols, carotenoids, vitamins, and amino acids, and so forth. *S. indica* have been reported phytoconstituents, such as Flavonoids, Steroids, Glycosides, Saponins, Carbohydrates, Proteins. Several studies have proven the pharmacological potential of different parts of mango trees such as leaves, bark, fruit peel and flesh, roots, and flowers as anticancer, anti-inflammatory, antidiabetic, antioxidant, antibacterial, antifungal, anthelmintic, gastroprotective, hepatoprotective, immunomodulatory, antiplasmodial, and antihyperlipemic. Several studies have proven the pharmacological potential of different parts of *saraca indica* trees such as leaves, bark, stem and flowers as antihemorrhagic activity, anti-microbial activity, uterine tonic, anti-helminthic activity, anti-inflammatory, antiarthritic effect, anti-diabetic property, antioxidant activity, anticancer effect, larvical activity. In the present review, a comprehensive study on, pharmacological activities, and bioactive compounds of *M. indica* and *S. indica* has been described.

Keywords: Ashoka, *Saraca asoca*, *Mangifera indica*, Pharmacological activity, medicinal uses.

INTRODUCTION

M. indica L. is considered as one of the main tropical fruits in the world believed to be originated from Asia [1]. It has been reported that China, India, Brazil, Nigeria, Pakistan, Mexico, Thailand, and Philippine are well-known for mango cultivation with India being the highest mango cultivating country [2]. World production of mango is approximately 42 million tons. Mango is known by various names around the world, for example, Manja in Arabic, Mannko in Greek, Am or Ambi in Hindi, Amba in Sinhala, Mangué in French, Mango in Finnish, Mango in Dutch, Mangué in German, Mángguō in Chinese, and Mampalam in Tamil [3]. Mango fruit peel and flesh are reported to be a rich source of fiber, vitamin C and A, essential amino acids, and polyphenols [4]. Mango seed has also been reported as a rich source of polyphenols [5]. Despite the common use of mango fruit as a food item, various parts of mango trees have also been used for medical purposes since ancient times, mostly in Southeast Asian and African countries [7].

Whereas the *Saraca asoca* medicinal plants were thus one of the main plants used since ancient times. Asoka or Ashoka is a Sanskrit meaning, "no sadness" or "no pain." Ashoka is one of India's most mythical and holy trees. Ashoka, known as *Saraca asoca* or *Saraca indica* of the family Caesalpiniaceae. Universally recognized as the binomial Latino name. *Saraca asoca* is an evergreen shrub or small tree with a thick horizontal crown of up to 10 meters in height. The circumference of the bole may be 10cm. The tree is a key herbal medicine in Ayurveda. Bark is picked from the wild, and sold on local markets, alone and in a range of formulations. *Saraca asoca* is one of India's largest sacred trees, both Hindus and Buddhists, with beautiful flowers widely used to decorate temples. In certain parts thereof, this small tree has been affected largely by the loss of its habitat and over-exploitation⁴⁻⁶. Much evidence is found in literature on pharmacological and ethnomedicinal uses of *M. indica* and *S. indica* however, there is no complete review on phytochemicals, biological effects of phytochemicals, and pharmacological and ethnomedicinal properties of *M. indica*. Therefore, we present this review as an up-to-date and comprehensive evaluation which mainly includes some reported bioactivities of phytochemicals, and pharmacological properties of *M. indica*.

Taxonomy and Botanical Description *M. indica*

The genus *Mangifera* belongs to the family Anacardiaceae. Genus *Mangifera* approximately contains 69 different species with *M. indica* being the most common species in the same genus [10, 11]. *M. indica* plant is an evergreen broad canopy tree which grows to a height of 8–40 m [12]. *M. indica* bark is a thick brown-gray colour and is superficially cracked [13]. Leaves are 15–45 cm in length with variable sizes [13]. Leaf petiole has a variable length from 1–10 cm [13]. *M. indica* leaves (Figure 1) possess different shapes (lanceolate, ovate-lanceolate, linear-oblong, roundish-oblong, oval, and oblong) [13]. Green, red, and yellow leaves are seen in some mango varieties and upper leaf surfaces are normally shiny [13, 14]. In case of *M. indica* flowers, male and hermaphrodite flowers are produced in the same panicle; its size can vary from 6–8 mm in diameter. There are about 4000–5000 small flowers in panicles with red/purple spots on petals [13, 14]. Even though a large number of flowers present in panicles, very few will be developed as fruits. Flowering season is mainly from January to April and most of the flowers are subsessile and have a sweet smell. *M. indica* fruit (Figure 1) is drupe with different sizes, shapes, and colours. Fruit peel is green, yellow, red, or orange. Seeds are ovoid- or oblong-shaped covered with a hard endocarp having a woody fiber covering [15].

Whereas *S. indica* Parts used: such as Bark, leaves, Flower.

Externally: The medication is applied locally to treat a variety of poisonings and pain.

Internally: It is recommended for uncomfortable visceral conditions.

Systematic

- Digestive system: in cases of dysentery, diarrhea, worm infestation, and thirst.
- Heart and circulatory system: Edema and hemorrhages are suggested by the flower.
- Menorrhagia, dysmenorrhoea, leucorrhoea, and other uterine illnesses are cases of the reproductive system.
- Urinary system: Powdered leaves are used to treat urinary tract stones and dysuria. Bark has uterine sedative and strong astringent properties. It directly affects the uterine muscle

fibers. It stimulates the ovarian tissue as well as the endometrium. It appears that the ketosterol found in Ashoka bark has androgenic properties.

Synonyms: Ashok, Shoknashan, Smaradhivas, Kankeli, Vanjuldrum, Raktapallava, Hempushpa, Nata, Pindapushpa, Gandhapushpa, Madhupushpa5 .

Vernacular Names: In Indian literature, this tree is known by several different names. The Ashoka tree goes by a few names.

Latin Name: *Saraca indica* Common name: Asoka, Hempushpa

English Name: Asoka

Habitat: It can be found throughout the Indian subcontinent. The Western Ghats and Deccan plateau are thought to be the tree's original habitat. The eastern and central Himalayas are also home to it. It can grow up to 750 meters above sea level, according to reports.

Pharmacological Properties of *M. indica*

A number of in vitro and in vivo studies have been carried out to reveal various pharmacological potentials of *M. indica*. Different parts of *M. indica* trees have been demonstrated to exert anticancer, anti-inflammatory, antidiabetic, antioxidant, antibacterial, antifungal, anthelmintic, gastroprotective, hepatoprotective, immunomodulatory, antiparasmodial and antihyperlipemic effects [69].

Antioxidant Properties of *M. indica*

Antioxidants are substances which inhibit/delay oxidative damage by trapping free radicals to a target molecule [70]. Several classes of natural compounds including polyphenols, phenolic acids, and flavonoids are reported as good free radical scavengers [71]. It has been reported that reactive oxygen species (ROS) and some other oxidants cause various disorders and diseases to human [71]. Humans possess antioxidative mechanisms which fight against reactive oxygen species (ROS) and some other oxidants by deactivating free radicals before they attack targets in human body [72]. Naturally occurring antioxidants have gained much attention recently as they possess a remarkable ability to fight against free radicals and reactive oxygen species [72]. As almost all the parts of the mango tree are reported to possess polyphenols, which are well-known antioxidants, most of the pharmacological studies have proven that antioxidant properties with extract(s) of various parts of the *M. indica* tree are related to polyphenolic content.

Anti-Inflammatory Effects of *M. indica*

Several naturally found polyphenols are reported to possess anti-inflammatory effects via inhibition of nuclear factor kappa-B (NF- κ B) [84]. However, anti-inflammatory activities of these compounds depend on their chemical structures and their cellular targets [84]. Production of a large amount of proinflammatory cytokines (IL-1, 2 and 6 and TNF) increase the expression of enzymes such as COX-2 and iNOS which are associated with anti-inflammations [85]. Nuclear factor kappa-B (NF- κ B), a transcriptional factor, is reported to control expression of proinflammatory cytokines [86]. Ulcerative colitis and inflammatory

bowel disease are considered as main diseases that occur due to chronic inflammation [87]. Several studies have shown that mango extracts can exert anti-inflammatory effects in experimental models of ulcerative colitis. In a recent study, treatment with a mango beverage prepared from fruit (Mexican variety) which consists of polyphenols and vitamins has caused attenuation of colitis symptoms by expressing the PI3K/AKT/mTOR pathway [88]. Another study conducted by the same authors showed that the same mango polyphenols-rich beverage can inhibit the IGF-1R/AKT/mTOR pathway in ulcerative colitis [89].

Analgesic Effects

Analgesic effects of stem-bark aqueous extract of *M. indica* have been studied by Ojewole, 2005. Hot-plate and acetic acid test models of pain in mice have been used to study analgesic effects, and results of this study have demonstrated significant analgesic effects in mice with nociceptive pain. Islam et al. 2010, have demonstrated analgesic effects of methanol extract of leaves of *M. indica*. Results have demonstrated a significant reduction in writhing response in an acetic acid-induced writhing response rat model. Garrido et al., 2001 [93], have shown possible analgesic effects of Vimang. Acetic acid-induced abdominal restriction and formalin-induced licking were used to test analgesia. Results of this study have shown that Vimang can exhibit antinociceptive effects in mice. Moreover, a considerable dose-dependent inhibition in formalin-induced pain was also observed in rats after administration of Vimang.

Immunomodulatory Effects of *M. indica*

Immunomodulation is a process that adjusts the immune system of an organism upon any change caused by a foreign agent. Immunomodulation can be of two types, namely immunostimulation and immunosuppression. Immunostimulation includes stimulation of the immune system with immunostimulating agents that activate components of the immune system (macrophages, certain T-lymphocytes and granulocytes). 2, COX-2, IL-1 β , TNF- α , and colony-stimulating factor (GM-CSF) mRNA levels were found to decrease in experimental mice model(s).

Antitumoral Effects of *M. indica*

Cancer is considered as one of the major causes of death in the world and any practical solution in fighting this dreadful disease would be very important in public health. It is the main cause of death in economically developed countries and the second leading cause of death in economically developing countries. Cancer is caused by several factors such as chemicals, radiations, tobacco, infectious microorganisms, hormones, gene mutations, and immune conditions. Though, modern surgeries have considerably reduced the cancer death rates, use of radiotherapy, chemotherapy, and hormone therapy treatments cannot completely reduce the number of deaths due to cancer. Plant-based treatments have been used in traditional medicine to treat different diseases including cancer since ancient times and a number of *in vitro* and *in vivo* studies have already been reported in literature to validate these uses. Different organic extracts and decoctions prepared from parts of mango trees and compounds isolated from mango trees have shown anticancer effects and Haden, found in Brazil) have been evaluated in leukemia (Molt-4), lung (A-549), triple negative breast (MDA-MB-231), prostate (LnCap), and colon (SW-480) cancer cells by Noratto et al. 2010. Among the studied mango varieties, two (Ataulfo and Haden) were more sensitive to SW-480 and MOLT-4 cells. Moreover, apoptotic effects of Ataulfo and Haden varieties have also been studied in SW-480 cells in this study.

Antibacterial Effects of *M. indica*

Resistance to antibiotics has become one of the biggest problems worldwide. Unnecessary use of antibiotics for viral infections, prolong use of antibiotics for diseases, wrong prescriptions given to patients without determining the exact cause of infection, and discontinuation of antibiotics without completing treatments by patients are some of the major causes for occurrence of antibiotic resistance. Approximately half of all deaths in tropical countries are due to bacterial infections. Therefore, discovery of novel antibacterial agents for drug resistant bacteria is essential. A number of studies have proven the antibacterial effects of certain plant crude drugs and natural compounds isolated against drug resistant bacteria. Herbal remedies for bacterial infections have gained much attention recently as they are readily available, cause fewer side effects, and cheap.

Antifungal Effects of *M. indica*

Fungal diseases have been identified as an important health problem nowadays. *Candida*, *Aspergillus*, and *Cryptococcus* species are known to causes many fungal diseases worldwide. *Candida albicans* is reported to be the most common pathogen in fungal infections. Although fungal infections are common, few antifungal drugs are currently used to treat infections. Therefore, the identification of novel drugs as antifungal agents is necessary. Plant-based treatments and natural compounds derived from plants have been identified as ideal drug leads for fungal diseases. A number of pharmacological investigations have confirmed antifungal effects of organic/aqueous extracts of different parts of *M. indica*.

Anthelmintic Effects of *M. indica*

Helminth infections which are caused by parasitic worms are commonly seen in tropical regions. They live either as parasites or in some cases in a free-living form. Intestinal nematodes (IN) or soil-transmitted helminths (STH) are the most common types of nematodes. It has been estimated that approximately 30% of world population is primarily infected with helminth parasites annually. Development of resistance to helminth parasites has become a major problem in the treatment of the helminth infections.

Antiplasmodial Effects of *M. indica*

Complete eradication of malaria appears to be a major challenge in the world due to the development of resistance to antimalarial drugs. Many parasites in genus *Plasmodium* cause malaria and *Plasmodium falciparum* is the most predominant in genus *Plasmodium*. It has been estimated that malaria affects approximately 280–290 million people annually. Quinine and artemisinin are naturally derived antimalarial drugs, which have been used for almost 400 years in the treatment of malaria. However, *P. falciparum* has developed complete resistance to almost all the antimalarial drugs in clinical use. Therefore, it is of paramount importance to investigate novel treatment methods/drugs which can target the malaria parasites.

Antihyperlipemic Effects of *M. indica*

Hyperlipidemia is considered as a major reason for atherosclerosis and coronary heart disease [247]. Coronary heart disease is the main cause of death in the world [247]. Scientific investigation of herbal remedies for antihyperlipemic effects will give a strong support for the development of drugs for hyperlipidemia. A recent study by Gururaja et al., 2017 [248], reported cholesterol lowering effects of a methanolic extract of *M. indica* leaves in albino Wistar rats. A significant decrease in plasma cholesterol levels has been observed in rats administrated with cholesterol in this study. Results of the studies conducted with aqueous extracts and ethanolic extracts of *M. indica* leaves have shown promising antihyperlipemic effects in hyperlipemic rat models.

Antidiabetic Effects of *M. indica*

Diabetes mellitus is a metabolic disease resulting from a defect in insulin action or secretion. It has now become a major health problem affecting 442 million people worldwide. 90% of diabetes cases are type 2 and the remainder is type 1. Blood glucose homeostasis is the key to prevent diabetes associated complications such as cardiovascular diseases, kidney diseases, eye problems, and peripheral neuropathy. Several plant-based remedies have been used to treat type 2 diabetes in traditional medicine and a number of pharmacological studies have been conducted to validate these claims. Fruit peel, flesh, seed kernel, leaves, and bark of *M. indica* have been extensively studied for their antidiabetic properties. Gondi and Prasada Rao, 2015 have showed that an ethanolic extract of mango fruit peel can successfully reduce blood glucose level in streptozotocin-induced diabetic rats. Significant decrease in fructosamine and glycated hemoglobin, which are considered as status indicators of diabetes, has also been observed after treatment with the ethanolic extract of mango peel.

Gastroprotective Effects of *M. indica*

Peptic ulcers are mainly present in the lining of stomach or in the duodenum. Nonsteroidal anti-inflammatory drugs, mental or physical stress, alcohol, diet, life style, and antibiotics are considered as main causes of peptic ulcers. Peptic ulcers are usually treated with proton pump inhibitors that reduce the secretion of gastric HCl. As peptic ulcer cases are rising at an alarming rate worldwide, it is necessary to discover novel methods or drugs that can effectively reduce peptic ulcers. Assessment of gastroprotective effects of different extracts of *M. indica* has been carried out. A study conducted by Lima et al. 2006 found that a decoction prepared from *M. indica* flowers can significantly increase gastroprotective properties in an experimental rat model by reducing gastric juice volume and acidity.

Pharmacological Activity of Leaves and Bark of *Saraca Asoca*

Numerous pharmacological properties are present in *Saraca asoca*, including antimicrobial, anticancer, antimenorrhagic, antioxytotic, antihelminthic, antitumor, antioxidant, anti-inflammatory, antihyperglycemic, central nervous system depressant, analgesic, antiinflammatory, antiarthritic, and cardioprotective properties. The following properties: antifungal, antiulcer, larvicidal, uterine tonic, and antidiabetic. A few of them are talked about here¹².

Anti-menorrhagic Activity

Saraca asoca is regarded as a woman's buddy due to its ability to heal a variety of gynecological conditions. In India, dried bark has been used to treat menorrhagia. In cases of uterine problems, females are administered dried bark and flower as a tonic. All disorders related to the menstrual period are also treated with the stem bark of *Saraca asoca*. Research on this leaf action is still possible¹²

Antimicrobial Activity

By using the micro broth dilution experiment, different components of *S. asoca* were investigated for their antimicrobial activity against six different bacteria (*P. aeruginosa*, *K. pneumoniae*, *S. aureus*, *E. coli*, *A. fumigatus*, and *A. flavus*). By measuring the minimum inhibitory concentration and determining that plant internal tissue exposed to an external environment increased the synthesis of anti-infective molecules, it was determined that LHWE (leaves hot water extract) and RBHWE (renewed bark hot water extract) exhibited

superior anti-microbial activity. The antimicrobial activity of *S. asoca* was attributed to the presence of catechin^{12,13}

Uterine Tonic

Because of its stimulating effects on the endometrium and ovarian tissue, *Saraca asoca* is used as a plant as a uterine tonic. An herbal remedy called U-3107 was created using two distinct plant extracts, bark and leaf, which are beneficial for treating a range of menstrual diseases, including premenstrual syndrome, menorrhagia, dysmenorrhea, puberty, abnormal bleeding, and impending abortion^{12,13}. 8.4

Anti-helmintic Activity

In Leaves: The human body becomes malnourished, feeble, and vulnerable to bacterial and viral illnesses when parasitic worms are present. It has been claimed that mature Indian earthworms can be killed or paralyzed by methanolic preparations of *S. asoca* leaves^{12,13}. The stem bark of the *Saraca indica* plant exhibits strong anthelmintic properties because it contains flavonoids, terpenoids, alkaloids, glycosides, saponins, and tannin^{12,13}.

Anti-inflammatory & Anti-arthritis effect

It has been demonstrated that the ethanolic and methanolic extracts of *S. asoca*'s leaf and bark have anti-inflammatory potential by strongly preventing the binding of different transcription factors to their target DNA sequences, such as NF- κ B, AP-1, GATA-1, etc., and so reducing the levels of proinflammatory cytokines. It has also been demonstrated that *S. asoca* extract lowers levels of TNF- α and IL-1, two pro-inflammatory cytokines¹³. Several studies use the model system of Carageenan-induced paw oedema and brine shrimp assay to describe the antiarthritic potential of *S. asoca* leaves and bark¹³.

Antidiabetic Property

In leaves: Studies have demonstrated that the flavonoid fraction of *S. asoca* flowers and leaves inhibits the type-2 diabetes-related enzymes α -glucosidase and α -amylase as well as prevents the oxidation of low-density lipoprotein (LDL)^{13,14}. In bark: Ashoka bark decoction is used to treat diabetes by taking two doses each day. When consumed with milk, dried powdered *Saraca asoca* herb has anti-diabetic properties^{13,14}.

Antioxidant Activity

In Leaf, Jayita Saha and colleagues investigated the antioxidants found in several *Saraca asoca* sections. In an in-vitro model for DPPH radical scavenging, the antioxidant activity of methanol extracts was evaluated at various doses. By comparing the IC₅₀ values of the various plant sections of *S. asoca*, antioxidant activity was demonstrated. The *asoca* plant's methanol extract of the leaves had an IC₅₀ value of 28.6 ± 0.62 mg/ml, which was slightly higher than the IC₅₀ values of the plant's flower and bark, which were 6.83 ± 0.07 mg/ml and 6.6 ± 0.10 mg/ml, respectively¹⁴.

Navneet Kumar et al. investigated the in-vitro antioxidant activity of a bark extract from *Saraca indica* in stem bark. It was discovered that plant phenolic compounds exhibit potent free radical scavenger action by preventing lipid peroxidation through the neutralization of peroxy radicals produced during lipid oxidation^{15,16}.

Anticancer effects

The cytotoxic activities of various extracts of *Saraca indica* L. leaves were screened, and the results showed that the total ethanolic extract was active against MCF-7, HEPG-2, and HCT-

116 ($IC_{50} \leq 30 \mu\text{g/mL}$ [20]) and inactive against the HeLa cell line; on the other hand, the EtOAc extract demonstrated potent cytotoxic activity against HCT-116, as well as active against MCF-7, HEPG-2, and HEPG-2, with IC_{50} values of 0.038, 3.29, 10.14, and 19.21 $\mu\text{g/mL}$, respectively, in comparison to standard doxorubicin, which was found to be 0.175, 0.155, 0.9, and 0.69 $\mu\text{g/mL}$ [15-17].

Larvicidal Activity

Fighting the threat posed by insects like mosquitoes is crucial in the fight against infectious diseases including dengue, filariasis, malaria, and others. It has been demonstrated that the bark, leaves, and flowers of *S. indica*, when extracted using petroleum ether and chloroform, dramatically reduced the population of the mosquito *Culex quinquefasciatus*, so preventing the reproduction of insect vectors [21,22].

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