



Plant Profile, Phytochemistry and Pharmacology of Ashoka (*Saraca Asoca* (Roxb.), De. Wilde) – A Comprehensive Review.

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Abstract

Ayurveda is a traditional system of medicine in which herbal therapies were used systematically. *Ashokai.e.Saraca asoca* (Roxb.) Wilde belonging to Caesalpinaceae subfamily of the Legume is one of the indigenous plants with lots of traditional significance. The all partsof this plant are considered pharmacologically important and has especially been used to manage various gynecological disorders like menorrhagia, leucorrhoea, dysfunctional uterine bleeding. *Saraca asoca* has been reported to contain phytoconstituents like flavoinoids, steroids, glycosides, saponins, tannins, carbohydrates, proteins along with lot of pharmacological activities such as spasmogenic, oxytocic, uterotonic, anti-bacterial, anti-menorrhagic, anti-cancer, anti-esterogenic, anti-progestational, dermatoprotective, anti-mutagenic and genoprotective activities. This review describes the socio-ethnobotanical usage, different reported pharmacological actions, phytoconstituents and pharmacognostical information about *Ashoka* herb. The information about lacunae in improving the Pharma worth of *Ashok* such as lack of tissue culture techniques in *Ashoka* planting has been also gathered. *Saraca asoca* is the ideal candidate for screening of its endophytes for pharmaceutical related compounds.It is hoped that this review will provide sufficient, ideal and unique information under one umbrella and also give new direction for the researchers and pharmaceutical industry to extend the Pharma worth of this natural product.

Keywords: Ashoka, Phytoconstituents, pharmacology, pharmacognocny, adulteration, endophytes, gynaecological disorder.

Introduction:

Plants have been used for medicinal purposes long before prehistoric period.*Ayurveda*, the traditional system of medicine continue to be widely practiced on many accounts. Population rise, inadequate supply of drugs, prohibitive cost of treatments, side effects of several synthetic drugs and development of resistance to currently used drugs for infectious diseases have led to increased emphasis on the use of plant material as a source of medicines for a wide variety of human ailments.*Ashoka* is one the most ancient and sacred tree of India.It is known by its binomial nomenclature *Saraca asoca*(Roxb.) De. Wilde and *Saracaindicia* Linn. Belongingto Caesalpinaceae subfamily of the legume. *Asoka* or *Ashoka* is the Sanskrit word that means “Without sorrow.”*Ashoka* is specially sacred to the Hindu god of Love, Kamadeva, for whom it is worshipped every year on December 27; it is mentioned in Hindu mythology that the Indian philosopher and founder of Buddhism, Gautama Siddhartha (c.563-483 B.C.) was said to have been born under this tree.^[1] In *mahakavya*, or Indian epic poetry the *Ashoka* tree mentioned in the Ramayana in reference to the ‘*Ashoka Vatika*’, where Hanuman first meets Sita. The *Ashoka* is a rain- forest tree. Its original distribution was in the

central areas of Deccan plateau, as well as the middle section of the Western Ghats in the western coastal zone of the Indian subcontinent. The *Ashoka* is valued for its beautiful foliage and fragrant flowers. The flowers being much used for religious ceremonies and temple decorations. It is a small, erect, evergreen tree, with deep green leaves growing in dense clusters. Its flowering season is around February to April. The *Ashoka* flowers come in heavy, lush bunches. They are bright orange- yellow in color and turns into red before they fall. ^[2]In classical *Ayurvedic* text *Ashoka* has been mentioned in *vedanasthapana mahakashaya* and *Kashayaskandha* by *aacharya caraka*. ^[3] *Aacharya Sushruta* included *Ashoka* in *Rodhradigana*. ^[4] As we all know *Ashoka* is the drug of choice in *Raktapradara* (dysfunctional uterine bleeding) but this action of *Ashoka* was not mentioned in *Ayurvedic* text like *Caraka samhita*, *Sushruta samhita* and in *Nighantus*. *Vrundamadhava* was the first who described use of *ashoka* in *Raktapradara*. ^[5] *Ashoka* is the famous drug for feminine disorders, in spite of these *aacharya Sushruta* has been mentioned the use of *Ashoka* in *Kalyanaka lawana* of *Vatvyadhi chikitsa*, in *Tilvakasarp*, *Vran avachooran*, *krushabha agada*, *Dundubhiswaniya* chapter, in eye disorder (specially pitta-kaphaj), in *Mahakalyanaka ghruta*. ^[6] Also *aacharya Vagbhata* has been mentioned the use of *Ashokaghruta*. ^[7] Generally in practice the bark of *Ashoka* is used for treatment. The bark is bitter and acrid; refrigerant, astringent to the bowels, alexiteric, anthelmintic, demulcent, emollient; cures dyspepsia, thirst, burning sensation, diseases of the blood, biliousness, effects of fatigue, tumors, enlargement of the abdomen, colic, piles, ulcers, bloody discharges from the uterus, menorrhagia; useful in fractures of the bones; beautifies the complexion. The bark is much used in uterine affections and especially in menorrhagia. The seeds are useful in urinary discharges. ^[8]

Synonyms:^[5]

Ashok, Shoknashan, Smaradhivas, Kankeli, Vanjuldrum, Raktapallava, Hempushpa, Nata, Pindapushpa, Gndhapushpa, Madhupushpa,

Vernacular names:^[10]

Sanskrit – Kankeli, Asoka; Gandhpushpa ; **English** – Asoka tree ; **Hindi** – Ashoka, Anganpriya ; **Marathi** – Ashoka ; **Bengali** – Ashoka, Oshok ; **Gujrati** – Asupala, Ashopalav **Telugu** – Asok ; **Tamil & Mal.** – Asogam ; **Cannad** – Asokada, Kankelimara ; **Panjabi** – Ashok

Habitat:

Ashoka is one of the sacred trees of Hindus and is found plentifully along the road side in Eastern Bengal, South India, Aracan and Tenasserium, U.P. near Kumaon, It is also cultivated in gardens throughout India for its Handsome flowers. ^[10] It occurs almost throughout India upto an altitude of 750 meters, in the Central and Eastern Himalayas and the Khasi, Garo and Lushai hills; it is also found in the Andaman Islands. ^[11] In Kerala region it is found in Patagiri, Kaikatty and Pothundi of Palakkad district, Thirsur, Kollam and Kannur districts. ^[12]

Scientific Classification:^[13]

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Fabales
Family : Caesalpinaceae
Genus : Saraca
Species : asoca

Morphology:^[8, 13]

A tree 6-9 meters high; branches glabrous. **Stems** are erect or ascending, more than 2 meters tall, solid, glabrous or sparingly glabrate. **Leaves** 15-25 cm long; rachis glabrous, corky at the base; petioles very short; **stipules** intrapetiolar, completely united, 10- 13 by 6mm. scarious, ovate, oblong, obtuse, parallel-nerved. **Leaflets** 4-6 pairs, 10-20 by 3-5.7 cm., oblong-lanceolate, obtuse or acute, quite glabrous, base rounded or cuneate, slightly oblique; **petiolules** 4.5- 6.5 mm. long, stout, wrinkled; **stipels** deciduous. The **bark** is brown or grey or almost black with warty surface. **Stem bark** are rough and uneven due to the presence of rounded or projecting lenticles. Bark channeled, smooth with circular lenticles and transversely ridged, sometimes cracked. Fracture splitting exposing striated surface, a thin whitish and continuous layer is seen beneath the cork leaver. **Flowers** are actinomorphic or somewhat irregular fragrant, numerous, in dense axillary corymbs 7.5- 10 cm. across; peduncels stout; **pedicels** 8-13 mm. long, red, glabrous; bract ovate, subacute; **bracteoles** 2, appearing like a calyx, 4mm. long, spatulate- oblong subacute, ciliolate, amplexicaul, colored. **Calyx** passing from yellow to orange and finally red; tube 1.3-2 cm. long. **Petals** 0. **Stamens** 7 or 8, much exerted; filaments filiform, thrice as long as the calyx segments; **anthers** purple. **Ovary** pubescent, especially on the sutures; **Style** curved into a ring. **Pods** black, 10-25 by 4.5-5 cm., linear-oblong, tapering to both ends, compressed, glabrous, veined, **seeds** 4-8, ellipsoid-oblong, 3.8 cm. long, slightly compressed.

Properties and action^{[12, 14]:}

Rasa – Kashaya, tikta

Veerya – Sheeta

Vipaka – Katu

Guna – Laghu, Ruksha

Karma – Kaphapittashamaka (alleviates kapha and pitta), varnya (improves complexion of skin), sothaghna (anti-inflammatory), kusthagana (cure skin diseases), rasayan (rejuvenating), stambhana (astringent), shonitsthapana (anti-haemorrhages), vrsya (aphrodisiac), artavjannan (improve ovulation), krimighna (anti-helminthic), pramehaghna (anti-diabetic).

Part used:^[14]

Bark, Seed, Flower.

Externally – The drug is used as a local application for pain and in various types of poisoning.^[12]

Internally – It is indicated in painful condition of viscera.^[12]

Systemic:^[12]

- i. **Gastro-intestinal tract** – In diarrhea, dysentery, worm infestation and thirst.
- ii. **Cardiovascular system** – The flower is indicated in edema and haemorrhages.
- iii. **Reproductive system** – In menorrhagia, dysmenorrhoea, leucorrhoea and other uterine disorders.
- iv. **Urinary system** – Powdered seed is used in dysuria and stones in the urinary tract.

Adulterant:^[12]

Because of the destructive extraction and the absence of an organized cultivation programme, the availability of the crude drug is diminishing and this has resulted in the sale of adulterants. The commonly used adulterant is the bark of *Polyalthia longifolia* Benth & Hook belonging to family Annonaceae. In Marathi it is called as 'Khota ashoka' whereas in Hindi and Bengali it is called as *Devdaru*. Also *ashoka* bark is mixed with bark of Rohitaka (*Afanamexis polystakis*) and *Sicalpineae pulchirena*.

S. V. Lal in 1953 reported that both the plant *Saraca indica* and *Polyalthia longifolia* contain two pharmacologically active fractions which have similar action on pain muscles, though the mode of action of

the stimulant fractions is quite different in each case; Thus he concluded that the stimulant fraction of *Saraca indica* acts by liberation of acetylcholine, that of *Polyalthia longifolia* acts directly on the plain muscle fibre.

Cultivation:^[11]

Soil & Climate:The plant requires slightly acidic to neutral soils for better growth with medium to deep well drained fertile soils. It grows well in tropical to sub-tropical situations under irrigation.

Nursery raising & planting: The crop can be propagated by seeds and stem grafting. The seedlings are planted in the well manured field during the rainy season.

Thinning & Weeding: Weeding and thinning of the plants may be done when required usually after 15-30 days for better growth.

Manures, Fertilisers and Pesticides: The medicinal plants have to be grown without chemical fertilizers and use of pesticides. Organic manures like, Farm Yard Manure (FYM), Vermi – compost, Green Manure etc. may be used as per requirement of the species. To prevent diseases, bio- pesticides could be prepared from Neem, Chitrakmool, Dhatura, Cow's urine etc.

Irrigation: Normally grown as rainfed crop but for better yield irrigation may be done as per requirement (weekly/ fortnightly)

Action of drug:^[9, 10]

Bark is strongly astringent and uterine sedative. It acts directly on the muscular fibers of the uterus. It has a stimulating effect on the endometrium and the ovarian tissue. The Ketosterol present in the bark of *Ashoka* seems to be androgenic in nature. The activity of the drug appears to be due to the presence of the steroidal component and the calcium salt. Aqueous extract of the bark is reported to contain two active principles, one stimulating and other relaxing the plain muscle of the ilium of the guinea-pig. The drug is reported to stimulate the uterus, making the contractions more frequent and prolonged without producing tonic contraction as in the case of pituitary or ergot. The crystalline glycosidal substance is also reported to stimulate uterine contraction. It is suggested that the drug may prove useful in all cases of uterine bleeding where ergot is indicated. The drug is reported to have a stimulating effect on the endometrium and ovarian tissue, and is useful in menorrhagia due to uterine fibroids, in leucorrhoea and in internal bleeding, haemorrhoids and haemorrhagic dysentery.

Preparations:

Official preparations listed in the Indian pharmaceutical Codex are *Decoction Asoka* and *Extraction Asok Liquidum*.^[10] Decoction of the bark prepared by boiling 4 ounces of the bark in 4 ounces of milk and 16 ounces of water till the water is evaporated and this quantity is given with milk in 2 or 3 divided doses during the course of the day in menorrhagia.^[15] It must be advised from the 4th day of the monthly period and continued till the bleeding ceases. *Asoka ghrita* is prepared with a decoction of the bark and clarified butter with the addition of a number of aromatic substances in the form of a paste. Decoction of the bark in water with dilute sulphuric acid is also used. Liquid extract of the bark was tried in cases of menorrhagia and found to do considerable good.^[16, 17, 18]

Doses:^[1, 14]

Ashokarishta: 15-30 ml b.i.d. / t.i.d.

Ashokaghrita: 5 gm b.i.d.

Tvaka kwath: 50 ml

Seed powder : 3-6 gm

Flower powder: 3-6 gm

Traditional uses:

Ashoka has been mostly used as a traditional medicine for feminine disorders, like Leucorrhoea, menorrhagia, dysfunctional uterine bleeding etc. Bark is reported to cure biliousness, dyspepsia, dysentery, colic, piles, ulcers and pimples. Leaves possess blood purifying properties and their juice mixed with cumin seeds is used for stomach-ache. Flowers, pounded in water are used in haemorrhagic dysentery and the dried flowers in diabetes. Flowers are considered to be an excellent uterine tonic as well as in biliousness and syphilis. In Assam fruits are chewed as a substitute for areca-nuts. Pods are reported to make very good forage for cattle. Wood is light, reddish, brown, soft used for making ploughs and shafts in Assam and for house building purpose in Ceylon. The seeds are useful in urinary discharges. The bark is much used in uterine affections and especially in menorrhagia. A decoction of the bark in milk is generally prescribed. According to aacharya *Sushruta* the bark, flowers and fruits are prescribed in combination with other drugs for the treatment of Snake-bite and scorpion-sting but *Mhaskar* and *Caius* has been concluded that the bark, flower and fruits are equally useless in the treatment of snake-bite and scorpion-sting.^[8, 10]

Ashoka is also effectively used in *Ayurveda* for clearing congestion from Medas and Mamsa Dhatus, especially when there may be leucorrhoea, endometriosis, cysts and fibroids from excess kapha and ama in Artava srotas. The *ashoka* herb also has a nourishing effect on the circulatory system, thereby making it an effective remedy in arrhythmia and cardiac weakness. The *Ashoka* herb benefits the endometrium and uterine muscles and this makes it effective as a uterine tonic for irregular menstrual cycles and miscarriage. *Ksheerapaka* of 6 gm bark powder of *Ashoka* is useful in *Pradara roga* of females; also this *ksheerapaka* is effective in uterine inertia, uterine pain, urinary calculus, and dysuria. In pain local application of paste of bark should be effective. The womenfolk of Chhattisgarh boil the bark of *Ashoka* in cow's milk, add the sugar and consume it once a day for three days and repeat the same after three months to prevent the gynecological disorders. On "*Ashoka Shasthi day*", in India married Hindu women eat the flower buds of *Ashoka* herbs to protect their child from grief and sorrow. The persons suffering from mental disorder are advised to take bath under the shade of *Ashok* tree. For mental piece, the natives prepare special '*Herbal Mala*' using root pieces of *Sita Ashok* and give it to the patients. The patients are advised to put the powdered seeds inside the Pan (Betel) and eat it empty stomach. The healers prepare decoction of the bark of *Ashok* is used for external wash. In patients of *Safed pani* (leucorrhoea), the healers boil the bark in mixture of milk and water, after evaporation of water the combination is given to the patients.^[16, 17, 18]

The specific analgesic properties present in *Ashoka* can used to calm the nerves when they have been aggravated by *vata dosha*. The *ashoka* herb is also effective in purifying blood naturally and in preventing skin allergies. This herb is also useful to improve the complexion of the skin.^[19]

API standard:^[20]

IDENTITY, PURITY AND STRENGTH:

Foreign matter	Not more than	2	per cent, Appendix	2.2.2.
Total Ash	Not more than	11	per cent, Appendix	2.2.3.
Acid-insoluble ash	Not more than	1	per cent, Appendix	2.2.4.
Alcohol (90 per cent)	Not less than	15	per cent, Appendix	2.2.6.
Soluble extractive				
Water-soluble extractive	Not less than	11	per cent, Appendix	2.2.7.

Analytical parameter^[11]

Description:

A. Colour	-	Brown
B. Odour	-	Characteristic

- C. Taste - Characteristic
D. Appearance - Free flowing powder

Identification: TLC method

- PH (1% w/v solution): 5 to 7
Loss on drying: NMT 5% w/w
Moisture Content by K.F.: NMT 5% w/w
Volatile oil content: Do Not Available
Assay of active principle by HPTLC / HPLC: Tannins NLT 30 % w/w

Microbiological analysis:

- A. Pathogens (E. coli, S. aureus) absent
B. Total Bacterial Count (CFU/gm) NMT 800 CFU/gm
C. Total Fungal Count (CFU/gm) NMT 500 CFU/gm

Heavy Metal:

- A. Arsenic NMT 1ppm
B. Lead NMT 5ppm

Phytochemical study:

Jayita Saha and Taniya Mitra et al has conducted the phytochemical and HPTLC analysis in *Saraca asoca*(Roxb.) Wilde and they were concluded that, the experimental yield of chloroform, ethanol, methanol, and water extracts of *Saraca* flower were found to be 1.80%, 11.90%, 15.10% and 22.00% respectively. Water soluble extractive value showed the presence of sugar, acids and inorganic compounds and alcohol soluble extractive values determined the presence of polar constituents. The physicochemical parameters total ash, acid insoluble ash and water soluble ash value were found to be 3.00%, 2.02% and 1.12% respectively. Total ash value percentage showed the amount of mineral and earthy material present in the plant sample. The amount of acid insoluble siliceous matter present in the plant sample was 2.02%. Alkaloids were found to be absent in all the four extracts. Carbohydrates, tannin, flavonoid, saponin, glycosides, proteins and steroids were found to be present in methanol and ethanol extracts. The chloroform extract contained only carbohydrates whereas the water in addition to carbohydrates, contain tannin, flavonoid, saponin and steroids. Methanolic extract of flower and leaves confirmed the presence of gallic acid using HPTLC assay. Jayita Saha et al has firstly reported the presence of gallic acid in *Saraca asoca* leaf. The presence of gallic acid in leaf is very important because flowers are only seasonal, while leaf is available throughout the year.^[21]

Thus the preliminary phytochemical screening revealed the presence of tannins, proteins, steroids, glycosides, carbohydrates, saponins, flavonoids in different extracts of the flower of *Saraca asoca*. In this study the researchers has been observed that, the most active principles present in the flowers are flavonoid, steroids, tannins and glycosides. These phytoconstituents may be responsible for various pharmacological actions of this plant part, like antibacterial, antiulcer, anticancer, larvicidal and chemoprotective activities.^[22, 23, 24, 25, 26]

Bark:

Bark of *S. asoca* is the most important organ for its medicinal value. It is known to contain flavonoids, tannins, steroids, volatile oil, glycosides, steroidal glycosides such as β -sitosterol glucoside^[1,27,28,29,30] reducing sugars, and many compounds of potassium, sodium, calcium, aluminium, strontium, calcium, iron, magnesium and phosphate.^[1,21,27,29,31,] Powdered bark also carries cellular species

such as tracheids, stone, parenchyma, sieve tubes and other cells.^[1] Lignin glycosides such as lyoniside, nudiposide, 5-methoxy-9- β -xylopyranosyl, isolariciresinol and schizandriside; flavonoids such as catechin, epicatechin, epiafzelechin-(4 β -8)-epicatechin, procyanidin B2, deoxyprocyanidin B, leucocyanidins and leucopelargonidin^[32,33,34]

and leucopelargonidin glucoside^[35] have been reported from *S. asoca* bark^[1,27,28,29,32,33,34] Antioxidant such as polyphenolics, gallic acid and ellagic acid have also been described from *S. asoca* bark.^[1,21, 27, 28,35,36,37,38,]

Leaves:

leaves of *S. asoca* have been reported to contain alkaloids, steroids, flavonoids, tannins, saponins, terpenoids, polyphenolics, glycosides and many carbohydrates.^[1,21,36,39,40,41] The antioxidant activity of the leaf extracts has been described to be due to the presence of polyphenolics such as gallic acid and ellagic acid.^[36]

Flavonoids such as quercetin, β -sitosterol, ceryl alcohol, and glucosides such as quercetin-3-*O*- α -rhamnoside and kaemferol-3-*O*- α -L-rhamnoside have been reported from *S. asoca* leaves^[1,27,30,33,35,36, 38,40,42]

Flowers:

The flowers of *S. asoca* have been shown to contain tannins, flavonoids, saracasin, saracadin, waxy substances, carbohydrates, proteins and steroids.^[21] They are especially known for the presence of many fatty acids such as oleic, palmitic, stearic, linolenic and linoleic acids; glucosides such as quercetin-3-*O*-*P*-*D*-glucoside, apigenin-7-*O*-*p*-*D*-glucoside, pelargonidin-3,5-diglucoside and cyanidine-3,5-diglucoside; steroids such as *p*- and *y*-sitosterols; flavonoids such as quercetin, leucocyanidin, and polyphenolics such as gallic acid and ellagic acid.^[1, 27, 36, 40]

Seeds:

Seeds of *S. asoca* have been reported to contain various fatty acids such as oleic, linoleic, palmitic and stearic acids; sterols such as catechol and epicatechol; and a flavonoid, leucocyanidin.^[1,27] Saracin, a lectin from *S. asoca* seeds has been reported as an inducer of apoptosis or even mitogenic in human T-lymphocytes.^[24,40] Phenols, flavonoids, tannins, saponins, carbohydrates, glycosides and salicylates have been demonstrated in the acetone extracts of *S. asoca* seeds.^[40]

Fruits (pods):

Fruits have been reported for the presence of various fatty acids such as oleic, linoleic, palmitic and stearic acids; sterols like catechol and epicatechol, and a flavonoid, leucocyanidin.^[1, 27]

Roots:

Roots contain resinous and extractive matter, gum, sugar, colouring matter and salts of lime. Colouring matter consists of red crystalline principle purpurine; a yellow principle glucoside garancin, alizarin (orange red) and xanthine (yellow).^[43]

Pharmacognostical characteristics:

Microscopical characters:

1) Bark: Transverse section of stem bark shows periderm consisting of a wide layer of cork, radially flattened narrow cork cambium, secondary cortex wide with one or two continuous layers of stone cells with many patches of sclereids, Parenchymatous tissue contains yellow masses and prismatic crystals; secondary phloem consists of phloem parenchyma, sieve tubes with companion cells and phloem fibres occurring in groups, crystal fibres are present.^[44]

2) Stem: Transverse section of stem is circular. Small rounded to oval projecting lenticles are present on the surface. Epidermis is single layered with thin cuticle. Below the epidermis, 5-6 layers of cork are seen. Cortex is 12-16 layered. In the middle region of cortex, 3-5 layers of stone cells are visible. Just above, the phloem region is very distinct and contains tannin cells. Cambium is very clear and is 2-3 layered. Xylem

region is mostly composed of tracheids and a few vessels. Primary xylem is prominent. There is prominent pith, composed of thin walled parenchyma and many of the pith cells contain polygonal calcium oxalate crystals.^[44]

3) Root: In transverse section root is appears somewhat circular in outline. The outermost zone is cork, composed of 8-10 layers of tangentially elongated thick walled cells. Phellogen is not distinct. Inner to the cork region, secondary cortex having two distinct zones are seen. The upper zone consists of 5-7 layers of thin walled parenchymatous cells, some of them containing few small rounded starch grains. Below this parenchymatous one, 3-5 layers of mechanical cells are distinctly seen, of these the outer layer is sclerenchymatous and the inner layers are stone cells. Following this supporting region is a broad zone of primary and secondary phloem. The cells are parenchymatous, thin walled and polygonal. 4-6 cambial layers are very prominent below the bast zone. In secondary xylem region tracheids, vessels and parenchyma cells are arranged in a peculiar manner, i.e., xylem parenchyma and tracheids are in alternating patches. The ray cells in the secondary xylem region are filled with starch grains. Primary xylem groups are seen towards the centre which is in a line with the medullary rays.^[44]

Powder characters:

Ashoka bark powder is brown in colour, under microscope it contain some tracheids, large quantity of fibres, stone cells, parenchyma cells, sieve tube fragments and many unidentified cells.^[45]

Pharmacological activity:

Saraca asoca possesses lot of pharmacological activity such as Antimicrobial, Anticancer, Antimenorrhagic, Antioxytotic, Antihelminthic, Antitumor, Antioxidant, Antipyretic, Antihyperglycemic, Central nervous system depressant activity, Analgesic, Antiinflammatory, Antiarthritic and cardioprotective effect, Antidiabetic, Uterine tonic activity, Larvicidal activity, Antiulcer activity, Antifungal activity, Hypolipidemic effect, Anti-nephrolithiatic, Dermatoprotective, Antimutagenic and genprotective activity etc.

Antimenorrhagic activity:

Ashoka dried bark has been used in India for menorrhagia.^[46, 47] In case of uterine disorder *Saraca asoca* dried bark and flowers are given as a tonic in females of India. *Saraca asoca* stem bark is also used to treat all the disorders related with menstrual cycle.^[48,49] In Sri Lanka *Ashoka* bark is used for menstrual disorders and in menorrhagia.^[50,51] In India *Saraca asoca* bark is used as a uterine sedative and its hot water extract administered to human adult female to stimulate the uterus similar to ergot, but without producing tonic contractions. Also given in menorrhagia, as an emmenagogue, uterine sedative, uterine affections as well as used in many preparations related to female disorders.^[52,53,54,55] In Pakistan *Saraca indica* bark is used to cure uterine affection and menorrhagia. In India dried bark of *Saraca asoca* is used as an astringent to stop excessive uterine bleeding.^[56] Aqueous extract of the bark is reported to contain active principles, one is stimulating and the other is relaxing the plain muscles of ileum in guinea pig. The drug is reported to stimulate the uterus, and making the contractions more frequent and prolonged. The crystalline glycoside substance is reported to stimulate the uterine contractions.^[57]

Antimicrobial activity:

Saraca asoca possesses antibacterial activity (ethanol: water, 1:1) on agar plate with different organisms such as *Bacillus subtilis*, *Salmonella typhosa*, *Staphylococcus aureus*, (plant pathogen). *Agrobacterium tumefaciens* showed negative activity.^[58] *Ashoka* dried flower buds are tested against antibacterial activity of

methanol extract on agar plate against *Shigella boydii*, *Escherichia coli*, *Salmonella viballerup*, *Shigela flexneri*, *Vibro cholera* and *Shigella dysenteriae* showed positive result.^[59] *Saraca asoca* leaves tested against antibacterial activity of ethanol (95%) and water extract on agar plate *Escherichia coli* and *Staphylococcus aureus*. *Escherichia coli* found active whereas tested against *Staphylococcus aureus* showed negative result.^[60] The methanolic extract of *Saraca asoca* was tested against *Alternaria cajani*, *Helminthosporium sp.*, *Bipolaris sp.*, *Curvularia lunata* and *Fusarium sp.*, at different concentrations (1000, 2000, 3000, 4000 and 5000 ug/ml). The extracts exhibited good inhibitory activity against *A. Cajani*, also it effective at lower concentrations against other fungi.^[61] Four different extract of *Saraca asoca* bark tested antibacterial activity against *Escherichia coli*, *Salmonella typhi*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Bacillus cereus*, *K. Aerogenes*, *Sh. Boydis*, *P. vulgaris*.^[62] different extract of *Saraca asoca* bark were tested against the enteric pathogen isolates namely *Escherichia coli*, *Shigella sonnei* and *Salmonella enteritis*. All the extract except aqueous extract showed antimicrobial activity and highest percentage of activity was observed with the methanol extract.^[63] Methanol and water extract of Ashoka leaves having good activity against *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Salmonella typhimurium* also both the extract showed marked activity against *Alternaria alterate*, *Colletotrichum gloesporioides* and *Drechlera specifera*.^[64] Bark extract of *Saraca asoca* were investigated for in vitro antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Bacillus aureus* and *Klebsiella pneumonia* at 4 mg/ml using agar well diffusion method. The ethanol and distilled water extract showed significant broad spectrum antibacterial activity.^[65]

Uterine tonic activity:

In Ayurvedic medicine *Saraca asoca* is a drug of choice for its stimulant activity on the endometrium and ovarian tissue. The estrogenic effect of U- 3107 (1mg/kg p.o) was considered in healthy and ovariectomised rats. U-3107 was administered as an aqueous suspension for a period of 21 days. The management of ovariectomised rats did not any expand on uterine weight. Only in the presence of functional ovary U-3107 perform the estrogenic activity and is devoid of any progestational activity. U-3107 is a herbal preparation which is formulated by using various plant extract and is useful in variety of menstrual disorders like puberty, menorrhoea, Dysmenorrhoea, premenstrual syndrome, abnormal bleeding and threatened abortion.^[66]

Larvicidal activity:

The pet ether extract of the leaf and the chloroform extracts of the bark of *Saraca asoca* effective against the larva of *C. Quinquefasciatus* with respective to LC50 value. The larvicidal bioassay follow the WHO standard protocols for experimental treatment, 1ml of plant extract dissolved in absolute ethanol was added to 99ml of distilled water in 150 ml disposable wax coated paper cup, which was shaken lightly to make a homogeneous test solution. Then 25 early fourth Instar larvae of vector mosquito were transfer to each experiment was performing in four replicates with a final total of 100 larvae for each concentration. The test container was held at 27 +/-2c, 80-90% relative humidity and photoperiod of 12h dark. After 24 h exposures larval mortality was recorded. The experiments were repeated twice. The pet ether extract of leaves of *Saraca asoca* showed Larvicidal activity with LC50 and LC90 values of 228.9- 458.3 ppm respectively whereas the chloroform extract of the bark of *Saraca asoca* showed Larvicidal activity with LC50 and LC90 values of 291.5 and 499.3 ppm respectively.^[25]

Anti-oxytocic activity:

Oxytocic activity of *Saraca asoca* herb was seen in rat and human isolated uterine preparations. Estrogen primed or gravid uterus was more sensitive to the action of the alcoholic extract. Oxytocic action was

completely blocked by Pentolinium bitartrate. Seed extract is found effective against dermatophytic fungi. In-vitro tests on rat uterus preparation, extract of Ashoka did not show oxytocic activity. Saraca asoca has been tested twice previously with negative result and once with positive result.^[47]

Anti- cancer activity:

The Saraca asoca flowers contain an anticancer principle(a flavonoid fraction) proved to prevent two stage skin carcinogenesis and is indicated 50% cytotoxicity (in vitro) in Dalton's lymphoma ascites and Sarcoma-180 tumour cells at a concentration of 38 mug and 54 mug respectively, while being non-toxic to normal lymphocytes but there is preferential activity against lymphocytes derived from leukemia patients.^[67]The ethanolic extract of Saraca indica was shown to inhibit the breast cancer.^[68] Recently, the lectin 'Saracin' isolated from the seed integument has been reported to induce apoptosis in human T- lymphocytes in an in-vitro assay.^[24]

Anti-inflammatory activity:

Chronic arthritis and cardiovascular diseases are mostly seen as a result of inflammatory response mediated by pro- inflammatory cytokines. The ethanolic and methanolic extract of leaf, bark and root of Saraca asoca possesses an anti-inflammatory potential which significantly inhibited the binding of various transcription factors such as NF-kB, AP-1, GATA-1, etc. To their target DNA sequences, thereby lowering the level of pro-inflammatory cytokines.^[21] Saraca asoca extract has been shown to reduce the level of pro-inflammatory cytokines IL-1 and TNF- α .^[69] The leaves of Saraca asoca has been shown the anti-inflammatory activity against Carrageenan induce paw oedema in animal. The ethanolic extract of Saraca asoca reduce the paw oedema significantly and is caused 56.95% inhibition increase paw volume, though of a short duration and intensity, as compare to that of 10mg/kg diclofenec .^[70, 71]

Anti- arthritic activity:

Saraca asoca plant extract has been shown to lower the level of liver and lysosomal enzymes, serum collagen and restoring the normal histological structure of joints, thereby reducing rheumatoid arthritis in rats.^[21]

Cardioprotective activity:

The ethanolic extract of Saraca indica reported to have an anti-inflammatory activity and also shown to protect the cardiac tissue from infiltration of inflammatory cells. Saraca asoca extract has been proved for its blood purification activity.^[1]

Analgesic activity:

There is lot of information available about the analgesic action of Saraca asoca in classical text of Ayurveda. The leaf and bark extract of Ashoka like Petroleum ether, chloroform, methanol and water extract was evaluated by using tail immersion method, tail flick method and formalin induced pain method in albino mice. The analgesic property of Saraca indica has been attributed to its ability to inhibit sensory nerve stimulation(early phase). Analgesic effect of petroleum ether, chloroform, methanol, and aqueous extracts create dose dependent analgesic activity, in the early phase of formalin test pain arise due to the direct stimulation of the sensory nerve fibres by formalin while in the late phase pain was arise due to inflammatory mediators like histamine, prostaglandins and bradykinins. Thus it is assumed that extract of Saraca asoca typically relieved the pain by acting on both central as well as peripheral nervous system.^[21,67, 72]

Anti-ulcer activity:

The aqueous suspension of Ashoka flowers, dried flower buds, bark and seeds were shown to produce ulcer in albino rats by using two models, namely pyloric ligation and aspirin- induced gastric ulcer. As compared to control rats, in both experiments the volume of gastric juice produced, the acidity and an ulcer index were shown to be reduced remarkably when treated with water extract of saraca asoca.^[21,27,42,72-75] The anti-ulcerogenic effect of these extract may be due to the presence of saponins, triterpenes, tannins, catechin, sterols, phenolic glycosides and flavonoids^[73,74] Thus, the aqueous suspension of saraca asoca flowers produced the anti-ulcer potential activity either by inhibition of basal gastric secretion and/or stimulation of mucus secretions and /or endogenous gastric mucosal prostaglandin synthesis and /or antioxidant activity of flavonoids present in the water extract of saraca asoca^[27,95,73]

Anti-fungal activity:

Traditionally, compromised immune response of an individual has been responsible for fungal infections and do not causes any major danger to the population on large scale. The antifungal activity of methanolic and hot water extracts of Ashoka leaves, flowers and bark against *Alternaria alternate*, *Colletotrichum gloeosporioides*, *Drechlera specifera*, *Alternaria cajani*, *Helminthosporium sp.*, *Bipolaris sp.*, *Curvularia lunata*, *Aspergillus flavus*, *A. Fumigates* and *Fusarium sp.*, have been reported by various groups. Further detailed investigations are required to find out the bioactive principle.^[32, 61, 76]

Anti-helminticactivity:

Parasitic worms present in the human body are responsible for malnutrition, weakness, and more susceptibility to bacterial and viral infections. The methanolic and ethanolic extract of *Saraca asoca* leaves has been used for antihelmintic activity and piperazine citrate used as a positive control against Indian earthworm. The methanolic and ethanolic extract has been reported to paralyze and kill the adult Indian earthworm. The glycosides, alkaloids, tannin, flavonoids and terpenoids from the ethanolic and methanolic extract of Ashoka seems to be the important phytochemical constituents for performing anti-helmintic activity^[42, 77, 78, 79]

Anti-oxidant activity:

A number of study has been reported to described the presence of various antioxidant compounds such as Catechin, flavonoids, β - sitosterol and its glucoside form, ascorbic acid, lignin glycosides, polyphenols like gallic acid in petroleum ether, chloroform, and methanol extract of Ashoka leaves, bark and flowers.^[21, 28,29,37,38,39,80-84]

Anti-diabetic and hypolipidemic activity:

The flavonoid fraction of *Saraca asoca* flowers and leaves has been shown to inhibit α - glucosidase and α -amylase enzymes linked to type-2 diabetes and also prevent LDL oxidation.^[39,82,84] These study have also been reported that Ashoka extract lower lipid and cholesterol level and reduce the elevated glucose levels in a dose dependant manner an STZ- induced diabetic albino rats and mice.^[39,84] Several study have also been reported to reduce the diabetes induced renal oxidative stress. Use of these extract also improve the pancreatic, renal and hepatic profiles and overall health in diabetic mice.^[30, 84, 85]

CNS depressant and brain tonic:

The petroleum ether, chloroform, methanol and aqueous extracts of leaves of *Saraca asoca* shows CNS depressant activity depending upon their polarity out of which the methanol extract shows maximum CNS depressant activity in albino mice. The activity was examined by using phenobarbitone induced sleeping

time with the help of actophotometer. The extract of *Saraca asoca* significantly reduced the locomotor activity in mice by 67.33%. The mechanism of the depressant activity can be associated with activation of γ -aminobutyric acid (GABA) receptors in the CNS by glycosides, flavonoids, saponins and tannins present in the plant extract which culminates in anxiolysis, muscle relaxation and sedation.^[1, 86-88]

Anti-nephrolithiatic :

When there is condition like urinary passage obstruction due to renal stones, *Saraca asoca* root has been reported to give relief in such situation and is also known for its potential to breakdown the oxalic acid crystals present in the kidney.^[1, 89, 90]

Dermatoprotective activity:

In classical text references are available about *Saraca asoca* to improve skin complexion. Lot of researches has been performed on *Ashoka* plant extracts and reported that the root, bark and seed extract of *S. asoca* useful in the treatment of skin complications such as eczema, psoriasis, acne, dermatitis, herpes- kushta/visarpa, scabies, pruritis, tinea pedis and skin cancer.^[69,91] The flower extract of *S. asoca* contain flavonoids, has been shown to reduce the skin tumours induced by 7,12- dimethyl benzanthracene.^[69] It also improve skin complexion, induce quick healing of skin injuries, reduce freckles and external inflammation of the skin. Seed extract have been reported to be effective against dermatophytic fungi.^[1]

Anti-mutagenic and genoprotective activity:

Mutagenesis is one of the important causative factors for cancer and other debilitating diseases. *Saraca asoca* has been known as a good source of antioxidants which can reduce mutagenesis. *S. asoca* bark extract has been reported to prevent mutagenesis in *Salmonella* strains.^[92] This extract has been shown to protect Swiss albino mice against cyclophosphamide- induced genotoxicity.^[93] From the stem bark of *S. asoca* a lignin glycoside 'Saracoside' was isolated, it has been reported as a potent inhibitor of DNA topoisomerase IB, an important enzyme involved in many processes where DNA unwinding is essential such as replication, transcription, recombination etc.^[92,93]

Endophytes from *S. asoca*:

Endophytes i.e. microorganisms (eg. fungi, bacteria etc.) without any symptoms living inside the internal tissue of the plant hosts are known to symbiotically benefit the host.^[94] These endophytes are classically isolated for pharmaceutical bioprospecting purposes. Some of these endophytes acquired the biosynthetic credentials for various compounds which the host is known for. Some of the noticeable examples of such endophytes includes anticancer drugs like taxol, podophyllotoxin, camptothecin, vinca alkaloids such as vincristine and vinblastine^[95] *Saraca asoca* is the ideal compound for screening of its endophytes for pharmaceutically relevant compounds because of its well known medicinal value, this in principle help for identifying single chemical compound from *Saraca asoca* extract which could be responsible for biological effect of its extract. Only a limited number of reports describe biomolecules of pharmaceuticals or commercial significance from the endophytic fungi isolated from *Saraca asoca*.^[96-101] These include an endophytic *Acremonium sp.* Producing an enzymes an amylase and a protease.^[96,97] also *Lasiodiplodia theobromae* an endophytic fungi produced an antioxidant and anticancer steroidal saponin named cholestanol glucoside.^[98-101] The isolation of 37 endophytic fungal species belonging to 22 different genera, including *Lasiodiplodia*, *Camarosporium*, *Pestalotiopsis* and *Fusarium*, the same group reported significant *in vitro* cytotoxicity of 18 fungal extracts against three human cancer cell lines- HeLa, HepG2 and PC3, also the classical apoptosis- based *in vitro* anticancer activity of *Pestalotiopsis sp.* 6 has been reported by

them.^[101] Thus, pharmaceutical bioprospecting of *Saraca asoca* associated endophytes could provide a new dimension to expand the pharma worth of this natural pharmacy.

Limitations in supporting the high pharmaceutical potential of *S. asoca*:

- 1) Lack of studies on proper scientific standardization and quality control of preparation of Ashoka formulations. This would seem especially when this plant was adulterated by other non effective plants e.g.adulteration with the bark of *Polyalthia longifolia*.^[1,89,102,103] Therefore, for identification of original plant materials different modern methods like spectroscopy, spectrometry, metabolomics, DNA barcoding based techniques, etc would prove valuable in ensuring a uniform and safe raw material of high quality.^[104-106]
- 2) Investigations are required on Ashoka plants which help to identify proper parameters for its cultivation, sample collection and process technologies to assure maximum drug standardization which in turn leads to optimal clinical efficacy of its formulations.^[60,107]
- 3) Ashoka formulations are the mixture of many compounds, it remains unknown as to which components, if at all, plays more significant role in the biological effects known from *Saraca asoca* extract. For example, the bark extract of ashoka known to act on the endometrium of uterus but the mechanism of its action and its active principle remain largely unknown.^[60,107]
- 4) At present there remain inadequate research on the chemistry and molecular biology- based studies on physiology, metabolism and pharmacology of this plant by using standard methodologies. For example, there is no information available on the biosynthetic origin of any pharmacologically important compound reported from this plant.^[107] Also, Chloroplast matK gene investigation and PCR- based identification of *S. asoca* – specific microsatellite markers remain the only molecular biology related reports from *Saraca asoca*.^[108,109]
- 5) Ashoka cell culture system have not been established yet, which can help for investigating the different aspect of the bioactive metabolite production by this plant with the help of already established tools and methodologies, As the plant take many years to reach at maturity, the tissue culture techniques such as ‘callus’ and ‘suspension culture’ could be explored to assess the production of useful secondary metabolites by them.^[107]

Conclusion:

Saraca asoca is regarded as a universal panacea in the classical Indian text. Ashoka is used to treat feminine disorders since ages, such as menorrhagia, leucorrhoea, dysfunctional uterine bleeding, haemorrhoids etc. There are lot of references found in the Ayurvedic literature that, ashoka is the drug of choice in female troubles as it is endowed with large scale of pharmacological activities such as, anti-cancer, anti-menorrhagic, anti-microbial, larvicidal, anti-oxidant, anti- tumour, CNS depressant, anti-diabetic, anti-estrogenic, anti-progestational, dermatoprotective, anti-mutagenic, genoprotective. It is used extensively in Ayurveda, Unani and Homeopathic science of medicine. This versatile plant is the source of many phytochemical compounds such as, flavonoids, tannins, saponin, glycosides, proteins, steroid etc. Beyond this important characteristic of Ashoka some lacunae remains in the research studies of Ashoka plant like lack of comprehensive modern scientific investigations like spectroscopy, spectrometry, metabolomics, molecular and physio-chemical-based research studies for its known pharmacological value. Also purpose oriented, rapid, scientific standardization for evaluation of raw material and quality control processes are required to develop more effective and safer therapeutic natural products from this important medicinal plant. Ashoka cell culture techniques are also essential to study different aspect of its metabolite production. Ashoka is the well known source of new and host plant – associated bioactive secondary metabolites. Pharmaceutical bioprospecting of *Saraca asoca* associated endophytes provide a new dimension to expand the pharma worth of this plant.

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