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A REVIEW ON UTILIZATION OF ASHOKA PLANT IN OXIDATIVE STRESS INDUCED WOMEN REPRODUCTIVE HEALTH COMPLICATIONS

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Abstract: Along with their role as crucial signal molecules in physiological processes, reactive oxygen species (ROS) can contribute to pathological processes that have an impact on the female reproductive system. Oxidative stress is implicated in the pathoysiology of infertility and assisted reproduction, according to numerous research. Its involvement in endometriosis, tubal and peritoneal factor infertility, as well as unexplained infertility, is partially demonstrated. Synthetic hormones and hormonal medications that are frequently prescribed have been shown to disturb the endocrine system and may negatively impact metabolic, neurological, developmental, and reproductive processes. Ashoka is widely used for the treatment and management of a variety of menstrual anomalies, skin conditions, easing liver issues, managing cough and cold, sore throat, treating respiratory diseases, promoting digestion, healing ulcers and wounds, and many other conditions due to the presence of essential bio-active components and the host of medicinal properties is well-known for being helpful for a range of reproductive health issues of women, including issues with the menstrual cycle. In future, there is a need for more study to characterize the biological activity of numerous metabolites present in various Ashoka extracts.

Index Terms - Oxidative stress, Reproductive health, Natural products, Ashoka plant, Pharmacological properties.

1. Oxidative stress

Reactive oxygen species are highly reactive oxygen-containing chemical species that are generated continuously in the body due to the metabolism of cells. The enhanced production and insufficient sequestration of ROS result in oxidative stress (Anwar et al., 2022a). Oxidative stress is a condition that shows up as an imbalance between the body's capability to quickly detoxify reactive intermediates (through antioxidant defences) and the systemic production of reactive oxygen species (ROS), as well as between that capacity and the body's ability to repair the damage that arises from this process. Oxidative stress causes oxidative damaging of protein, nucleic acids and lipids, lipoproteins, carbohydrates and connective tissue macromolecules (Anwar et al., 2020a). Reactive oxygen species are produced during the conversion of ethanol to acetaldehyde, which is then converted to acetate, amplifying the oxidative state of cells. Oxidative stress and ROS have been implicated in the pathophysiology of several serious diseases such as aging, inflammation, cancer, diabetes, cardiovascular disease, arthritis, cataract, muscular degeneration, impaired wound healing, etc (Sakat et al., 2010). Alcohol dehydrogenase are enzymes that catalyse the reversible oxidation of alcohols (Haque et al., 2012) reducing the oxidative stress in cell. Oxidative stress and antioxidants have a significant effect in liver diseases (Yahia and Anwar, 2020).

The body's essential metabolic activities can naturally produce free radicals and other ROS, or they can come from external factors like X-ray radiation, ozone exposure, smoking, air pollution, and industrial pollutants. Free radical generation occurs continually in cells as a result of both enzyme-dependent and enzyme-independent activities. Enzymes can generate free radicals through events involving the cytochrome P-450 system, phagocytosis, prostaglandin synthesis, respiratory chain, and phagocytosis. Non-enzymatic oxygen-organic compound reactions can also produce free radicals in addition to ionising reactions (Lobo et al., 2010).

Oxidative stress becomes exacerbated by the denaturation of antioxidant enzymes like Cu-Zn superoxide dismutase (SOD) by glycation (Anwar et al., 2014; Yunus and Anwar, 2018) or other factors It has been demonstrated that the antioxidant enzyme activity of Cu-Zn superoxide dismutase (SOD) and glutathione peroxidase (GPx) are lower in the erythrocytes of obese individuals than in nonobese controls (Habdous et al., 2003). Total antioxidant status (TAS) and ferric reducing antioxidant power (FRAP) have been utilised as comprehensive measures of antioxidants' ability to dampen plasma radicals. Through a number of physiological mechanisms, including the production of superoxide by NADPH oxidases, oxidative phosphorylation, glyceraldehyde auto-oxidation, activation of protein kinase C, and pathways involving polyol and hexosamine, obesity can itself result in systemic oxidative stress (Manna et al., 2015). Oxidative damage can affect many different types of molecules, including lipids, proteins, nucleic acids, and

sugars. As a result, complex carbohydrates, RNA, DNA, and membranes such as those in cells, nuclei, and mitochondria may all be subject to oxidative stress (Rahmani et al., 2022).

2. Oxidative stress in reproductive health of an adult woman

ROS play a part in pathological processes affecting the female reproductive tract in addition to acting as important signal molecules in physiological processes. The development of oocytes, fertilisation, embryo development, and pregnancy are only a few of the physiological processes that ROS have an impact on all of them. Age-related reproductive decrease may be slowed by OS, according to some research. Preterm labour can start at any time during pregnancy, normal delivery, or both. Repetitive ovulation is regarded to be a contributing factor in the development of the majority of ovarian malignancies, which manifest in the surface epithelium (Agarwal et al., 2005). Oxidative stress can be quite damaging since gonads have exceptionally fast rates of metabolism and cell division. The ability of gonad tissues to act as antioxidants is essential as a result of this. Excessive nitrosylated oxygen radicals (NO) exacerbate the harm to the testicles and ovaries. Peroxynitrite, commonly known as $ONOO_2^-$, is a potent oxidant that is produced when superoxide radicals and NO interact. Furthermore, NO and CO_2 can react to form nitrogen dioxide, a radical with less activity than peroxynitrite but a longer diffusion distance (Asadi et al., 2017).

Experimental studies on both animals and people have shown that the most major DNA mutagenic lesion, 8-oxoguanine, is increased in surface ovarian epithelial cells during ovulation. It has been suggested that the first line of defence against ovarian cancer should be to restrict oxidative stress to the ovarian epithelium (Amano et al., 2021). Reactive oxidants are created in excess during the processes of ovulation and luteinization. Additionally, ovarian surface epithelial cells undergo genetic damage that results in apoptosis as a result of periovulatory remodelling processes, and neighbouring cells are exposed to an excessive amount of reactive oxygen species (Murdock and Martinchick, 2004).

Figure 1 shows multiple health complications in women mediated by oxidative stress (figure 1). Potential ROS generators in the female reproductive system include the granulosa cells, oocytes, cumulus cells, and endometrial cells. A few of the ROS produced by granulosa cells during follicular development that are involved in controlling ovulation and corpus luteum activity are nitric oxide (NO), hydrogen peroxide (H_2O_2), and superoxide anions (O_2^-) (Kaltsas et al., 2023).

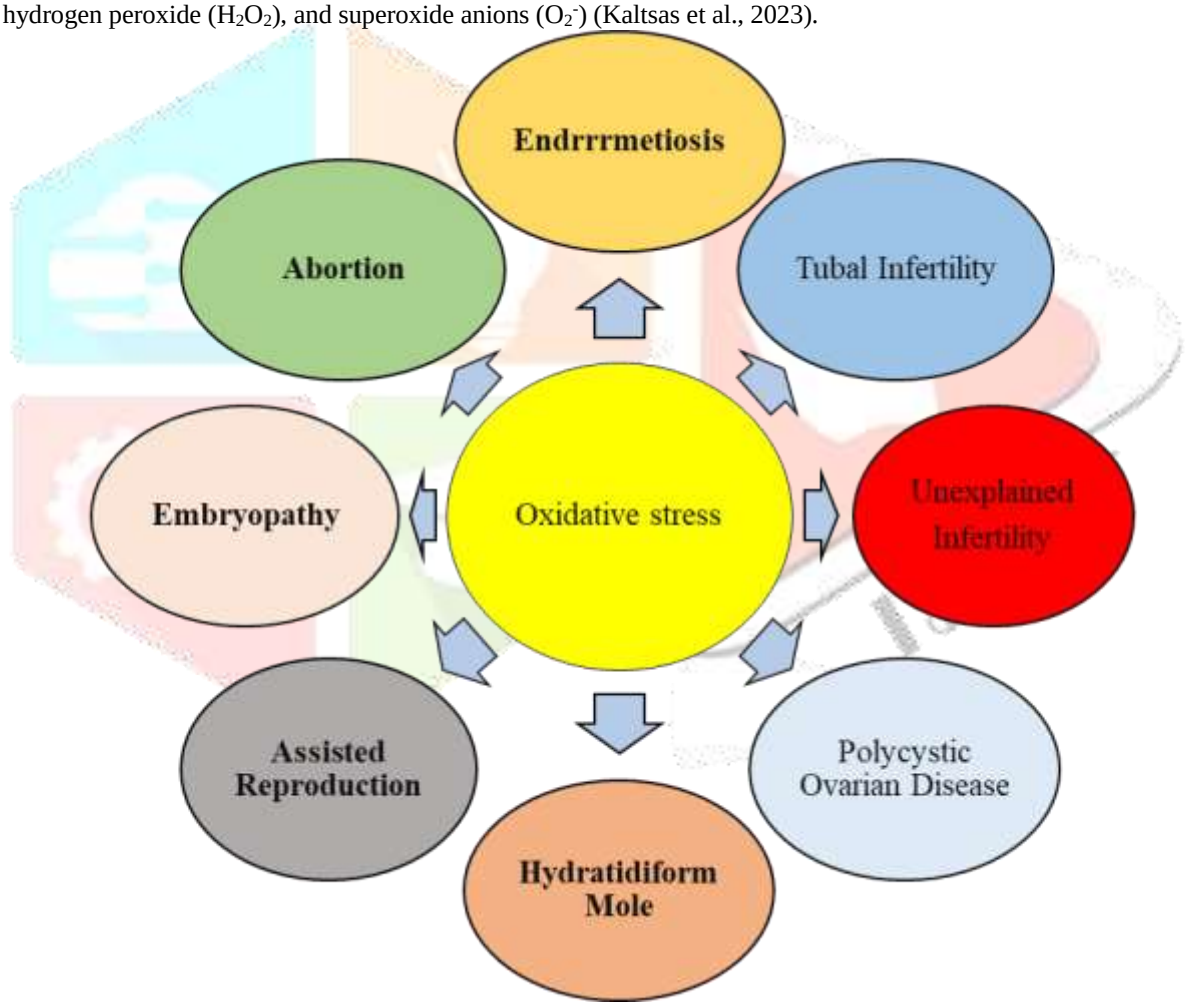

Figure 1. Various reproductive health complications in women induced by oxidative stress.

Oocytes are especially susceptible to OS due to their abundance of mitochondria, which are the primary sources of ROS. During meiosis, oocytes produce ROS. The cumulus cells release H_2O_2 and O_2^- which control fertilisation and implantation, during ovulation. In addition to producing ROS during menstruation and pregnancy, the endometrial cells that line the uterus are essential for fertilisation and implantation (Khazaei and Aghaz, 2017). O_2^- and H_2O_2 production by endometrial cells has been demonstrated. This pathway of programmed health decline has become a serious concern for doctors and scientists because OS also contributes to poor fertility, poor embryonic development, pregnancy loss, birth abnormalities (including autism), and paediatric cancer. Oocytes and follicles in the female reproductive system are impacted by oxidative stress in ways such as defective implantation, reduced endocrine function, and endometrial damage. Oocytes and follicles in the female reproductive system lose some of their viability and functionality as a result of lipid peroxidation's harm to the cell membrane (Archibong et al., 2018).

Additionally, oxidative stress and cell damage are made worse by proinflammatory cytokine production brought on by lipid peroxidation. In contrast to protein oxidation, which decreases the viability and functionality of proteins in the developing oocytes and follicles of the female reproductive system, protein oxidisation results in the loss of the ability of amino acid residues in proteins to carry out their original functions (Agarwal et al., 2012). Oocytes and follicles in the female reproductive system are impacted by

OS in ways such as defective implantation, reduced endocrine function, and endometrial damage. Oocytes and follicles in the female reproductive system lose some of their viability and functionality as a result of lipid peroxidation's harm to the cell membrane (Agarwal et al., 2012; Yan et al., 2022). OS and cell damage are also made worse by the proinflammatory cytokine production that is generated by lipid peroxidation. Protein oxidation impairs the survival and functionality of proteins in the developing oocytes and follicles of the female reproductive system, whereas protein oxidisation renders the amino acid residues in proteins incapable of carrying out their original functions (Kaltsas et al., 2023).

2. Use of natural products in therapeutics

The use of natural products and their derivatives to treat many human disorders dates back to antiquity and they are generally harmless and affordable (Anwar et al., 2020b). More than 80% of people utilise traditional plant-based medicines for their primary healthcare, according to a report from the World Health Organisation (WHO). Natural products and secondary metabolites have already been mentioned as a rich source of therapeutically significant biomolecules for the development of new drugs (Amaral et al., 2019). Poor diet significantly increases the chance of developing a number of chronic diseases, such as obesity, diabetes, and cardiovascular disease. Food deficiencies from an inadequate diet will almost probably contribute to chronic disease. An increase in death rates has been associated with diets high in sodium and poor in whole grains, fruit, vegetables, nuts, and seeds (Anwar et al., 2022b).

Antibiotics (e.g., penicillin, tetracycline, erythromycin), antiparasitics (e.g. avermectin), antimalarials (e.g., quinine, artemisinin), lipid control agents (e.g. lovastatin and analogues), immuno suppressants for organ transplants for example, cyclosporin, rapamycins) and anticancer drugs (eg, paclitaxel, doxorubicin) have revolutionised new medicines (Anwar et al., 2020b). Myrrh is a natural resin and its therapeutic Potential in health management through modulation of oxidative stress, inflammation, and advanced glycation end products formation using in vitro and in silico analysis has been reported (Rahmani et al., 2022). A large number of plants and other natural products have been discussed to have anticancerous effects (Lin et al., 2020; Lichota and Gwozdzinski, 2018). A recent study indicates that around 60 % of chemotherapeutic drugs originate from natural compounds (Cragg et al., 1997). Hesperidin, a bioflavonoid in cancer therapy has been discussed for its mechanism of action through the modulation of cell signaling pathways (Rahmani et al., 2023). So far, many taxonomical groups of organisms have been studied as sources of new anticancer drugs such as algae, bacteria, fungi, higher plants, arthropods and marine invertebrates (Anwar et al., 2020b).

A number of researchers believe that ayurveda is an ancient type of traditional medicine. In the practice of ayurveda, there are actually three fundamental categories of vibrations or fundamental concepts that exist in everything and every individual (Jiaswal and Williams, 2016). Traditional Sanskrit words including vata, pitta, and kapha are being very popularly used in Ayurveda because there fails to be just one phrase in the English language that effectively expresses all of these concepts. Vata is the energy of movement; pitta is the energy of digestion or metabolism and kapha, the energy of lubrication and structure (Dey and Pahwa, 2014). All humans have vata, pitta, and kapha features. However, but one is usually primary, one secondary and the third is usually least prominent. In accordance with Ayurveda, a disease is caused on by inappropriate activity in the cells carried on by a high or low level of vata, pitta, or kapha. Toxic substances directly are capable of resulting diseases (Travis and Wallace, 2015).

Synthetic drugs that are prescribed for the treatment of female reproductive health concerns, such as hormones and hormonal medicines, have been found to have negative effects on a number of bodily systems. Therefore, the purpose of the current review is to talk about the pharmacokinetic characteristics of the Ashoka tree with a focus on its usage for women's reproductive health.

3. Ashoka tree: A women friendly plant

The *Saraca asoca* plant, commonly known as the Ashoka plant, is significant in many different ways and is well recognised for promoting happiness and optimism in the home. In India's history, this tree played a significant role. Ashoka is the largest and most revered tree in India. The native plant known as Ashoka plant, belongs to the Caesalpiniaceae subfamily of the Legume family. It is an evergreen tree of medium size (Smitha and Thondaimin, 2016). It is a resilient tree that requires little maintenance and can withstand a variety of environmental factors. However, it is a beautiful ornamental tree with appealing foliage, fragrant blossoms, and attractive bark, and its cultural and religious significance adds to its cultural worth. The Ashoka tree can make a nice accent to an interior or outdoor space. For a range of medical disorders, Ashoka can be taken in a variety of forms, including seed powder, juice, decoction, tablets made from the processed leaves of the Ashoka plant, and paste. Depending on the situation, there are a variety of ways to use the Ashok plant.

Sanskrit- Hemapushpa, Vanjul, Ashoka, Kankakeli, Tamrapallava, Pindapushpa, Gandhapushpa; Hindi -Ashoka, Sita Ashoka; Odia- Oshoko,Asupal, Devdaru; Kannada – Ashoka, Ashuge; Ubbina, Hessare; Gujrati-Ashopalava, Asopalo; Tamil- Ashogam, Asogu; Nettilingu; Telegu- Nara mamidi, Asokamu, Devdaru; Bengali- Debdaru, Devdaru; Asok;Nepali- Ashau;Marathi- Rankasvinda, Jasundi; Malayalam –Ashokamu Arana, Chorani, Aranei.; English- Sorrow-less tree, Indian fir, Buddha tree, Indian willow; Persian- Bargh-e-ashok

4. Geographical distribution and cultivation of Ashoka tree

In India, Sri Lanka, and Myanmar, the evergreen Ashoka tree has lovely blossoms. Rainforest and monsoon forests compose its main habitat. Its native habitats were located along the western coastal region of the Indian subcontinent, in the center of the Deccan plateau, and in the Western Ghats. The Ashoka is a species considered endangered since it is a naturally occurring tree. Although Ashoka trees are getting less common in their natural environment, it are still to be seen in limited sites in the northern Indian plains, nearby Mumbai on the subcontinent's west coast, in the valleys of the middle and eastern Himalayas, and in a number of additional places (Smithi and Thondaimin, 2016). There are a few varieties of the Ashoka tree (Vignesh et al., 2022). It is one among the Indian subcontinent's rarest blooming trees. Ashoka are beloved because of their attractive leaves and attractive blossoms. It is a lovely little standing up evergreen tree with beautiful bunches of dark green leaves (Urumarudappa et al, 2023). It blooms during the period February to April. Ashoka flowers grow in dense, weighty clusters. Bright orange-yellow in hue, they first become crimson after wilting. The Ashoka tree occurs in a few distinct varieties. One kind is bigger and more widely scattered. Columnar variants are frequently grown. The Ashok plant requires medium to deep, rich in organic material soil with pH levels ranging from moderately acidic to neutral and are properly irrigated for its best growth (Smithi and Thondaimin, 2016). A tropical and subtropical climate is ideal for the Ashoka plant, which can grow to a height of 20 to 30 feet. Ashoka trees need loamy, sandy loamy, or clay-loamy soil types that are moderately to slightly acidic, productive, and within the pH range of 5-7.5. It needs a temperature between 16 and 32 °C, roughly (Bhalerao et al., 2014).

5. Biochemical composition of Ashoka bark

Reducing sugars, tannins, saponins, and fixed oils were found in both the methanolic and aqueous extracts of S. asoca bark during phytochemical examination, but alkaloids were also found in the latter (Bendigeri et al., 2019). In particular, acetone extract of *Saraca* asoca (Roxb.), De. Wild bark revealed the presence of steroids, carbohydrates, phenols, and glycosides; diethyl ether, petroleum ether, and ethanol extract all contained carbohydrates, glycosides, saponins, and steroids; and acetate extract contained glycosides, steroids, and phenols. Distilled water extract contained steroids, carbohydrates, glycosides, saponin, and other substances (Divya et al., 2017). There have been reports of the presence of many bioactive substances in Ashoka bark extract, including phenolic compounds such phenolic acids, phenolic alcohols, and flavonoids (Ahmad and Ghosh, 2022). These substances have been suggested to be implicated in a number of signalling pathways (Zhang et al., 2019). Inflammation, oxidative stress, endoplasmic reticulum stress, mitochondrial dysfunction, and insulin resistance may all be prevented by activating these signalling pathways, according to some research (Almatroodi et al., 2020).

6. Medicinal value and pharmacological activity

Ashoka, particularly its bark and leaves, has a variety of therapeutic advantages. Women who suffer heavy, irregular, or painful menstruation may gain relief from treatment with Ashoka for a variety of gynecologic and menstrual disorders. To relieve discomfort in the stomach and muscle spasms it may be taken two times daily after meals in either the form of powder or tablet. Because of their blood-purifying properties, Ashoka bark juice may also promote good skin. In brief, Ashoka show multiple pharmacokinetic properties. Multiple interesting medicinal properties of Ashoka plant is provided in figure 2.

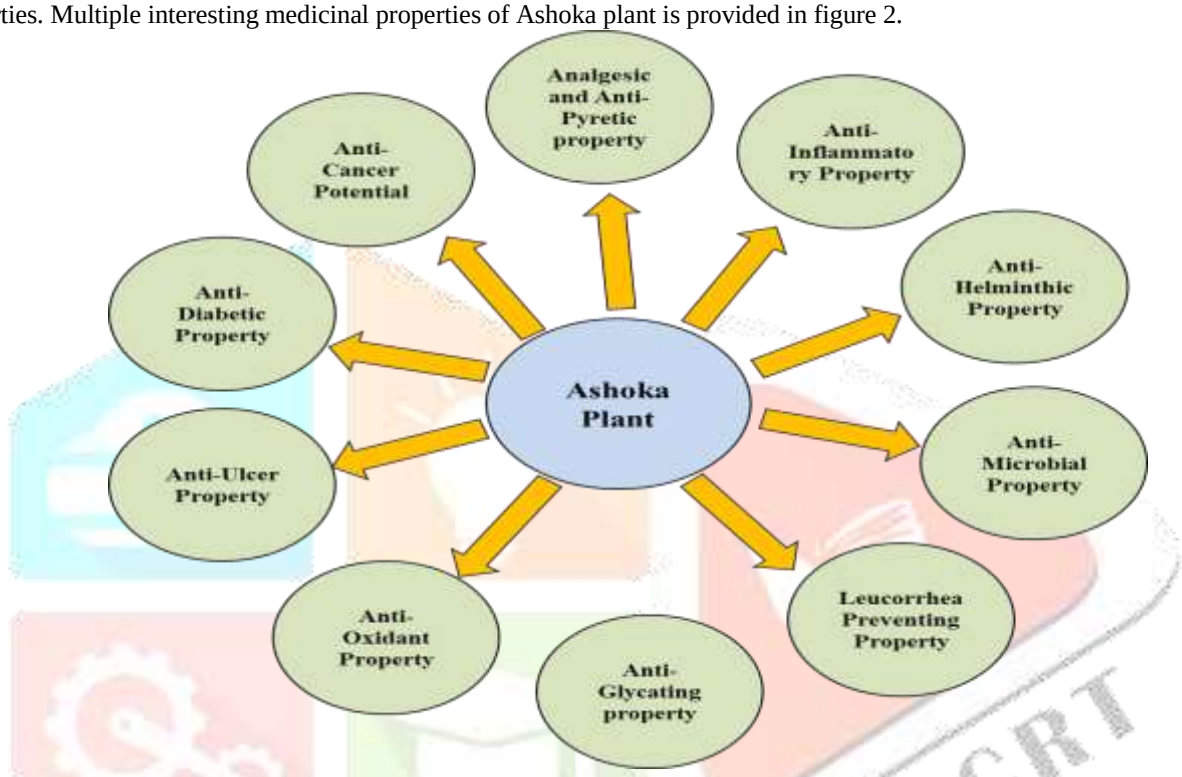

Figure 2- Various medicinal properties of Ashoka plant

6.1. Leucorrhea

Vaginal discharge that is thick, white or yellowish is known as leucorrhea. Leucorrhea can have numerous causes, with estrogen imbalance being the most common one. It is typically a non-pathological symptom that results from inflammatory conditions of the vagina or cervix. The amount of discharge may increase due to vaginal infection or STDs, and it may also disappear and reappear from time to time. In this case, the discharge becomes more yellow and foul-smelling (Kaur and Kapoor, 2014). Recently, 363 females were randomly assigned to the placebo, standard medicine, and four research drug groups for this double-blind, randomised clinical investigation, which was conducted on them for 15 days. Vaginal fluid was examined both before and after treatment, along with subjective primary and secondary symptoms, objective biochemical markers, and other data. According to the findings of the clinical investigation, all four research drug groups displayed equivalent, and occasionally even greater, therapeutic efficacy when compared to normal medication. The research formulation revealed robust and significant antibacterial action and caused an 80–90% inhibition of subjective symptoms, demonstrating its excellent therapeutic efficacy (Gupta et al., 2020).

6.2. Antimenstrual, oxytocic, and uterine tonic properties

In India, the dried bark, root, and flowers of S. asoca are widely used to treat uterine irregularities, menorrhagia (excessive menstrual bleeding), ammenorhea, painful periods, endometrosis, and menstrual cycle disorders. After birth, the root infusion of S. asoca is also eaten for increased lochial discharge. Experiments have shown that bark aqueous extract can stimulate and calm the intestinal muscle, as well as prolong uterine contractions and function as a uterine sedative (Singh et al., 2015).

6.3. Antibacterial potential

Numerous studies show that methanolic, ethnolic, acetone, and aqueous extracts of S. asoca bark, dried flower buds, and leaves have antibacterial effects. These have been tested against many pathogenic bacteria including Bacillus subtilis, Escherichia coli, Salmonella typhosa, S. typhimurium, S. typhii, S. viballerup, S. enteritis, Staphylococcus aureus, Bacillus cereus, Klebsiella pneumonia, K. aerogenes, Shigella boydis, S. sonnei, S. flexneri (Singh et al., 2015). Using the disc diffusion method, extracts of several S. asoca explants were tested for antibacterial activity against gramme positive and gramme negative bacteria. The activities of the compounds were compared with a standard strain for antibacterial characteristics of the imine base and its solvent extract analysed and presenting in show that the compounds are active in demonstrating antibacterial role (Mohan et al., 2016).

6.4. Anticancer properties

Plant-based therapy for cancer prevention is becoming more popular due to its unique properties such as natural chemical composition, lower cost, readily available, easily orally administrable, significant chemo-protective activities, nontoxicity to normal cells in the body, and fewer side effects when compared to other synthetic chemotherapeutic drugs. Chemotherapeutic medicines are toxic to both cancer and normal cells. Furthermore, some common side effects or health consequences of chemotherapeutic drug treatment in cancer (Anwar et al., 2020b). Natural substances may reduce cancerous tumours by increasing the susceptibility of chemotherapy drugs to cancer cells. Through the prevention of drug efflux, it also increases the chemotherapeutic drug deposition in malignant cells. Natural substances can be used alone or in conjunction with other chemotherapeutic medications as a kind of therapy. Sereca indica bark extract's antiproliferative ability was assessed against breast cancer cells (MCF-7, MDA-MB-231) using the MTT assay, and its safety was assessed using normal human cell (HEK-293) culture. SIE also exhibit strong anticancer and antioxidant activities in vitro. *Saraca indica* bark extract's antibreast cancer, antioxidant, and toxicological studies are encouraging and suggest that this herbal remedy may have the potential to be employed in complementary and alternative medicine for breast cancer treatment (Yadav et al., 2015).

6.5. Anti-inflammatory activity

The ability of an ethanolic leaf extract from *Saraca indica* to reduce inflammation was tested using an animal model. It was done using the carrageenan-caused paw edema method. The ethanolic extract, at a dosage of 200 mg/kg of *Saraca indica*, considerably (P 0.01) reduced the edema in the paws. Diclofenac 10 mg/kg did not inhibit as rapidly as *Saraca indica*'s ethanolic extract did (Mujumdar et al., 2000). Paw edema was significantly decreased by the ethanolic extract of *Saraca asoca*. Rats were used to test the immediate anti-inflammatory impact using a model of paw edoema caused by carrageenan. The Carrageen agent at 300 mg/kg and 500 mg/kg pharmacological dose exhibited a considerable decrease in the circumference of paw oedema over 4 hours of 76.74% and 93.02% as compared to standard medicine Indomethacin, which resulted in 97.67% inhibition when compared with control group. The outcomes confirm the strong analgesic, antipyretic, and anti-inflammatory pharmacological effects of *Saraca asoca* seed aqueous extract (Gupta et al., 2014).

6.6. Action against fungi

The disc diffusion technique was used to evaluate the antifungal effectiveness of acetonic and methanolic extracts of Sarca ascoca (Mahesh and Satish, 2008). Aspergillus fumigatus and Aspergillus niger are two separate aspergillus species. Filter paper discs (6 mm in diameter) soaked in acetonic and methanolic extracts were placed on test organism-seeded plates. The organisms employed for testing were Aspergillus fumigatus and Aspergillus niger. Distilled water that has undergone an autoclave was used as the control. After a 24-hour incubation period at 280°C, the results were expressed in terms of the zone of inhibition. The zones were measured in millimeters for their diameter (Alhajj et al., 2019),

6.7. Activity in the uterus

The ayurvedic herb *Saraca asoca* is well known for its capacity to stimulate ovarian and endometrial tissue. The estrogenic activity of U3107 (1 mg/kg p.o.) in normal and ovariectomized rats was investigated. U-3107 was given in an aqueous solution over the course of 21 days. The care of rats with ovariectomies didn't make the uterus weigh more. U-3107 only displays estrogenic activity when an ovary is active and has no pregestational effects. U-3107 is a herbal medication manufactured from multiple plant extracts that is used to treat a variety of menstrual illnesses, such as menorrhagia, puberty, premenstrual syndrome, dysmenorrhea, approaching abortion, and abnormal bleeding (Mitra et al., 1999).

6.8. CNS depressing effects

An extract of *Saraca indica* leaves in chloroform, petroleum ether, water, and methanol displays CNS-depressing effects depending on the polarity of the solvent. The actophotometer approach was used to monitor this activity during a phenobarbital-induced sleep period. A leaf extract from *Saraca indica* significantly reduced the locomotor activity of mice (67.33%) (Verma et al., 2010).

6.9. Analgesic property

Swiss albino rats were used to test the efficiency of aqueous and alcoholic extracts of the bark skin from Shorea robusta (Shal) and *Saraca indica* (Ashoka) for pain relief. The *Shorea robusta* and *Saraca indica* extracts, at 300 mg/kg body weight, significantly reduced pain when compared to the control group. These plants may include phytoconstituents like alkaloids and steroids that have analgesic properties. The results of the investigation indicated that Ashoka and Shal seemed to have analgesic properties, but more experimental and clinical research is required (Poonam et al., 2014).

6.10. Anti-Larvicidal property

The *Saraca asoca* leaf and bark extracts in pet ether and chloroform, respectively, have an LC50 value that make them effective against the larva of C. Quinquefasciatus. The larvicidal bioassay adheres to the WHO's established standards for experimental treatment. To create the test solution, a homogenous shaking of 1 ml of plant extract in 100% ethanol was added to 99 ml of distilled water in a 150 ml disposable wax-coated paper cup. Following that, 25 early fourth instar vector mosquito larvae were transferred to each experiment, which was being run in four replicates, for a final total of 100 larvae for each concentration. The test container was maintained at a temperature of 27°C with a margin of error of 2°C, relative humidity of 80–90%, and a photoperiod of 12 hours of darkness (Mathew et al., 2008).

Screening of the efficacy of methanol extract leaves of *Saraca indica* was done by performing bioassay studies against different developmental stages of insecticidal efficacy of methanol extract of leaves of *Saraca indica* L. against four insect pests causing severe damage to stored grains. The larvicidal activity of methanol extract of leaves of Saraca indica against four insect pests viz. *Ostrinus nubilalsis*, *Spodoptera littoralis*, *Callosobruchus maculatus* and *Tribolium confusum* was found to be directly related to the exposure time and concentration of the methanol extract (Savita et al., 2018).

6.11. Cytotoxic activity

In the recent study, *Saraca indica* bark extract (SIE) was tested for antioxidant, antibreast cancer, and toxicological properties. SIE also exhibit strong anticancer and in vitro antioxidant activities. The toxicological examination of *Saraca indica* bark extract's antibreast cancer, antioxidant, and other properties appears encouraging (Yadav et al., 2015).

On lead-induced toxicity in HepG2 and HEK293 cell lines, the antioxidant activity and in vitro cytotoxicity of *Saraca indica* extract were evaluated. At concentrations of 800 µg/ml for aqueous extract and 1000 g/mL for ethanolic extract, it was discovered that cell viability for HepG2 and HEK293 cell lines was 50%. The *Saraca indica* extract significantly and dose-dependently enhanced the viability of the HepG2 and HEK293 cell lines, according to data from the MTT experiment (Shivhare et al., 2023).

Using the MTT assay, the crude methanolic bark extract of *Saraca indica* was found to be cytotoxic in vitro to HeLa cell lines. The extract had a significantly significant percentage of cell line inhibition, and the IC50 value was found to be 14.63 g/ml. These findings back up the ethnomedical use of *Saraca indica* by demonstrating a sizable anticancer and cytotoxic impact of extract against human cervical carcinoma HeLa cell line (Asokan and Thangavel, 2014).

6.12. Anti-hyperglycemic property

In streptozotocin-induced diabetic mice, Kumar and colleagues studied the antihyperglycemic and antioxidant activities of a petroleum Ether, chloroform, and methanol extract of *Saraca asoca* (Roxb.) De Wild leaves. The extracts were given orally to diabetic mice for 21 days, and this resulted in a significant decrease in blood glucose levels. After daily extract treatment, the body weight of diabetic animals also improved. Other diabetes-related biochemical indicators that had been changed were similarly improved by all of the extracts. The histological modifications of the pancreas, liver, and kidney in STZ-induced diabetes mice are also positively impacted by the extracts. At 500 µg/ml, every extract exhibited significant antioxidant activity. *Sraraca asoca* has antihyperglycemic and antioxidant qualities, as well as the ability to enhance body weight, liver profile, renal profile, and total cholesterol levels. It may justify the plant's legendary usage in diabetes. (Kumar et al., 2012).

Thilagam et al investigated the anti-hyperglycemic and anti-hyperlipidemic effect of ethanolic extracts of *Saraca asoca* (EESA) flowers in alloxan-induced diabetic rats. *Saraca asoca* ethanolic floral extract reduced blood glucose and increased lipid levels in alloxan-treated diabetic mice in dose and time-dependent ways (Thilagam et al., 2021).

6.13. Anti-glycating property

Prathapan and colleagues looked at the antioxidant, antiglycation, and inhibitory ability of a flavonoid fraction of *Saraca asoka* flowers (SAF) against α-glucosidase and α-amylase (the enzymes connected to type 2 diabetes) and LDL oxidation. The antioxidant, antiglycation, and inhibitory activity of a flavonoid fraction of *Saraca asoka* flowers (SAF) against α-glucosidase and α-amylase (the enzymes connected to type 2 diabetes) and LDL oxidation were examined in this work. Under in vitro circumstances, SAF also displayed effective antiglycation and reduced LDL oxidation (Prathapan et al., 2012). Inhibition of advanced glycation end-product formation by quercetin and Catechin components of *Saraca indica* was studied. With inhibitory concentration values of 15.58 mM and 35.01 mM, respectively, the ARIs quercetin and catechin prevented early glycation (Julius and Hopper, 2017).

6.14. Skin-protective properties

Saraca asoca is mentioned in classical texts as having skin-improving properties. Many studies on Ashoka plant extracts have shown that the root, bark, and seed extract of *Saraca asoca* are effective in treating skin conditions such eczema, psoriasis, acne, dermatitis, herpes-kushta/visaropa, scabies, pruritis, Tinea pedis, and skin cancer (Cibin et al., 2012; Kapoor, 2001).

Since 7,12-dimethyl benzanthracene causes skin cancers, it has been demonstrated that the flower extract of *Saraca asoca*, which contains flavonoids, can reduce these tumours [69]. Additionally, it helps to lighten freckles and reduces external skin inflammation while also promoting quick healing of skin wounds. In some cases, dermatophytic fungus can be successfully combated using seed extract (Pradhan et al., 2009).

Cibin et al investigated chemoprevention of Two-Stage Skin Cancer *in vivo* by Saraca asoca. Swiss albino mice were exposed to a single topical application of 7,12-dimethyl benzanthracene (100 µg/50 µl of acetone) that was followed by a 20-week treatment with croton oil three times per week. The number of tumours per mouse and the percentage of tumor-bearing mice were significantly reduced by pretreating the FF with *Saraca asoca*. When compared to the untreated animals, the levels of reduced glutathione, catalase, and protein in the skin of the plant-treated animals increased significantly. The levels of lipid peroxidation, on the other hand, significantly decreased. The expression of ornithine decarboxylase, a crucial enzyme in the promotion stage of 2-stage skin cancer, was significantly reduced in the group treated with plants. These results point to the chemopreventive action of S asoca flavonoids on two-stage skin carcinogenesis (Cibin et al., 2012).

6.15. Anti-estrogenic activity

A study was conducted to evaluate antiestrogenic and toxicological evaluation of methanolic extract of *Saraca asoca* and *Cynometra travancorica*. The increased levels of oestrogen (20 µg/animal) in Wistar female rats may be greatly reduced by a methanolic bark extract of both plants (600 mg/kg) (Suhail et al., 2022). Results of a recent study suggest that the ethanolic extract of *Saraca asoca* flowers showed discernible estrogenic activity in ovariectomized (OVX) female albino Wistar rat model, adding support to the plant's traditional use in treating female reproductive diseases. If the plant extract is clinically confirmed to be helpful, local women who live in areas where the plant is naturally abundant may benefit (Swar et al., 2017).

6.16. Anti-oxidant properties

In vitro DPPH (1,1-diphenyl-2-picryl hydrozyl) radical scavenging activity was carried out to investigate the antioxidant activities of *Saraca asoka* stem bark. The test compounds were found to scavenge free radicals in a concentration-dependent manner (Panchawat and Sisodiya, 2010). In vitro Breast Cancer Prevention and Antioxidant Activity of *Saraca indica* Bark Extract were assessed. According to the study's findings, this herbal remedy possesses antioxidant and antibreast cancer properties (Yadav et al., 2015). *In vitro* antioxidant activity of leaves and stem bark of *Saraca indica* L. was assessed. This plant's leaf and bark extracts in methanol and n-hexane have high antioxidant activity, it can be said (Sabita et al., 2020). Aqueous and ethanolic extractions Saraca indica were characterised for their antioxidant capability and metabolic properties. The antioxidant activity seen may be attributed to the phenolic and flavonoid content in the aqueous and ethanolic extract of Saraca indica, which is a fantastic source of natural antioxidants (Shivhare et al., 2023). Vignesh and colleagues conducted a comparative LC-MS analysis of bioactive compounds, antioxidants and antibacterial activity from leaf and callus extracts of *Saraca asoca*. Callus methanol extracts produced in vitro had the highest concentration of phenolics and flavonoids. Better scavenging activities were also demonstrated using the 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay. The callus methanol extract significantly inhibited *Salmonella typhi* (ZOI 14 mm) and *Enterococcus faecium* (Zone of Inhibition 17 mm) germs (Vignesh et al., 2022). The methanole and n-hexane leaf and bark extracts of this plant possess significant antioxidant activity (Sabita et al., 2020).

6.17. Anti-arthritic property

A systemic inflammatory and chronic illness, rheumatoid arthritis (RA) primarily affects the periarticular tissues and joints and causes debilitating deformities and a variety of functional limitations, including cartilage degradation. Due to their failure to stop the degeneration of their joints and cartilage, RA sufferers have decreased functional abilities. According to *in vitro* models, the hydro ethanol extract-based gel formulation of *Saraca asoca* bark has demonstrated considerable anti-arthritic efficacy (Lil et al., 2022). The anti-inflammatory effects of acetone extract of saraca asoca seeds were investigated in rats with adjuvant-induced arthritis. Comparatively to the control (normal saline) and standard (Indomethacin) groups, regular administration of Saraca asoca acetone

extract (at 300 and 500 mg/kg doses) up to 21 days in adjuvant-induced arthritic rats increases RBC and Hb, decreases WBC, ESR, and prostaglandin levels in blood, and restores body weight. Significant inhibitory effects on paw edoema, ankle joint inflammation, and urine concentrations of hydroxyproline and glucosamine were also seen at higher doses (Gupta et al., 2014).

6.18. Antiulcer property

Saraca indica plant has been reported to have antiulcer properties. In order to treat stomach ulcers, albinos rats were made to receive an aqueous extract of *Saraca asoca* flowers. Flavonoids, saracasin, fatty acids, waxy compounds, and saracadin are the main ingredients in the flowers of *Saraca asoca*. In order to treat stomach ulcers, Albinos rats are treated with an aqueous preparation of Saraca asoca flowers. Flavonoids, saracasin, fatty acids, waxy substances, and saracadin are the main components of *Saraca asoca* flowers. Consequently, the potential antiulcer effect of the *Saraca asoca* solution can be explained by at least one or more plausible mechanisms, such as the suppression of basal gastric secretion, the encouragement of mucus secretion, and the production of endogenous gastric mucosal prostaglandin (Maruthappan and Shree, 2010; Njar et al., 1995).

6.19. Antihelminthic activity

Using solvents like ethanol and methanol, the maceration and soxhelet methods of extraction was conducted to determine the anthelmintic properties of *Saraca indica* leaves. The anthelmintic activity of each extract was evaluated using a protocol. The *Saraca indica* ethanolic and methanolic extracts (obtained from both techniques of extraction) demonstrated anthelmintic property in a dose-dependent manner. Ethanolic and methanolic extracts, when it came to anthelminthic properties, were more potent than the positive control in both extraction procedures. Phytochemical evaluation of the extracts was also carried out to link phytochemical screening with anthelmintic activity (Nayak et al., 2011).

7. Use of Ashoka in female reproductive health

Synthetic hormones and hormonal medications that are frequently prescribed have been shown to disturb the endocrine system and may negatively impact metabolic, neurological, developmental, and reproductive processes. They might also have detrimental effects including polycystic ovarian syndrome, endometriosis, early adolescence, infertility or toxicity to the gonads, testicular germ cell cancer, breast or prostate cancer, problems with brain development, or even birth defects (Asim and Gul, 2021).

Given the enormous developments in biology, chemistry, medicine, and engineering that could be applied to contraception for both women and men, the market for contraceptive products is ripe with opportunity (Callahan et al., 2020). New innovations in contraception are possible as a result of the rising global interest in natural products for reproductive health. Science is interested in the hunt for natural contraceptives or contraceptive medicines that are safer alternatives. Several formulations and medications of plant, mineral, and animal origin that are said to have sterilising, contraceptive, and similar qualities are reviewed in this analysis of ancient, mediaeval, and modern publications, including erotica material (Bhatt and Deshpande, 2021). Some of these are not very common and some are known to be poisonous. However, due to problems with consumer compliance, restrictions on standardisation, and a lack of suitable validation modalities, the majority of the formulations, constituents, or modes of administration have gone neglected. Many of these components have undergone research into determine their phytoconstituents and range of pharmacological actions (Bhatt and Deshpande, 2021).

Additionally, pre-eclampsia, intrauterine growth restriction, and premature birth are among the obstetrical problems linked to polyphenols. Additionally, it has been demonstrated that polyphenols have an impact on foetal health, nutrient absorption, and sexual and reproductive development (Christina et al., 2015). The Ashoka tree's herb can work on the endometrium and uterine muscles, relieving spasms and other pains associated with the abdomen. In addition, it aids in the treatment of conditions like amenorrhea, leucorrhea, cysts, fibroids, and irregular menstrual periods. In order to cure gynaecological and menstrual issues in women, the Ashoka tree is frequently employed. It has been demonstrated that ashka tree has a stimulating impact on ovarian and endometrial tissue. Internal bleeding, haemorrhoids, ulcers, uterine diseases, menorrhagia—especially caused by uterine fibroids—meno-metrorrhagia, leucorrhoea, and pimples might all benefit from it (Nayeem et al., 2017). Ashoka has been reported to be beneficial for treating a variety of hormonal issues in women. It not only aids in the treatment of endometriosis, a condition that results in the inflammation of the uterine lining, but it also controls the blood's levels of the hormones FSH and LH, which in turn aids in regulating pubertal maturation, pubertal development, the strengthening of the female reproductive system, the menstrual cycle, the onset of ovulation, and the development of the corpus luteum. Besides, the Ashoka formulations increase fertility when a person is attempting to get pregnant since they are strong uterine tonics (Sushma and Yadava, 2021).

In addition, it also has a significant impact on the control of periods, the treatment of postnatal health problems, and even the management of excessive abdominal pain and bleeding. It also promotes easy menstrual blood flow and relieves the discomfort associated with dysmenorrhea (kashta artava). Further, it relieves cramping and abdominal pain associated with the menstrual cycle and regulates the aberrant Vata Doshas. By aggressively cleaning the blood and restoring the health of the uterus, Ashoka formulations assist women with PCOD have regular, healthy menstrual periods. In addition to being used during menstruation, Ashoka bark has considerable benefits on non-period days by reducing excessive vaginal discharge or leucorrhoea.

8. Concluding remarks and future perspective

In view of numerous health beneficial properties, Ashoka plant is known to have the properties beneficial for women health. While the powdered formulation is helpful for treating vaginal infections, the decoction of the bark, when eaten with water and taken after meals, helps treat menstruation difficulties. It has been shown to act on the endometrium, ovarian tissue and has many other properties. Ashoka bark extract has reportedly been shown to have a number of bioactive compounds. These substances may have a role in the regulation of numerous signalling pathways that prevent insulin resistance, endoplasmic reticulum stress, oxidative damage, and inflammation. Further research is needed to characterise the activity of the metabolites rather of just the native compounds, which are currently the most frequently examined agents in in vitro experiments, as the active component responsible for the biological action may not be the native polyphenol found in food. Finally, if researchers want to know whether the effects of a specific dose in an experimental trial are physiologically meaningful, they must first discover the normal physiological range of various polyphenols of Ashoka and their metabolites in good maintain of women reproductive health.

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Conflicts of interest

All authors declare that they have no conflicts of interest.

Ethical approval

There was no need of any ethical approval due to the lack of any experiments.

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