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Pterocarpus angolensis: Botanical, Chemical and Pharmacological Review of an Endangered Medicinal Plant of India

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ABSTRACT

Herbal products for primary health care are gaining huge interests of the people and the various healthcare professionals. This is mainly because of the local availability and cost-effectiveness of plant remedies over expensive modern treatments. *Pterocarpus angolensis*, a deciduous plant belonging to the family of Fabaceae is mainly found in the tropical regions of Africa. This tree is rich in medicinal properties which are immensely used by the locals in Africa for the treatment of ringworm infections, ulcers, urinary schistosomiasis, skin injury, etc. The extracts of *P. angolensis* are treasured in Africa for their effectiveness against many diseases like gonorrhea, mouth diseases, diarrhea, etc. It is reported to have inhibitory activity against various pathogens like E*scherichia coli, Staphylococcus aureus,* and *Salmonella typhimurium* because of the high concentration of bioactive compounds like flavonoids, tannins, and other phenolic compounds in the bark and leaves of the tree. Various research papers demonstrated the polar and nonpolar constituents of this plant showing antimicrobial, anti-plasmodial activities against *Streptococcus agalactiae, Candida krusei,* etc. In India, very few of these plants have been reported to be alive in the Darjeeling district, West Bengal. But, lack of proper documentation or research paper led to negligence related to the importance of this species and it has already been listed in the IUCN Red List of threatened species. The main objective of this review is to spread awareness about the conservation of the plant possessing such remarkable properties. Secondly, to provide an overview of the phytochemical screening of various important medicinal constituents that this plant possesses and this might lead to change in the field of modern medicine.

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1 Introduction

Human beings have been known to use plants as medicine for many health related problems since the pre-historical period. This practice forms the origin of much of modern medicine. Many drugs which are used even today are of plant origin. Quinine (from cinchona bark), morphine (from the opium or poppy seeds), aspirin (from willow bark) are well known examples (Vickers et al. 2001). There has been a huge increase in the consumption of herbal products in the last three to four decades. According to WHO's report published in 2010 about three fourth of the world, the population depends on herbal products for their day-to-day health care (WHO 2010). Firstly, the cost of the present-day hospital treatments is too costly as compared to traditional medicines (Maroyi 2013). Secondly, resistance to drugs has led people to resort to more affordable traditional medicine. Lack of efficacy of modern-day treatment is reported by The World Health Organization (Brand Features 2018). Moreover, scarcity of medicines in developing countries has also compelled people to depend on herbal medicines (WHO 2013). Herbal supplements have been used to treat various ailments such as asthma, rheumatoid arthritis, migraine, gastroenteritis, and cancer (Maroyi 2013).

P. angolensis commonly known as the Blood wood tree is a deciduous tree belonging to the family Fabaceae, which is mostly found in southern and eastern Africa. The sap of the tree resembles blood and hence the name Bloodwood. The tree is famous for its quality timber (Mojeremane and Lumbile 2016). Moreover the sticky deep red or maroon-colored sap is used as a dye for fabric. Also, medicinal values of treating several ailments like ringworm, ulcers, and urinary schistosomiasis (Chipinga et al. 2018; Ndamba et al. 1994), antibacterial and antifungal properties of this plant are well documented. Hence exploitation of the tree for above mentioned medicinal as well as a commercial utility has already made it marked as a "decreasing" species in the IUCN Red-List of threatened species (Barstow and Timberlake 2018).

On Indian soil, *P.angolensis* is known as Ram Supari. It has been reported to be alive in the Darjeeling district of West Bengal but is surprisingly few. Therefore, the tree needs to be conserved immediately. Because of the lack of proper documentation of ethnobotanical and pharmacological aspects of this plant in India, the importance of this plant has been completely neglected to lead to the impending extinction of this species from India.

Considering the above facts, this review provides an overview of the botanical, chemical, and pharmacological aspects of *P.angolensis*. It presents the various beneficial properties of the plant in the field of medicine as well as its commercial value. The main aim of this review is to provide an overview of the phytoconstituents that the plant possesses and to spread awareness about the conservation of the plant with such significant medicinal properties.

2 Botanical Aspect

P.angolensis is a deciduous tree having a slightly flat crown with a high canopy. It reaches up to 16 m high and reaches 28 m under favorable conditions. They have straight stems that are occasionally swollen at the base (Mojeremane 2016). The leaves exhibit alternate arrangements and are drooping in nature (Takawira-Nyenya et al. 2005). The plant has sweet-scented, orange-yellow flowers that have distinctive round pods surrounded by brown and papery wings (Mojeremane 2016) which are pear-shaped and are bisexual (Takawira-Nyenya et al. 2005). Very few stems in the younger age classes are present currently. The reason behind this is the exacerbation by loggers to supply timber for commercial purposes (Stahle et al. 1999). This indicates that it is under threat of extinction and therefore calls for immediate measures to conserve it.

3 Chemical or Phytochemical Aspect

The family of Leguminosae has been substantially investigated and various secondary metabolites with a wide range of diversity in their chemical structures have been reported to date (Ramawat and Mérillon 2008). Phytochemical investigations of different parts of *P.angolensis* have revealed the presence of many phytochemicals such as flavonoids, isoflavonoids, pterocarpans, triterpenes, epicatechins, deoxybenzoin, and chalcones (Abouelela et al. 2019) (Table 1). The non-polar extracts of such plants are mainly composed of essential oils and other bioactive compounds. These are obtained from different plant parts such as flowers, bark, wood, twigs, leaves, and roots(Abubakar and Majinda 2016). Preliminary screening of the extracts of the plant from various parts revealed the presence of a high concentration of tannins in the bark, saponins are found in the root as well as bark. Researchers have confirmed phytochemicals such as tannins, flavonoids, terpenes are mainly found in the leaves (Chipinga et al. 2018).

3.1 Non-polar Profile

Nonpolar (*n*-hexane and chloroform) extraction of the stem bark followed by GC-MS analysis is performed to analyze the different metabolites. Identification is done by comparing the acquired spectra with the existing NIST library (National Institute of Standards and Technology). The structures of the phytochemical are elucidated using NMR (Nuclear Magnetic Resonance) spectroscopy. GC-MS (Gas Chromatography-Mass Spectroscopy) analysis of the chemical constituents from the n-hexane and chloroform extracts reveals the presence of glycosides, ketone, saturated and unsaturated fatty acids, alcohols, and sterols. Ten volatile phytoconstituents, viz. tetratriacontane 11, n-hexadecanoic

Table 1 List of compounds isolated from *P. angolensis*

NOS.	COMPOUND NAME	SOURCE (PLANT PART)	REFERENCES
1.	Liquiritigenin	Wood	Maurya et al. 1984
2.	Prunetin	Wood	Seshadri 1972
3.	Muningin	Wood	Bezuidenhoudt 1987
4.	Epicatechin-3-O-galate	Stem Bark	Noufou et al. 2012
5.	Epicatechin(4b-8)-epicatechin(B2)	Stem Bark	Samie et al. 2009
6.	(-)-Epicatechin	Bark	Bezuidenhoudt 1987
7.	Hexamer of Epicatechin	Stem Bark	Samie et al 2009
8.	Isoliquiritigenin	Wood	Seshadri 1972
9.	α,2'-Dihydroxy-4,4'-di-methoxy chalcone	Wood	Bezuidenhoudt 1981
10.	(-)-Pterocarpin	Wood	Shah 1975
11.	Angolensin	Wood	Seshadri 1972
12.	α (S)-4-O-methylangolensin	Wood	Bezuidenhoudt 1980
13.	(αR,1"R,4"S,4"αR,8"αR)-4-O-α-cardinylangolensin	Wood	Bezuidenhoudt 1980
14.	(αR,1"R,4"S,4"αR,8"αR)-4-O-T-cardinylangolensin	Wood	Bezuidenhoudt 1980

acid 1, 7-dehydrodiosgenin 12, stigmasta-3,5-dien-7-one 14 , lupeol 13, octadecanoic acid 10, friedelan-3-one 15, hexadecanoic acid, methyl ester 9 and tetradecanoic acid 8 are reported to be the most abundant in the n-hexane extract of *P. angolensis*. While from the chloroform extract 1-octacosanol 16 was reported to be present (Abubakar and Majinda 2016).

3.2 Polar Profile

Phenolic compounds are found to be universal in almost all plants as secondary metabolites. Various researchers have estimated the different phenolic compounds in *P. angolensis* using Folin-Ciocalteu's reagent. Mainly phenolic compounds are present in the water extract of the plant. However, some amounts of these compounds are also present in methanolic extracts. Leaves of *P.angolensis* are reported to have more polyphenols as compared to barks (Santos et al. 2020). Further analysis of the phenolic profile by HPLC-DAD (High-Performance Liquid Chromatography with Diode Array Detection) verified the presence of gallic acid, caffeic acid, and taxifolin in the crude extracts and fractions of *P.angolensis* but not in abundance. The presence of hexadecanoic acid and lup-20(29)-en-3β-ol has been revealed in the GC-MS analysis of a methanolic extract of the leaves (Santos et al. 2020). The thick bark of the plant that secretes blood-red sap is found to be rich in organic compounds such as tannin (76.7%) and mining when damaged (Mojeremane 2016).

4 Pharmacological Aspect

Many researchers have revealed that the various parts of the plants such as the bark, roots, flowers, sap, and seeds have different medicinal values and are used to treat various ailments. The red sap rich in various organic compounds is to stop nose bleeding. It is also efficient in killing ringworms and curing ulcers. Several studies have reported that the sap is used in treating eye cataracts, malaria, skin inflammations, and urinary schistosomiasis. Cold infusion from the bark is used as a remedy for rashes as well as to relieve headaches, mouth ulcers, corneal ulcers, and various stomach-related disorders (Mojeremane 2016). The seeds are crushed to form powders that are used as a wound dressing (Takawira-Nyenya et al. 2005) to speed up healing. Apart from the above-mentioned benefits of the plant, various researches have revealed the surprising pharmacological properties of the plant.

4.1 Antiplasmodial Activity

In a study, some researchers have explored the efficacy of the *P. angolensis* extract to inhibit the survival of the malarial parasite *Plasmodium falciparum*. Although malaria is a treatable disease, the growth of parasites resistant to antimalarial drugs is growing day by day (WHO 2017a & b).

Heat shock proteins (Hsps) are universal chaperone molecules that facilitate protein folding. Hsp70 family of chaperones has been reported to be expressed by the malarial parasite. The Hsp70s show a low basal ATPase activity (Kampinga and Craig 2010). Hsp 70s in their ATP-bound state, exhibit low affinity for substrates, which results in the release of the substrate. It expresses six members of the Hsp 70 family out of which two of them are located in the cytosol-PfHsp70-1 and PfHsp70-z (Shonhai et al. 2007). These two Hsps are thought to function towards facilitating protein folding for the survival of the parasite. It has been studied

that the maintenance of protein quality is important for the survival of the parasite as about 24 percent of the parasite proteome is made up of arginine repeats that tend to aggregate under stressful conditions that the parasite encounters during its life cycle (Singh et al. 2004). So the two proteins have been considered as potential targets to inhibit the survival of the parasite.

Growth inhibition assays were conducted using *P .falciparum* 3D7 that were maintained at the blood stage. Chloroquine was used for the validation of the antimicrobial sensitivity of *P. falciparum.* It was used as a positive control. *P. falciparum* 3D7 grown in absence of extracts was used as a negative control. The treatment of parasite cultures with *P.angolensis* extracts resulted in the inhibition of the growth of the parasite. They concluded that *P.angolensis* plants contain certain compounds which interfere with ATP binding by Hsp70 or do not allow the chaperones to bind the substrates. The result from this study has interestingly revealed that 50% ethyl acetate and 50% hexane fraction extract of *P.angolensis* exhibits potent antiplasmodial activity. However, the exact phytochemicals in that inhibited the parasite survival is unknown and further can be investigated (Zininga et al. 2017).

4.2 Anti-inflammatory Activity

In various diseases, including venereal diseases, inflammation becomes a prime risk factor and sometimes leads to various complications in the treatment (Mulaudzi et al. 2013). Among the different phenolic compounds, flavonoid has been reported to have the maximum anti-inflammatory property (Cushnie et al. 2005). The extracts of this deciduous tree are treasured for their anti-inflammatory property due to their high concentration of tannins and flavonoids (Chipinga et al. 2018; Cai et al. 2019). In a study, the scientist aimed to evaluate the anti-inflammatory property of the extracts of *P. angolensis*. They evaluated the anti-inflammatory activity against cyclooxygenase (COX-1 and COX-2) enzymes. They reported that the dichloromethane and petroleum ether extracts of the *P.angolensis* bark exhibited good anti-inflammatory activity in both COX-1 and COX-2 assays (Mulaudzi et al. 2013).

4.3 Antimicrobial Activity

Various scientists have reported that the extracts of *P.angolensis* shows anti-inflammatory activity and also high inhibitory activity against various bacteria such as *Staphylococcus aureus, Escherechia coli,* and *Salmonnella typhimurium* (Luseba et al. 2007). On further research, scientists have confirmed the anti-fungal property of the plant. They analyzed the phytochemicals present in the plant parts and evaluated the effectiveness against pathogenic bacteria such as *Staphylococcus aureus, Streptococcus agalactiae,* and fungus *Candida krusei.* Minimum inhibitory concentration (MIC), minimum bactericidal concentration/minimum fungicidal concentration (MBC/MFC) of crude extracts against pathogens was determined. They confirmed that the extracts exhibited antimicrobial activity. The antimicrobial activity varied in accordance to part of the plant used, the polarity of the bioactive compound, and concentration. They confirmed that more antimicrobial activity was exhibited by methanolic and dichloromethane extracts as compared to aqueous extracts (Chipinga et al. 2018). Various studies have revealed that the chloroform extracts *P. angolensis* stem bark showed activity against *Bacillus subtilis* with MIC of 50 µg (Abubakar and Majinda 2016).

Scientists have extracted and demonstrated the structures of seven different compounds from the ethanol extract of *P.angolensis* mainly phthalate and epicatechin and its derivatives. These compounds were tested against *S .aureus* and *Entamoeba histolytica*. The presence of epicatechin and derivatives in the stem bark extract revealed strong antibacterial activities against *S.aureus* but weak activities against *E.histolytica* (Samie et al. 2009).

Researchers have revealed that results phloem sap has bioactive compounds that possess antimicrobial activity of the plant against *S. aureus, Escherichia coli,* and *Pseudomonas aeruginosa*. The antimicrobial efficacy of the phloem sap was evaluated using the agar diffusion technique. They used tryptone – soya agar medium and impregnated it with the test organisms. However, the results obtained were proved to be negative as there was no formation of the clear zone for any of the test organisms. Further, they conducted the GC-MS analysis of the phloem saps and identified various compounds from the GC profile. The compounds identified are lactic acid, glycerol, phosphoric acid, succinate, D-ribofuranose, 3, 4-dihydroxybenzoic acid, silane, and D-fructose (van der Riet et al. 1998). However, with regards to lactic acid, it was found that, when used in combination with some other compounds such as sodium or potassium sorbate, it showed antimicrobial activity against the gram-negative test organism (Kim and Hearnsberger 1994)

Campylobacter sp. has been listed on the World Health Organization (WHO) list of global priority pathogens for research and development of new antibiotics (WHO 2017a; WHO 2017b). They belong to the groups of zoonotic bacteria which are the leading causes of human bacterial gastroenteritis (Cheng and Fischer 2018). Researchers have revealed the efficacy of *P.angolensis* extract and expressed the antibacterial activity as minimal inhibitory concentration (MIC) by the broth microdilution method. They confirmed that the ethyl acetate extract of the bark of the plant showed MICs of 90μg/ml (Hlashwayo et al. 2020).

4.4 Antioxidant Activity

The various reactive oxygen species induce oxidative stress which may result in DNA as well as protein damage that can lead to

aging and diseases such as cancer. Various studies have revealed the antioxidant property of *P.angolensis* that helps in scavenging the free radicals, thus inhibiting oxidative stress. The crude extract and the different fractions of *P.angolensis* were evaluated by the researchers to investigate the different phenolic compounds. Techniques such as UV-Visible and FT-IR (Fourier Transform Infrared Spectroscopy) were used to analyze the spectroscopic characteristics of the extract fractions. 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging and reducing power assays were used to assess the antioxidant efficacy. The results obtained showed that the fraction containing a low phenolic concentration displayed the highest DPPH radical scavenging activity while the fraction with high phenolic content exhibited the highest reducing power activity. Spectroscopic and IR spectroscopy details obtained by them revealed both the fractions from the stem bark are antioxidant rich fractions (Traoré et al. 2017).

4.5 Wound Healing activity

Healing of wounds occurs by the reconstruction of injured skin by the involvement of various cells (epithelial and mesenchymal cells) and molecules (cytokines and growth factors). The natural bioactive compounds extracted from the plants have always revealed wound healing activity from ancient times by causing the proliferation of fibroblasts and keratinocytes. Plant extracts contain growth factors and various cell adhesion molecules (Talekar et al. 2017)

Various studies have revealed the wound healing potential of *P.angolensis* and the researchers have confirmed that the methanolic extract of bark and leaf of the plant showed wound healing activity and clearly showed the decrease in size of the injuries (Santos et al. 2020).

Conclusion

This review presents an overview of the different phytochemical compositions and bioactivities of *P.angolensis*. As described; the plant exhibits versatile benefits such as anti-plasmodial activity; wound healing, antioxidant activity, anti-bacterial and anti-fungal activity, and many more. Firstly, as no research or proper documentation has been done with this plant in India to date, the detailed phytochemical screening of plant extract and various benefits presented in the review will enable us to systematically explore the possible medicinal impact of this plant in Indian perspective. Secondly, the objective of this review is to spread awareness about the conservation of the plant possessing such remarkable properties which can usher in a paradigm shift in the practice of medicine and encourage the people to cultivate and propagate such a threatened species and in protecting this valuable resource from extinction.

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Conflict of interest

All the authors declare that there is no conflict of interest.

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