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A COMPREHENSIVE REVIEW ON PHARMACOLOGICAL PROPERTIES OF *KYDIA CALYCINA*

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ABSTRACT: *Kydia calycina*, a member of the Malvaceae family known as Pulao, Boranga, or Pula, has been reported for its traditional uses as a medicinal plant. The presence of potentially active nutrients and their multifunctional properties make *Kydia calycina* leaves, root, bark, and stem perfect candidates for the production of phytopharmaceutical products. It is used traditionally as a remedy in different disease conditions like skin disease, hyperglycemia, antihyperlipidemic, analgesic, anti-inflammatory, anticancer, antioxidant, antiulcer, antifungal, immunomodulatory, febrifuge, wound healing, industrial uses, and nutritional important, *etc*. by tribal of Rajasthan Maharashtra and Himachal. It is important to clarify these health benefits to public due to the increasing need for prevention and treatment of chronic diseases. Although it is used widely around the country, single hand information about its ethnobotanical, phytochemical and pharmacological action is still lacking. Traditionally appreciated for its pharmacological properties by the various researcher's Pulao is still hardly recognized because of insufficient scientific information. The aim of this review is to summarise all the traditional pharmacological properties of *Kydia calycina*.

INTRODUCTION: India is known for its traditional medicinal systems as Ayurveda, Homeopathy, Siddha, and Unani. Traditional medicinal systems are found mentioned even in the ancient Vedas and other scriptures [1, 2]. These systems have rightfully existed side-by-side with Allopathy and are not in 'the domain of obscurity [3]. These systems are recognized globally for the prevention of disease, treatment, and generic health maintenance [4]. Herbal medicine has been the basis for medical treatments through much of human history, and such traditional medicine is still widely practiced today [5].

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Herbal medicine is also called phytomedicine or phytotherapy. Para herbalism describes alternative and pseudoscientific practices of using unrefined plant or animal extracts as unproven medicines or health-promoting agents [6].

Herbal medicine (HM) is the fulcrum of complementary and alternative medicine, which in recent times is increasingly gaining widespread popularity all over the world and gradually streaming toward integration into the mainstream healthcare systems [7]. Scientific validation of pharmacological activity of age-old drugs used in Ayurveda reinforces faith in the traditional system, in which plants are selected only on the basis of experience [8, 9]. Medicinal plants have always been an important source for finding new remedies for human health problems. Traditionally, numerous herbs have been recommended for the treatment of diabetes [10, 11].

About 80% of the human population in various countries said to be dependent directly or indirectly on traditional medicine for their primary healthcare services, and most of this comes from plants. Moreover, the prevalence of chronic illnesses in the nation is increasing, and previous studies showed that the use of herbal remedies among such patients is very high [12, 13]. Traditional knowledge of ethnic people is always a great source for the discovery of new drugs. The plant kingdom has proven to be the most useful in the treatment of diseases, and they provide an important source of all the world's pharmaceuticals. The most important of these bioactive constituents of plants are steroids, terpenoids, carotenoids, flavonoids, alkaloids, tannins and glycosides [14, 15].

Herbs had been used by all cultures throughout history. It was an integral part of the development of modern civilization. The herbal market globally increases due to safe drug delivery with fewer side effects compared to synthetic drugs [15]. In India, about 80% of the rural population uses medicinal herbs or indigenous systems of medicine.

Recently evidence-based studies are becoming increasingly essential for establishing the safety and efficacy of herbal products in the domestic and export market [16, 17]. Although herbal medicine is used mostly for treating mild to moderate illnesses, and participants were aware of its limits, the combination of self-medication, non-expert consultation, and missing risk awareness of herbal medicine is potentially harmful.

A traditional medicinal plant, widely distributed in the Rajasthan, known as pulao, sukhlai, pula, bhoti botanically identified as *Kydia calycina* Roxb of family Malvaceae [18, 19]. Distributed in the tropical Himalayas from the Indus eastwards to Myanmar and in peninsular India from northern Maharastra and Madhya Pradesh south-wards and in Rajasthan [20]. in Rajasthan it is found abundantly in Sariska tiger Reserve Alwar [21, 22]. These species become rare in Rajasthan by the time [23]. Malvaceae family plant members are distributed worldwide and have been used as a folk remedy for the treatment of skin diseases, as an anti-diabetic, as an antifertility agent, antiseptic and carminative. Compounds isolated from Malvaceae families such as flavonoids, phenolic acids, and carbohydrates are considered responsible for these Medicinal properties [24, 25].

Habitat: *Kydia calycina* is reported to grow in a wide range of habitats, but mainly in arid regions. It is common in the deciduous forests of India and the sub-Himalayan tract [18]. *Kydia calycina* is an evergreen tree growing 10-20 meters tall. The plant is harvested from the wild for its fiber. Small trees to 12 m. Leaves suborbicular to broadly ovate, $6^{-14} \times 6^{-16}$ cm, acute or obtuse, rounded to subcordate at base, margin irregularly denticulate, with scattered hairs above, densely tomentose beneath; petiole (1) 3-7 cm. Epicalyx segments 4.5- 5.5 mm, accrescent in fruit to 7-12(-15) mm, greyish tomentose. Calyx lobes 2.3-3 mm. Petals 7-8 mm, white or pink sometimes with reddish base. Male flowers with staminal column 3-4 mm, branches 2.5-3 mm. Female flowers with style c 4mm; stamens sterile. Fruit subglobose 4-4.5 mm [26, 27].

Tree of Pulao grow up to 15 m high, bark 5-6 mm thick, greyish-brown in color, irregularly flaking off in thin small scales; branchlets terete, stellate pubescent. Leaves simple, alternate, stipulate; stipules free, lateral, to 1 cm, subulate; petiole 2.5-10 cm long, slender, stellate-tomentose; lamina 5-15×4^{-13} cm, broadly ovate to suborbicular, 3-5 lobed, base obtuse, cordate, round or truncate, apex obtuse or acute, margin crenate-dentate or subentire, coriaceous, stellate-tomentose above, velvety beneath; 5-7 nerved from base, palmate, prominent, with a single raised elliptic nectary at the base of the midrib beneath or 3-nectaries on principle nerves beneath, lateral nerves 3-4 pairs, pinnate, prominent, intercostae scalariform, prominent.

Flowers polygamo-dioecious, white, in axillary and terminal panicles; peduncle stellate-tomentose; pedicel up to 5 mm long, stellate-tomentose; involucellar bracts 4-5, connate at base, obovate-spathulate, stellate-tomentose, accrescent; calyx 6 mm long, 5-lobed, divided to the middle, lobes ovate-acute, stellate-tomentose outside, silky glaucous within, accrescent; corolla 1.8 cm across in male flowers, to 1 cm across in female flowers, white; petals 4-5, adnate to the staminal column, spathulate, ciliate along the margins, clawed at base; staminal column 4 mm long, glandular throughout, hairy at base, 5-branched at apex with

4-6 sessile reniform anthers at its top; pistillode with a short style; ovary superior, 3-locular, ovules 2 in each locule; stylar branches 3, glabrous; stigmas large, peltate, minutely hairy; staminode with 3-5 clefted staminal column, each with 2-3 connate, rudimentary anthers at its apex. Fruit a capsule, 3-6 mm across, subglobose, stellate-tomentose, completely enclosed within the calyx; seeds one in each locule, reniform, concentrically striated, glabrous, brownish [28-32]. The anatomical character of Leaf shows epidermis on both side, distinct parenchyma with hypodermis and mesophyll tissue. It also consists of some unicellular hairy trichomes. Whereas stem also shows some cellular anatomy, but it shows secondary growth and prominent medullary rays with xylem [33].

Plant Classification: [34, 35]

Kingdom	:	Plantae
Phylum	:	Tracheophyta
Subphylum	:	Angiosperms
Series	:	Thalamiflorae
Class	:	Dicotyledon
Subclass	:	polypetalae
Order	:	Malvales
Family	:	Malvaceae
Genus	:	Kydia
Species	:	*K. calycina* *Kydia fraternal* *Kydia paterna*

FIG. 1: *KYDIA CALYCINA*

Synonyms: Pulao Pulu, Pula, Chourpultea, Pattha, Pulia, Choupultea, Potari, Bellaka [36, 37] Phuilau, Tumari [38] Puli Boranga [39] Baranga, Banakapsia, Pichela, Pula, Bhindi, Waring, Petari, Warang

Many species of Kydia e.g *K. calycina*, *K. angustifolia*, *K. paterna* were reported for their various Traditional-medicinal uses, and still have not been reported for its phytochemistry and pharmacological property. In this review, an attempt has been made to gather all the ethnomedicinal uses and pharmacological properties of *Kydia calycina*.

Ethnomedicinal Property: *Kydia calycina* has various traditional medicinal uses [40]. Traditionally it is used in the treatment of Diabetes or hyperglycemia but no pharmacological data available to date. Ethno medicinally used in Body swellings, to increases saliva and as anti-inflammatory drug [41-44.] Traditionally it is also used to treat jaundice, skin diseases, ulcers, body pains, arthritis and lumbago [45, 46] wounds, cuts, boils, veterinary medicine, timber, fibrous bark [47] fuel-wood [48]. This plant has a high Protein value Above 20% so used as Food [49, 50]. The plant also used for its antirheumatic property for curing arthritis [39, 51] lumbago, and relieving body pains [52]. According to other literature, also use as Febrifuge, antirheumatic, used for body pains and skin diseases [42, 43, 53] as an antifungal agent [54]. The leaves of the plant showed analgesic and anti-inflammatory action [20, 27, 55]. Leaves also have been proven to possess hepatoprotective potential [55, 56]. A paste of roots in butter, linseed oil & hen's egg is applied on fracture, or small tablets are taken orally [57]. The stem bark and leaf paste used by Chenchus people for skin diseases and ulcers [58].

Kydia calycina fibres also used in the textile industry [59] because this plant produces better quality bast fibers with respect to plants like jute and flax [60]. Flowers of *K. calycina* are rich in potassium and iron and were found inhibitory to Streptococcus mutans [61]. Recently, methanolic extract was reported to possess significant antioxidant activity [62,] whereas its antidiabetic activity has not been reported by earlier workers.

Plants of *Kydia calycina* are mucilaginous, anti-inflammatory, febrifuge 39 leaves and root are anti rheumatic, a paste of the leaves applied for body pains, and leaves are used in poultices for skin diseases. Leaves are chewed for stimulating saliva. Stem is used for clarifying sugars. The plant extracts are used in treating liver disorders and skin

related problems [27, 36, 55]. Studies on the application of leaf and bark extract of *Kydia calycina* showed phytotoxic effects on the germination and the radical growth of some food crops [63].

Pharmacological Properties:

Antioxidant Activity: In this research three plants have chosen for study *Kydia calycina*, *Aglaia elaeagnoidea,* and Alysicarpus monilifer. Results show that hydroalcoholic extracts of *Kydia calycina* plant have highest FRAP value (1.41) followed by *Aglaia elaeagnoidea* (1.36) and *Alysicarpus monilifer* showed the lowest value (0.88). Among the fractions of the selected plants tested, hexane fraction of *Kydia calycina* showed highest FRAP value (1.18) followed by hexane fraction of *Aglaia elaeagnoidea* (0.95) and the methanol soluble fraction of *Alysicarpus monilifer* showed the lowest value (0.51). Ascorbic acid was used as a standard. According to study *Kydia calycina* revealed the presence of bioactive triterpene and flavones glycosides such as squalele, friedelin, and tiliriside; they must have been responsible for the observed high FRAP value [62, 64, 65].

Analgesic Activity: Hot plate method was used to determine the analgesic activity of methanol extracts of *Kydia calycina*. In this study, the effect of extract (200 and 400 mg/kg; p.o.) on hot plate test and acetic acid-induced writhing in mice was deter-mine. The results of hot plate test and acetic acid-induced writhing test to indicate that the methanol extract (200 and 400 mg/ kg) showed the significant increase in reaction time and reduction in the number of writhes induced by acetic acid in a dose-dependent manner which were comparable with reference compounds, diclofenac and pentazocine respectively. A significant ($p< 0.0005$) analgesic effect to the thermal stimulus was observed at 60 min with 200 and 400 mg/kg of *K. calycina*, which is comparable to the effect of standard pentazocine [20, 55].

Anti Inflammatory Activity: Rat paw edema method was used to measure the anti-inflammatory activity of *Kydia calycina*. Results indicate that there was a dose-dependent inhibitory activity of methanol extract (200 and 400 mg/ kg) in Carrageenan induced paw inflammation at all assessment times. Diclofenac sodium, a COX-inhibitor at the dose of 20 mg/kg, p.o. used as standard [20, 55].

Hepatoprotective Activity: In this study Carbon tetrachloride (CCl_4) used as hepatotoxicants to induce hepato toxicity in female albino Wistar rats. In this study, the animals were also pretreated with test extract before inducing liver damage with CCl_4. Hepatoprotective activity of methanolic extract of *Kydia calycina* at doses of 250 and 500 mg/kg was evaluated. The toxic group which received 1 ml/kg (50% CCl_4 in olive oil) oral alone exhibited a significant increase in serum alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphate (ALP) and total bilirubin (TB) levels. It also exhibited a significant ($P < 0.001$) decrease in serum total protein (TP) and albumin (ALB) levels. The groups that received pre-treatment of *Kydia calycina* leaves extract at a dose of 250 and 500 mg/kg per oral showed reduced levels of the ALT, AST, ALP, and TB effects were compared with the standard drug (Silymarin 50 mg/kg) [56, 65, 66].

Hypoglycemic Activity: As a paste of Dried bark powder (5 gm), with a few drops of honey. The whole paste is taken at early morning in an empty stomach to reduce blood glucose concentration [67]. The grinded fruit, bark and root of Ficus is mixed with the grinded bark of *Kydia kalycina*, grinded leaves of *Bridelia scandens*, grinded bark and root of *Bombax ceiba*, bark and root of Syzygium tamilnadensis, grind together with required quantity of water and taken internally to reduce blood sugar lavel [68].

The bark of *Kydia calycina* mixes with fruit, bark and leaves of athi, leaves of Nenthravalli, bark & root of poolamaram & Njaval. Then the required quantity of water grind & Mix together. The drink is anti-diabetic. Exact mechanism of action is still unknown as experiments on anti-diabetic activity still not reported by earlier workers [41, 69].

Anti-cancer Activity: In this study *in-vitro* cytotoxicity of four different fractions of K. calycina such as toluene fraction (KT), ethyl acetate fraction (KE), butanone fraction (KB) and aqueous residue (KAq) were evaluated against three different cancer cell cultures, such as human cervical carcinoma (HeLa), human breast cancer

(MCF-7) and human neuroblastoma (IMR-32) cells using MTT assay, which is based on the reduction of MTT at different concentrations (10, 30, 100, 300 and 500 µg/ml). After 48 h of treatment, KE and KB fractions exhibited a higher inhibitory effect against all tumor cells, with varying efficiencies and selectivities, while others caused marginal cell inhibition. Among the four fractions, the KE and KB fractions have revealed that greater percentage inhibition in all types of cancer cells in a dose-dependent manner. Moreover, the KE fraction has shown superior cytotoxicity than KB fraction. The IC_{50} values of KE fraction were found to be 38.35, 40.47, and 36.83 µg/mL against HeLa, MCF-7, and IMR-32, respectively.69, 70

Antibacterial Activity: Result of this study indicate that the Methanolic extract of *Kydia calycina* shows significant antibacterial activity at various concentrations as 20, 40, 80, and 160 mg/ml. Methanol, Ethyl acetate, and Hexane soluble fractions were also tested at the same concentrations. According to the results, it was observed that hexane and ethyl acetate fraction showed prominent activity, whereas methanol soluble fraction showed moderate antibacterial activity. At the concentrations of 20 and 40 mg/ml, the hexane and ethyl acetate soluble fractions showed a significant inhibitory effect against *Basillus megaterium*, *Staphylococcus aureus*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa* and *Proteus vulgaris* moderately against *Streptococcus pneumonia*, *Bacillus subtilis*, and *E. coli*. Whereas at the concentration of 40 mg/ml, methanol soluble fraction showed significant activity against *Streptococcus pneumonia*, *Bacillus megaterium*, *Pseudomonas aeruginosa*, and *Proteus. vulgaris* when compared with the standard drug Rifampacine [71, 72].

Anti-cariogenic Activity: In this study, estimation of four major elements *viz.*, calcium, magnesium, sodium and potassium, and seven minor elements *viz.*, iron, manganese, zinc, copper, chromium-nickel, and lithium in microwave digested flower specimens was carried out. Flowers of *Kydia calycina* was found to contain a high quantity of most of the elements estimated. Among major elements, the content of potassium was highest, followed by calcium, magnesium, and sodium. Among the minor elements estimated, the content of iron and chromium was high and low, respectively. The inhibitory effect or Anti Cariogenic action of flowers chloroform extract against cariogenic bacteria was tested against 4 isolates of *Streptococcus mutans* (Sm-01 to Sm-04), which were recovered previously from carious teeth by Agar well diffusion assay. The zone of inhibition formed around the well was taken as positive for antibacterial activity. All the 4 isolates were found to be susceptible to chloroform extract of *Kydia calycina* with a zone of inhibition ranging from 1.3 to 3.3 cm [61, 73].

Free Radical Scavenging Activity: This property of *Kydia calycina* use to treat various disorders such as liver cirrhosis, cancer, aging, arthritis, diabetes *etc*. DPPH used to evaluate the free radical scavenging activity of *Kydia calycina*. The mean IC_{50} values for DPPH radical with hydroalcoholic extract, hexane, ethyl acetate, and methanol soluble fractions of *Kydia calycina* were found to be 73.5, 36.0, 23.0 and 25.9., with ascorbic acid was found to be 15.8 ug. Superoxide scavenging activity of the plant extract was determined by McCord and Fridocich method. The IC_{50} values for superoxide radical with hydroalcoholic extract, hexane, ethyl acetate, methanol soluble fractions of *Kydia calycina* and ascorbic acid were found to be 30.2, 21.6, 18.7, 25.9 µg and 14.4 µg. Ascorbic acid was used as the standard in both study [64, 74].

Anti-fungal Activity: In this study extract of three plant flowers *Calycopteris floribunda*, *Humboldtia brunonis* and *Kydia calycina* used for the study of antifungal activity. The effect of aqueous extracts of flowers against two pathogenic fungi *F. oxysporum* and *P. aphanidermatum* isolated from soft rot specimens of ginger was determined by using a poisoned food technique. The flower extracts have shown inhibition of mycelia growth of test fungi. The diameters of fungal colonies on poisoned plates were lesser than that of the diameter of fungal colonies on control plates, which indicated the presence of antifungal principles in the extracts of all plants [75].

Anthelmintic Activity: Leaves extract of *Kydia calycina* plant revealed anthelmintic activity using earthworms *Pheretima posthumain* in a dose-dependent manner and gave the shortest time of paralysis (TTP) and death (TTD) with 100

mg/ml concentration. The combination of (KC Aqueous + KC Methanol) extracts caused fast paralysis of worm followed by death at 4.47 ± 0.23 min and 10.14 ± 1.02 min at 100 mg/ml concentration, respectively. All the extract gave significant anthelmintic activity when compared with control ($p<0.001$). In this present study, albendazole was used as standard drug [76].

CONCLUSION: The research for alternate remedies (from the plant kingdom) for various disorders will continue all over the world as the various disease showing many challenges not only to the physician but also to the researcher. The present review reveals that different parts of *Kydia calycina* are being used traditionally to treat Diabetes, body swellings, skin diseases, body pains, arthritis, hepatoprotective, analgesic, and anti-inflammatory, febrifuge and to treat liver disorders. The drug has been studied for different pharmacological actions and found to possess antioxidant activity, antifungal, anti-leukemic activity, anti-inflammatory activity, and analgesic activity with good convincing results. No acute or chronic toxicity has been reported. But still, studies on various traditional uses are lacking.

The present review would further help for the renaissance of other pharmacological activities on the plant and can also give a lead to take clinical studies based on present reported activities.

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