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Pharmacological activities of wild turmeric (*Curcuma aromatica* Salisb): a review

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Abstract
Wild Turmeric (*Curcuma aromatica* Salisb.) is extensively used as an aromatic medicinal cosmetic in India. The plant has been in traditional use and in Ayurvedic literature it is mentioned as a remedy for various diseases related to skin, cardiovascular and respiratory system. For the last few decades, research works have been done to establish the pharmacological potential of wild Turmeric and its extracts. Some of them include anti-inflammatory, wound healing, anti-melanogenic, antioxidant and free radical scavenging activity, anti-tumor, anti-cancer, anti-repellent, antitussive, anti-platelet activity and anti-nephrotoxic activity. This review gives an update mainly on the pharmacological activities of *Curcuma aromatic* Salisb. and its extracts with plausible medicinal applications.

Keywords: *Curcuma aromatica* Salisb., Wild turmeric, Vana haridra, Kasturi manjal, Musk turmeric, Yellow zeodary.

1. Introduction
Curcuma aromatica Salisb. (family: Zingiberaceae) commonly known as wild turmeric (vana haridra) or yellow zedoary is a species that stands second among the widely used curcumin species next to common turmeric (*Curcuma longa* Linn.). The plant is distributed wild throughout India and mainly cultivated in Kerala and West Bengal [1]. It has been in traditional use as an aromatic medicinal cosmetic and is also a promising drug for therapeutic purpose. *Curcuma aromatic* (CA) is also a common Chinese herb used for treating diseases with blood stasis and has been regarded as a potent anticancer herb. It is used in indigenous medicine for external applications on skin diseases, sprain, bruise, in snake poison and also to enhance complexion. Compared to *Curcuma longa* it generally has a higher level of volatile content (4-8%) and the chemical and aroma characteristics of the volatile oil of two species are also different. They can be easily differentiated with thin layer chromatography (TLC) or gas chromatography (GC) due to the presence of camphene and camphor and a high boiling alcohol in the volatile oil of CA which are absent in C. longa [2].

2. *Curcuma aromatic* Salisb.
Plants of genus Curcuma belongs to zingiberaceae/ Scitaminae family and is known for their high therapeutic potentials. *Curcuma longa* Linn. (Haridra), *Curcuma aromatica* Salisb. (Vana Haridra), *Curcuma amada* Roxb. (Amragandhi Haridra), *Curcuma angustifolia* Roxb, *Curcuma caesia* Roxb.(Kali Haridra), *Curcuma zedoaria* Rosc. (Zedoary) are known important species among the hundred species seen in different parts of the world [3]. Among them CA is the second most important species cultivated for its rhizomes. It is an annual or biennial erect herb with light yellow (internally orange) coloured rhizomes having a camphoraceous odour and is commonly known as “kasturi manjal /arishne /pasuppu” (musk turmeric) in south India. It is a time tested medicinal cosmetic and is even in practice today in India for various skin ailments and cosmetic uses.

2.1 Traditional and folk value
CA is already known in India as a tonic, carminative, as an antidote to snake bites and astringent. It is used for bruises, corn, sprains and is a well-known for enhancing complexion. Paste of rhizome with milk is used for dysentery and gastric ailments. Aqueous extracts of CA rhizomes are used for curing indigestion, rheumatism and dysentery. Apart from rhizomes, leaves are also used for healing wounds and fractured bones. CA rhizomes are also used to remove stillborn baby from the womb. Khasi and Garo tribes of Meghalaya use the paste of CA rhizomes and consume it with water to prevent helminthes infections [4].

2.2 Medicinal values
According to Ayurveda the drug is used in various kinds of diseases related to skin, cardiovascular and respiratory system. CA is used in cosmetic formulations and traditional medicinal applications as an anti-inflammatory agent, to promote blood circulation, to enhance complexion, to remove blood stasis and also for the treatment of cancer. Rhizomes are used in combination with astringents and aromatics for bruises, sprain, hiccough, bronchitis, cough, leucoderma and skin eruptions. CA rhizomes are also used in snake poison. The paste of CA rhizomes is commonly used as a domestic remedy in headache [6].

3. Chemical constituents
Alpha-curcumene (ar-curcumene), beta curcumene, d-camphor, alpha and beta-turmerone. Also other compounds like d-camphene, p-methoxycinnamic acid, germacrene D, curzerene, germacrone, alpha-andd beta-pinenes, bborneol, alpha-terpeniol, myrcene, terpinolene, gamma-terpinene, limonine, beta-thujone, alpha-copaene, alpha-bergamotene, beta-bisabolene, cuminic aldehyde, cuminyl alcohol, hydroxyisogermafurenolide, xanthorrhizol, curcuphenol, beta –elemene, zingiberene, isoborneol, linalool, beta –farnesene, 1,8-cineole, curzerenone and curcumin [5]. The constituents identified in the oil were: alpha-pinene, beta-pinene, camphene, 1,8-cineol,isofurano-germacrene, borneol, isoborneol, beta-curcumene, ar-curcumene, xanthorrhizol, germacrone, camphor, and curzerenone and the constituent in oil was found to vary from place to place [16].

4. Pharmacological actions
Traditionally used as an anti- inflammatory agent CA possesses a wide range of activities. Many studies have reported Anti –inflammatory, anti-tumor, immunological effects, wound healing, anti -fungal, anti -oxidant, anti -microbial, anti-diabetic, antiplatelet and mosquito repellent activity of wild turmeric. CA is used for preventing and treating coronary heart disease, epilepsy, as anti-allergic and in auto immune disease. The extracts of CA roots find uses for the treatment of cholecystitis, biliary calculi and other related diseases. Ethanol extract exhibited potent anti-angiogenic and pro-apoptotic effects in mice bearing Ehrlich ascites tumor cells**.** Methanol extracts of CA showed an anti-proliferative activity against human cancer cells. It also showed *in vitro* estrogenic activity. Rhizomes yield 6.1% essential oil and exhibited anti-tumor activity. Oil is also used for treatment of early stage of cervix cancer. Volatile oil exhibited in vivo inhibitory effect on proliferation of hepatoma in mice. Essential oil also exhibited *in vitro* anthelmintic activity [5]. Various other reported activities include anti-microbial and anti-tumor activities of essential oil, anti-inflammatory activity due to curcumin, anti- diabetic due to (4S,5S)-(+)-germacrone-4,5-epoxide and anti-arrhythmic activity of aqueous extract due to the presence of dipotassium magnesium dioxalate dihydrate. The oil and methanol extract showed potent radical-scavenging activities. The extracts also exhibited remarkable superoxide radical-scavenging activities. The monoterpenoids, sesquiterpenoids and curcuminoids of CA have been reported to possess antimicrobial, anti-fungal, antioxidant and antitumour activities [6]. These are described in detail in the following section.

4.1 Anti- Inflammatory activity
Aqueous and alcoholic extracts showed anti –inflammatory activity in mice. The ethanol extracts and formulations exhibited significant anti- inflammatory activity in arachidonic acid –induced ear inflammations. The resulting anti -inflammatory activity was suggested to be due to effects on several mediators and arachidonic acid metabolism involving cyclo-oxygenase pathway [7]. A study was also done on Anti-inflammatory effect of the volatile oil from CA.

4.2 Wound healing activity
The powdered rhizome of CA exhibited wound healing activity in rabbits. Studies also showed significant wound healing activity in excision wound models, conducted to assess the wound healing activity of topical application of CA rhizome extracts and its cream formulations [7].

4.3 Anti-tumour activity
Germacrone is one of the major bioactive components of CA which has been proven to possess anti-tumor properties. In a study on the anti-proliferative effect of germacrone on human glioma cells and the molecular mechanism underlying its cytotoxicity concluded that Germacrone inhibits the proliferation of glioma cells by promoting apoptosis and inducing cell cycle arrest. It also suggested that germacrone may be a novel potent chemo preventive drug for gliomas via regulating the expression of proteins associated with apoptosis and G1 cell cycle arrest [8].
Studies were also conducted on Antitumor effect and pharmacological actions of beta-elemene isolated from the rhizome of CA**.**
As a part of study to reveal the inhibitory effects of *Curcuma aromatica* oil (CAO) on cell proliferation of hepatoma in mice, two tumor inhibitory experiments of CAO on hepatoma in mice were conducted. The inhibitory effects of CAO on proliferation of hepatoma in mice were evaluated by DNA image cytometry and immune-histochemical staining of proliferating cell nuclear antigen (PCNA). The resultant tumor inhibitory rates of CAO were 52% and 51% in two experiments, respectively. Compared with those of the saline-treated control groups, both differences were statistically significant ($P < 0.01$). The study concluded that the inhibition of CAO on the growth of hepatoma in mice might be associated with its depression on cellular proliferative activity [18].

4.4 Anticancer activity
A study was conducted to evaluate the anticancer effects of aqueous extract of *Curcuma aromatica* (AECA) and related molecular mechanisms of CA in human colon carcinoma LS-174-T cell line with wild-type p53 used as a model cell. AECA inhibited LS-174-T cell proliferation in a dose- and time-dependent manner and colony formation in a dose-dependent manner. This study suggested that AECA might be effective as an anti-proliferative herb for colon carcinoma [9].

4.5 Repellent activity
CA was selected for investigation of mosquito repellent activity under laboratory and field conditions**.** In a laboratory study, a 95% ethanol extract of CA extract showed repellency against *Ae. togoi* with ED50 and ED95 values of 0.061 and 1.55 mg/cm2, respectively. It also provided biting protection for 3.5 h when applied at a concentration of 25 g%. The ethanolic extract of CA was therefore chosen for further repellent activity under field conditions, where it had a protective effect against Armigeres subalbatus, Culex

quinquefasciatus, and Cx. tritaeniorhynchus. The ethanol-extracted CA did not cause dermal irritation when applied to human skin. No adverse effects on human volunteers were observed 2 months after application. Therefore, it concluded that CA extract can be applied as an effective personal protective measure against mosquito bites [17].

In a study on Chemical composition and anti-mosquito potential of rhizome extract and volatile oil derived from *Curcuma aromatica* against Aedes aegypti (Diptera: Culicidae), Crude rhizome extracts and volatile oils of *Curcuma aromatica* were evaluated for anti-mosquito potential, including larvicidal, adulticidal, and repellent activities against the Aedes aegypti mosquito. Results proved that volatile oil of CA possessed a significantly higher larvicidal activity against the 4th instar larvae of Aedes aegypti than that of hexane extracts, with LC50 values of 36.30 and 57.15 ppm, respectively [16].

4.6 Anti-platelet activity

Compounds isolated from CA and other drugs were evaluated for their ability to inhibit arachidonic acid- (AA), collagen- and ADP-induced platelet aggregation in human whole blood. An antiplatelet activity of the compounds was measured *in vitro* by the Chrono Log whole blood aggregometer using an electrical impedance method. Among the compounds tested, curcumin from CA and others showed strong inhibition on platelet aggregation induced by AA with IC (50) values of less than 84 microM. Curcumin from CA was the most effective antiplatelet compound as it inhibited AA-, collagen- and ADP-induced platelet aggregation with IC(50) values of 37.5, 60.9 and 45.7 microM, respectively [15].

4.7 Antitussive activity

Ethanolic extract of rhizomes of *Curcuma aromatica* was investigated for its antitussive effect on Sulfur dioxide induced cough model in mice. The results suggested that the extract exhibited significant antitussive activity in a dose dependent manner [14].

4.8 Free radical scavenging and antioxidant activity

In a study, methanol aqueous extracts of 100 plants were screened for anti-oxidative activity using Fenton's reagent/ethyl linoleate system and for free radical scavenging activity using the 1,1-diphenyl-2-picryl hydrazyl free radical generating system. The results suggest that *Curcuma aromatica* may be potential sources of anti-oxidants [13].

The chemical composition of hydro-distilled essential oil from leaves of CA was analysed. Twenty-three compounds representing 94.29% of the total oil was identified. The antioxidant activities of the oil and various extracts of C. aromatica were evaluated by using 2,2-diphenyl-1-picrylhydrazyl (DPPH) and superoxide radical-scavenging assays. The oil and methanol extract showed potent DPPH radical-scavenging activities, which were higher than butylated hydroxyanisole. The extracts also exhibited remarkable superoxide radical-scavenging activities and the activity in the methanol extract was superior to all other extracts. The results indicate that the oil and extracts of CA could serve as an important bio-resource of antioxidants for using in the food industries [10].

4.9 Antimelanogenic activity

Antimelanogenic effects of CA extracts were investigated by assessing tyrosinase activity, tyrosinase mRNA levels, and melanin content in human melanoma cells exposed to Ultraviolet A (UVA) irradiation which is said to be the main cause for melanogenesis which in turn is associated with melanoma skin cancer and hyperpigmentation. Protection against melanogenesis were examined by evaluating the inhibitory effects on UVA-induced cellular oxidative stress and modulation of antioxidant defenses including antioxidant enzymes, catalase (CAT) and glutathione peroxidase (GPx), and intracellular glutathione (GSH). Study demonstrated that UVA mediated melanin productions were suppressed by CA extracts at non-cytotoxic concentration. The extract showed protection against UVA-induced cellular oxidant formation and depletion of CAT and GPx activities and GSH content in a dose-dependent manner. This study also suggested that Inhibition of cellular oxidative stress and improving antioxidant defenses might be the mechanisms by which the extracts showed protective effects on UVA-dependent melanogenesis [12].

4.10 Anti-nephrotoxic activity

The protective effects of *Curcuma aromatica* leaf extract were studied on nephrotoxicity induced by arsenic trioxide in rats and the results revealed that CA leaf extract has a potential to modulate the renal dysfunction caused by arsenic trioxide [11].

5. Conclusion

It can be concluded that *Curcuma aromatica* is a medicinal plant with a wide range of biological activities which can be used for the preparation of various formulations for the treatment of inflammation, wound and microbial infections alone or associated with conditions like diabetes, tumor and cancerous growth. Pharmacological potentials proven through the present researches revalidate the traditional and Ayurvedic concept of wild turmeric as a potent herb in diseases related to skin, cardiovascular and respiratory system. The oil and extract of *Curcuma aromatica* also serve as an important bio-resource of antioxidants for using in the food industries. Moreover, it is a promising herb in the cosmetic industry with years of traditional practice updated with anti- melanogenic, anti-oxidative and free radical scavenging profile added with anti-inflammatory and anti -tumor activity. Hence it provides a wide area for research into the detail pharmacological actions of this drug which has not been explored much compared to its utility.

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