



Plants in traditional medicine with special reference to *Cyperus rotundus* L.: a review

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Abstract

The nutgrass, *Cyperus rotundus* L. (Family: Cyperaceae), is a colonial, perennial herb considered to have originated in India 2000 years ago and widely used in Ayurveda to treat several ailments. In addition to its prehistoric uses, it is used in several systems of medicine for treating variety of diseases. The synergistic actions of the *Cyperus*' compounds have added advantage over that of a single constituent. In the past decade, numerous studies proved analgesic, anti-allergic, anti-arthritic, anti-candida, anti-cariogenic, anti-convulsant, anti-diarrheal, anti-emetic, anti-helminthic, anti-histamine, anti-hyperglycemic, anti-hypertensive, anti-inflammatory, anti-malarial, anti-obesity, antioxidant, anti-platelet, anti-pyretic, anti-ulcer, anti-viral, cardioprotective, cytoprotective, cytotoxic, gastroprotective, hepatoprotective, neuroprotective, ovidical, and larvicidal, wound healing and inhibition of brain Na⁺ K⁺ ATPase activities of *C. rotundus* and its chemical constituents. However, the exact the mechanism of action is not very clear and requires further evaluation. These properties strongly suggest an extensive use of *C. rotundus* for clinical applications. In this review, we attempted to provide information about the pharmacological effects of *Cyperus* and its proposed mechanisms of actions.

Keywords Ayurveda · Nutgrass · Pharmacological activity · Secondary metabolites · Traditional medicine

Abbreviations

WHO World Health Organization
C. rotundus L. *Cyperus rotundus* L
bw Body weight

Introduction

Traditional medicine as defined by WHO refers to the complementary/alternative/non-conventional/indigenous medicine that is developed based on the theories, beliefs

and experiences innate to different cultures, whether interpretable or not, used to maintain health, as well as prevent, attenuate or cure physical and mental illnesses (WHO 2000). Out of the 7.5 billion world's population, 4.5 billion of them use traditional medicines for primary healthcare. India's population being equivalent to 17.84% of the total world population, around 0.93 billion Indians still use traditional medicines for maintaining primary health (Cordell 2002; Usha et al. 2018). These medicines are not only used by the rural masses in developing countries but are also used by urban masses in developed countries for their primary health care where modern medicines predominates (Ballabh and Chaurasia 2007). Medicinal plants are the back bone of traditional system used in Indian system called Ayurveda.

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Traditional system of medicines in India

Indian subcontinent is the largest storehouse of medicinal plants due to its diverse climatic and soil conditions, with 15 Agro-climatic zones (Supplementary Fig. 1) and 17,000–18,000 species of flowering plants of which 6000–7000 have been estimated to have medicinal usage in folk and documented traditional systems of medicine,

like Ayurveda, Siddha, Unani and Homoeopathy (Table 1). About 960 species of medicinal plants have been estimated to be in trade commerce of which 178 species have annual utilization levels of more than 100 metric tons (<http://www.nmpb.nic.in/>).

Plants in traditional medicine

Medicinal plants are the potential source of various secondary metabolites, which are critical for their existence and also to defend the plants from fungi, bacteria, animals and even other plants. These metabolites serve as pharmaceuticals, cosmetics, nutraceuticals, food additives, flavors and industrially important biochemicals. Many modern medicines are derived indirectly from medicinal plants. The current search for biologically active principles from plants has all the more enhanced the importance of medicinal plants (Middha et al. 2013; Usha et al. 2017).

One or more countries use notably 122 chemical substances derived from 94 plant species as an important drug (Farnsworth et al. 1985). In modern Ayurvedic medicine, herbs are primarily used for treating various ailments such as diabetes, diarrhoea, dysentery, fevers, food poisoning, indigestion, intestinal parasites, nausea, and vomiting (Nadkarni 1976; Williamson 2002; Middha et al. 2013, 2016; Usha et al. 2014, 2018) 25% drugs in modern inventories are derived from plants while many others are synthetic analogs built on prototype compounds isolated from plants (Ramawat 2007) (Supplementary Table I).

Cyperus rotundus L

Cyperus rotundus L, also known as purple nutsedge or nutgrass or java grass, belongs to the sedge family, Cyperaceae. It is the third largest family of monocotyledonous plants (Govaerts and David 2007). It is a colonial, perennial herb, 7–40 cm tall with fibrous roots and reproduces largely by rhizome and tubers. Rhizomes may grow in any direction in the soil. Those growing upward produces

shoot and roots. The rhizomes that are growing downwards or horizontally form individual tubers or chains of tubers. Mature individual tubers are dark reddish-brown, about 12 mm thick and vary from 10 to 35 mm long. The leaves are dark green, shiny, narrow and grass-like ranging in size from 5 to 12 mm wide to 50 cm long. The upright culms or stems support a much-branched inflorescence with bisexual flowers with three stamens and a pistil bearing three stigmas. Nutlets are rarely produced (http://Plants.usda.gov/plant_guide/pdf/pg.cyro.pdf). It is a widely used plant in traditional medicine around the world for treatment of various diseases as tabulated in Table 2. It is deemed with infinite medicinal properties authenticated by the scientific committee (Singh et al. 2012; Peerzada et al. 2015; Lydia and Sudarsanam 2014).

Therapeutic applications of *Cyperus rotundus* L

Cyperus rotundus (Ayurvedic name: Nagarmotha) is considered to have originated in India 2000 years ago and regarded as one of the best Ayurvedic herb. Studies indicated that the rhizomes of *C. rotundus* are used as traditional folk medicine for the treatment of stomach and bowel disorders and inflammatory diseases in Asian countries (Gupta et al. 1971; Seo et al. 2001; Dang et al. 2011). Clinical trials and animal research support the use of the plant as an analgesic, anti-arthritic, antibacterial, anti-cancer, anti-candida, anti-convulsant, anti-diabetic, anti-emetic, anti-histaminic, anti-inflammatory, anti-malarial, anti-obesity, anti-pyretic, anti-spastic, gastroprotective, hypotensive, sedative, and tranquilizing agent as tabulated in Table 1 (Lydia and Sudarsanam 2014; Peerzada et al. 2015; Singh et al. 2012). Studies on the ethnobotanical use of *C. rotundus* showed that the rhizomes were used to treat aging, apoptosis, atherosclerosis, cancer, cystitis, epilepsy, genotoxicity, hirutism, nociception and prostatitis disorders (Peerzada et al. 2015). It is reported that the tuber part of *C. rotundus* is used for the treatment of dysmenorrheal and menstrual irregularities from ancient times (Yu et al. 2004; Zeid et al. 2008). Chyawanprash and Ashokarishta, which are well-known ayurvedic formulas has *Cyperus* as one of the ingredients. External application of rhizome extract of *C. rotundus* is found to improve lactation and also relieve inflammation, itching and milk duct clogs. The 25th chapter of sutrasthana of *Charaka samhita* has mentioned *C. rotundus* as the best among all herbs in causing astringent effect. It is an excellent herb used as absorbent, digestive and carminative (<https://easyayurveda.com/2013/11/11/charak-samhita-sutrasthana-4-shad-virechana-shatahriteeya-adhyaya/>).

Table 1 Proportionate use of plants in different Indian system of medicine (<http://www.medicinalplants.in/aboutfrlhtdb>)

Traditional system of medicine	No. of plants used
Ayurveda	2559
Siddha	2267
Unani	1049
Homeopathy	460
Sowa Rigpa	671
Folk	6403

Table 2 Pharmacological activity of *Cyperus rotundus* Linn

Sl. no.	Plant part used	Solvent used for extraction	Pharmacological activity	References
1.	Rhizome	Ethanol Acetone	Anti-oxidant property	Pal and Dutta (2006) Kamala et al. (2018)
2.	Rhizome	Ethanol	Wound healing activity	Puratchikody et al. (2006)
3.	Rhizome	Ethanol	Anti-pyretic activity	Gupta et al. (1971)
4.	Tuber	Ethanol/ether/distilled water	Anti-inflammatory activity	Chithran et al. (2012)
5.	Rhizome	Methanol/petroleum ether/ethyl acetate	Anti-diarrheal activity	Uddin et al. (2006)
	Tuber	Water		Daswani et al. (2011)
6.	Rhizome	Hydro-ethanol	Anti-hyperglycemic activity	Raut and Gaikwad (2012) Tran et al. (2014)
7.	Rhizome	Ethanol	Anti-microbial activity	Sharma and Singh (2011)
8.	Rhizome	Ethanol	Anti-convulsant activity	Shivakumar et al. (2009)
9.	Tuber	Water	Anti-obesity activity	Athesh et al. (2014)
10.		Ethanol	Anti-platelet activity	Seo et al. (2011)
11.	Rhizome	–	Anti-ulcer activity	Mohammad et al. (2012)
12.	Essential oil	–	Analgesic activity	Biradar et al. (2010)
13.		Methanol	Anti-helmintic activity	Kasala et al. (2016)
14.	Rhizome	Methanol	Gastroprotective activity	Muhammet et al. (2010)
15.	Tubers-essential oil	–	Ovicidal and larvicidal effect	Kempraj and Bhat (2008)
16.	Rhizome	–	Anti-histamine activity	Sangeetha et al. (2014)
17.	Rhizome	Ethyl acetate	Hepatoprotective activity	Suresh Kumar and Mishra (2005)
18.	Rhizome	Ethanol	Anti-allergic activity	Jin et al. (2011)
19.	Tuber	Methanol	Anti-malarial activity	Weenen et al. (1990)
	Tuber	–		Thebtaranonth et al. (1995)
20.	Rhizome	Methanol	Cardioprotective and anti-hyperlipidemic	Jahan et al. (2012)
	Rhizome	Hydro-alcohol		Kumar et al. (2014)
21.	Rhizome	Ethanol	Cytoprotective effect	Zhu et al. (1997)
22.	Tuber	Ethanol	Hypotensive activity	Mansoor et al. (2013)
23.	Essential oil	–	Anti-arthritic activity	Biradar et al. (2010)
24.	Tuber	Water	Anti-emetic activity	Shinde et al. (1988)
25.	Rhizome		Neuroprotective effect	Kumar et al. (2013)
26.	Rhizome	Hexane	Inhibition of brain Na ⁺ K ⁺ ATPase activity	Ngamrojanavanish et al. (2006)
27.	Rhizome	Methanol	Cytotoxic effect	Kilani et al. (2008) Mannarreddy et al. (2017)
28.	Rhizome-essential oil	Ethanol	Anti-candida activity	Duarte et al. (2005)
29.	Rhizome	Hydro-alcohol	Anti-viral activity	Soltan and Zaki (2009)
30.	Tuber	–	Anti-cariogenic property	Yu et al. (2007)

Chemical constituents

The major chemical constituents as reported by Zhou and Yin (2012) in the rhizome of *C. rotundus* are α -cyperolone, β -cyperone, ρ -cymol, calcium, camphene, copaene, cyperene, cyperenone, cyperol, cyperolone, caryophyllene, cyperotundone, D-copadiene, D-epoxyguaiene, isocyperol, isokobusone, kobusone, limonene, linoleic-acid, linolenic-acid, mustakone, myristic acid, oleanolic acid, oleic acid, β -pinene, patchoulone, rotundene, rotundenol, rotundone,

α -rotunol, β -rotunol, β -selinene, selinatriene, sitosterol, stearic acid, sugeonol, and sugetriol.

Earlier studies on phytochemical constituents of *C. rotundus* revealed the presence of alkaloids, flavonoids, glycosides, phenols, tannins, steroids, starch and many novel sesquiterpenoids (Harborne et al. 1982; Umerie and Ezeuzo 2000; Kapadia et al. 1967; Trivedi et al. 1984; Sivapalan and Jeyadevan 2012). Sesquiterpene hydrocarbons such as cypera-2,4(15)-diene, isorotundene, norrotundene and the oxygenated compound cyperadione were isolated and

identified by Sonwa and König (2001). Tsoyi et al. (2011), reported the anti-inflammatory activity of sesquiterpenes such as nootkatone and valencene isolated from the rhizome of *C. rotundus*.

Kumar and Khanum (2013) and Kumar et al. (2013) explored the anti-apoptotic activity of *C. rotundus* using SH-SY5Y human neuroblastoma cells. 10,12-Peroxy-calamenene, an endoperoxide sesquiterpene, from the tubers of *C. rotundus* exhibit a strong anti-malarial activity (Thebtaranonth et al. 1995). Analysis of the active constituents of *C. rotundus* by GC-MS shows the presence of cyperene (Chen et al. 2011). Lydia and Sudarsanam

(2014) investigated the antidiabetic potential of a particular compound, 15-hydroxy-4-oxo-10-pentadecynoic acid lactone obtained by GC-MS study using in silico approach. In their recent study, Kamala et al. (2018) reported 1(2)-acetyl-3(5)-styryl-5(3)-methylthiopyrazole, a novel compound in *C. rotundus* (Fig. 1).

Kakarla et al. (2016) reported in their studies of hexane, chloroform and methanol extracts of 2 varieties of *Cyperus* such as *C. scariosus* and *C. rotundus* and reported 12 compounds such as stigmasterol, β -sitosterol, lupeol, gallic acid, quercetin, β -amyrin, oleanolic acid, β -amyrin acetate, 4-hydroxy butyl cinnamate, 4-hydroxy cinnamic acid (Seo

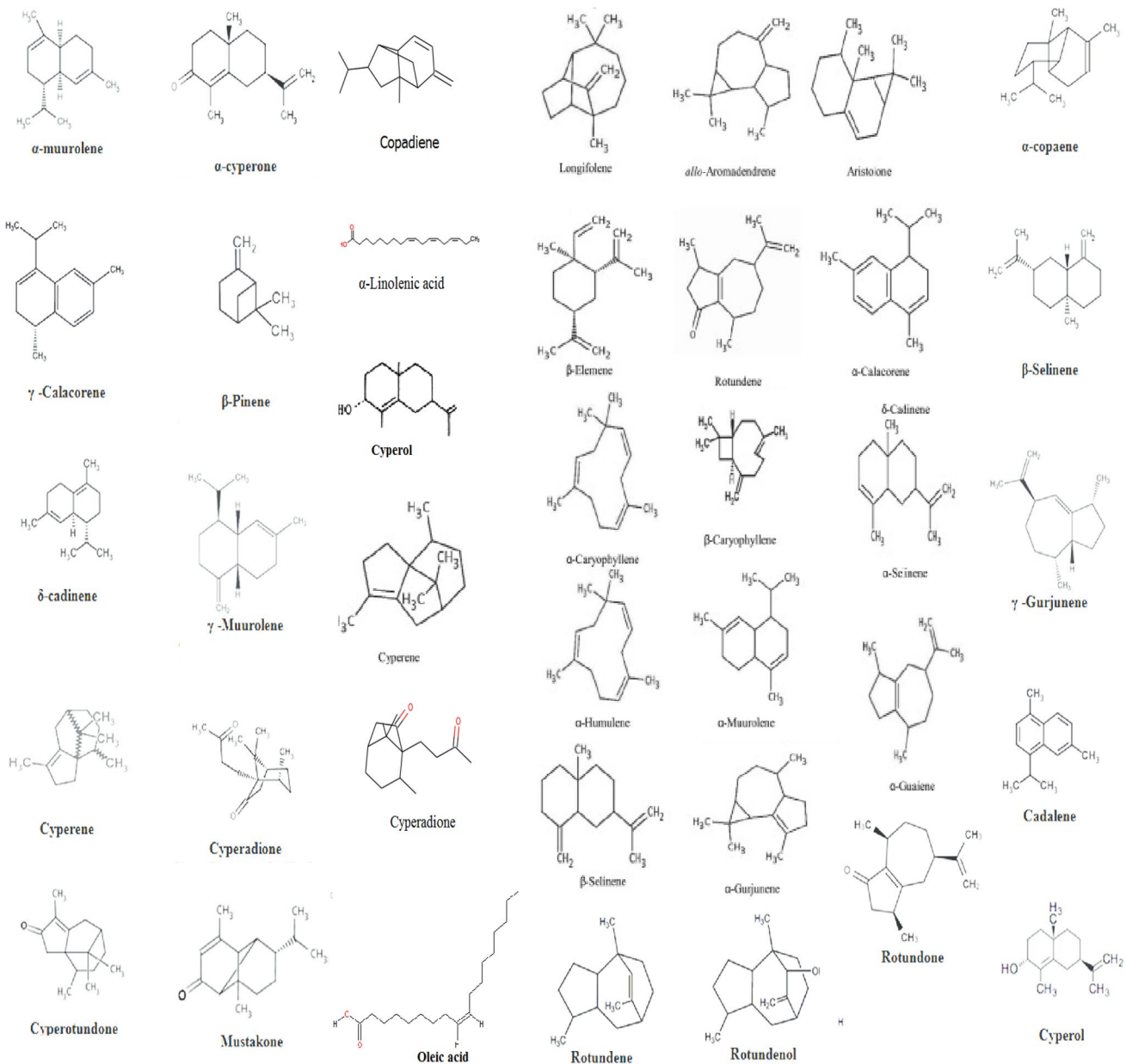


Fig. 1 Compounds in rhizomes of *C. rotundus*

et al. 2011; Lydia and Sudarsanam 2014) caffeic acid, and kaempferol (Fig. 1).

Pharmacological activities

Anti-oxidant property

In vitro anti-oxidant activity of ethanolic extract of *C. rotundus* rhizome was evaluated by Pal and Dutta (2006) through non-enzymatic hemoglobin glycosylation method. The measure of degree of hemoglobin glycosylation inhibition directly accounts for the anti-oxidant potential since haemoglycosylation being an oxidation reaction and anti-oxidant will inhibit the reaction. The anti-oxidant potential of the plant extract may be due to its high content of polyphenols, flavonoids, ascorbic acid, and other active principles. Our lab indicated 70% acetone extract possesses the best anti-oxidant activity when compared with other solvent extracts based on their polarity (Kamala et al. 2018).

Wound healing activity

An ethanolic rhizome extract of *C. rotundus* was examined by Puratchikody et al. (2006) for wound healing activity in three different rat models: the excision, the incision and dead space wound model and compared the wound healing activity with standard drug nitro furazone ointment (0.2% w/w NFZ). The extract was applied in the form of ointment. The recovery from wound was monitored through wound contractibility, time of wound closure and tensile strength 100% wound closure was observed on day 18 with 2% w/w of ethanolic extract of *C. rotundus*. It was found to have relatively more wound healing activity as compared to the standard NFZ. From the results obtained, it is suggested that the ethanolic extract of *C. rotundus* can serve as a potential source as natural wound healing agent which may be due to the presence of active terpenes, flavonol glycosides and β -sitosterol in tuber part of *C. rotundus* and this may be effective in reducing tissue swelling and oozing of tissue fluids accompanying inflammation revealed a positive healing profile.

Anti-pyretic activity

Gupta et al. 1971, reported significantly ($p < 0.001$) high anti-pyretic activity of 95% alcoholic extract of *C. rotundus* against pyrexia induced in albino rats through injection of suspension of dried Brewer's yeast in gum acacia in normal saline subcutaneously. Anti-pyretic effect of extract was found to be similar to acetyl salicylic acid when used on the same animal model.

Anti-inflammatory activity

The anti-inflammatory activity of *C. rotundus* tuber extract in carrageenan induced paw edema in albino wistar rats was evaluated by Chithran et al. (2012). The experiment was carried out in eight groups with six rats in each group. Paw edema was induced by injecting 1% carrageenan to all the rats and the paw volume was measured at regular time intervals after the administration of different solvent (ether, distilled water and ethanol) extract of *C. rotundus*. The results were compared with group administered with indomethacin standard and control group with 1% tween 80. Maximum % inhibition of paw edema was observed in the ethanolic extract which was similar to that of standard anti-inflammatory drug indomethacin, indicated that *C. rotundus* has anti-inflammatory activity.

Anti-diarrheal activity

Uddin et al. (2006), demonstrated anti-diarrheal activity of the methanolic, petroleum ether and ethyl acetate extract of *C. rotundus* rhizome in castor oil induced diarrhoea in mice. Among the orally given fractions at the doses of 250 and 500 mg/kg, 250 mg/kg of methanolic and petroleum ether fraction showed significant activity, the former being more active as compared to the control. Anti-diarrheal activity was not exhibited by ethyl acetate fraction.

The anti-diarrheal activity was also studied using the decoction of *C. rotundus* tubers by Daswani et al. (2011) on enteropathogenic *Escherichia coli*, enteroinvasive *E. coli* and *Shigella flexneri*. The anti-diarrheal activity was evaluated by the adherence of these pathogens to HEP-2 cells by measuring the effect on colonization. The bacterial adherence and invasion to HEP-2 cells were reduced by the decoction. The decoction also affected the production of cholera toxin and action of heat labile toxin. The anti-diarrheal action was found to be exerted by mechanisms other than direct killing of pathogens as decoction of *C. rotundus* does not have marked anti-microbial activity.

Anti-hyperglycemic activity

Anti-hyperglycemic activity of different fractions (chloroform, ethyl acetate, acetone and methanol) of hydro-ethanol extract of *C. rotundus* on the alloxan monohydrate (120 mg/kg) induced diabetes in Sprague–Dawley rats was screened by Raut and Gaikwad (2012). The anti-hyperglycemic activity can be attributed to its anti-oxidant activity due to high content of polyphenols.

Tran et al. (2014), isolated four compounds a new (2RS,3SR)-3,4',5,6,7,8-hexahydroxyflavane, together with three known stilbene dimers cassigarol E, scirpusin A and B from *C. rotundus* and investigated for their inhibitory

activity against α -glucosidase and α -amylase, enzymes involved in carbohydrate metabolism. The α -glucosidase activity was inhibited by cassigarol E, scirpusin A and B, whereas α -amylase activity was inhibited by (2RS,3SR)-3,4',5,6,7,8-hexahydroxyflavane and cassigarol E. All four compounds exhibited significant DPPH radical scavenging activity. This showed that the isolated compounds have marked anti-hyperglycemic effect.

Anti-microbial activity

Sharma and Singh (2011) evaluated the anti-microbial activity of *C. rotundus* rhizomes extracts against six pathogenic microbes viz. *Aspergillus niger*, *Bacillus cereus*, *Candida albicans*, *E. coli*, *Pseudomonas aeruginosa* and *Staphylococcus epidermidis*. The finely powdered rhizome of *C. rotundus* was successively extracted through soxhlation using petroleum ether, chloroform, ethanol, and water. The ethanolic extract showed highest anti-bacterial activity. However, the extracts did not exhibit any anti-fungal activity. Gentamicin and amphotericin were used as standard. The inhibitory effect was found to be similar to that of standard used.

Anti-convulsant activity

Rhizome of *C. rotundus* was evaluated for its anti-convulsant activity by Shivakumar et al. (2009), in albino rats against maximal electroshock (MES) and pentylenetetrazole (PTZ) induced tonic seizures. The ethanolic extract was assessed for anti-convulsant activity by calculating the period of tonic flexion, tonic extensor, clonus, stupor and recovery phase in rats. The oral administration of ethanol extract (100 mg/kg) reduced hind limb extension and duration of convulsion significantly, ($p < 0.001$). The result was comparable to standard drug phenytoin (25 mg/kg, i.p.) and diazepam (4 mg/kg, i.p.), respectively. The anti-convulsant effect can be accredited to the high flavonoids present in *C. rotundus*.

Anti-obesity activity

Anti-obesity potential of the aqueous tuber extract of *C. rotundus* was evaluated by Athesh et al. (2014), in high fat cafeteria diet fed obese albino rats. The rats were divided into six groups: group I served as normal control, group II served as disease control, group III, IV, and V served as test which received 100, 200 and 300 mg/kg bw respectively dose of aqueous extract of *C. rotundus* along with high fat cafeteria diet, group VI served as standard. Orlistat (50 mg/kg bw) was used as standard. The high fat cafeteria diet administered for 40 days to experimental groups induced obesity. While treatment with aqueous extract showed a significant weight reduction activity.

Anti-platelet activity

Anti-platelet activity of ethanolic extract of *C. rotundus* was reported by Seo et al. (2011). The extract and eight of its constituent compounds were examined for their effect on platelet aggregations in vitro, ex vivo, and bleeding time. Sprague–Dawley (SD) rats were used for platelet aggregation assay and ICR mice were used for tail bleeding time study. In vitro study on platelet aggregation showed significant and concentration based inhibitory effects on collagen, thrombin and arachidonic acid induced platelet aggregation. (+)-nootkatone was found to have the most potent inhibitory effect out of the eight constituents on rat platelet aggregation both ex vivo and in vitro. In addition both the *C. rotundus* extract and (+)-Nootkatone increased the bleeding time of mice. Hence, *C. rotundus* extract and its active component (+)-nootkatone can be used for the prevention of platelet-linked cardiovascular diseases.

Anti-ulcer activity

Mohammad et al. (2012) studied the anti-ulcer activity of rhizome powder of *C. rotundus*. The experiment was carried out on two different animal models. Gastric ulcer was induced in guinea pigs by administration of histamine (50 mg base i.p.) and albino rats were administered with aspirin (500 mg/kg orally) to develop ulcer. The rhizome powder of *C. rotundus* was given orally 45 min prior to histamine and 1 h prior to aspirin administration. In both cases, *C. rotundus* showed significant decrease in the ulcer index and was comparable to that of reference ranitidine. The anti-ulcer activity of *C. rotundus* can be attributed to its significant anti-oxidant activity.

Analgesic activity

Analgesic activity of *C. rotundus* essential oil was evaluated by Biradar et al. (2010). Swiss albino rats were injected with 0.05 ml of 2.5% formalin in the sub plantar of right hind paw to induce pain 30 min after the oral administration of essential oils (250, 500 mg/kg), indomethacin (10 mg/kg) and 1% CMC. After the injection of formalin the number of licks of the injected paw which symbolize pain is counted from 0 to 5 min (phase I) and 15–30 min (phase II) that corresponds to the neurogenic and inflammatory response respectively. Essential oils of *C. rotundus* were found to inhibit both neurogenic and inflammatory pain at higher dose, whereas at lower dose only inflammatory pain was inhibited. This shows that essential oils of *C. rotundus* have analgesic activity.

Anti-helmintic activity

Kasala et al. (2016) studied the anti-helmintic activity of *C. rotundus* methanolic extract on Indian earthworm *Pheretima posthuma* at two different concentrations (20 and 50 mg/ml). Albendazole was used as a standard. Anti-helmintic activity was judged by noting the time required for paralysis and death of the earthworms. Methanolic extract of *C. rotundus* showed significant anti-helmintic activity at concentration of 50 mg/ml and the result was comparable to that of standard.

Gastroprotective activity

The gastroprotective effect of methanolic rhizome extract of *C. rotundus* was studied by Muhammet et al. (2010). Damage of gastric mucosa was induced by ischemia and reperfusion in male wistar albino rats. The extract was given at the dose of 100 and 200 mg/kg of *C. rotundus*. The rats treated with the extracts were subjected to 30-min ischemia followed by 60-min reperfusion. The mean ulcer index of *C. rotundus* extract treated albino rats were significantly lower ($p < 0.05$) than that of control rats. The increased anti-oxidant activity of GSH-Px and decreased MDA levels were found in the *C. rotundus* rhizome extract treated rats when compared to the decreased anti-oxidant activity of GSH-Px and increased MDA levels in untreated rats. The results showed that the *C. rotundus* extract has a profound gastroprotective effect against the gastric mucosal damage.

Ovicidal and larvicidal effect

Kempraj and Bhat (2008), reported the ovicidal and larvicidal effect of essential oils of *C. rotundus*. Studies were carried out on eggs and larvae of *Aedes albopictus* (Skuse). The eggs and fourth instar larvae were exposed to the essential oil of varying concentration from 5 to 150 ppm for 24 h. The half maximum effective concentration (EC 50) value of < 5 ppm and lethal dose (LD50) value of < 20 ppm of essential oil indicated the effective ovicidal and larvicidal activity of *C. rotundus*.

Anti-histamine activity

Sangeetha et al. (2014), checked the anti-histamine activity of Amritha sanjeevi kuligai, a poly herbal formulation which has *C. rotundus* rhizome as one of the ingredient using male albino rats. The rats were divided into four groups with six animals in each group. 0.1 ml of histamine was injected to the hind paw for all rats. Group I served as negative control without any drug treatment, group II served as standard, was administered with standard phenyl butazone (100 mg/kg) through oral route. Group III and IV served as test which received 200 mg/kg body weight and 400 mg/kg body

weight of the herbal formulation, respectively. The increase in paw volume after the induction of oedema was estimated at regular time intervals of 0–240 min. Plethysmometer was used for the measurement of swelling. The decreased paw volume in rats reflected the anti-histaminic activity of the herbal formulation.

Hepatoprotective activity

Studies on hepatoprotective activity of ethyl acetate rhizome extract of *C. rotundus* against carbon tetrachloride-induced hepatotoxicity in rats was carried out by Suresh Kumar and Mishra (2005). The study was evaluated by measuring the levels of aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatases (ALP) and total bilirubin. Oral dose of 100 mg/kg was showed remarkable defensive effect. Further, the assay was supported by histopathological examination.

Anti-allergic

Jin et al. (2011), isolated sesquiterpene derivatives (valencene, nootkatone, and caryophyllene α -oxide), monoterpene derivatives (β -pinene, 1,8-cineole, and limonene) and 4-cymene from the 70% ethanolic extract of rhizome of *C. rotundus* and evaluated their anti-allergic activity both in vitro and in vivo. Out of the various constituents of the extract, Valencene strongly inhibited 5-lipoxygenase (5-LOX)-catalyzed leukotrienes (LTs) production in RBL-1 cells, β -hexosaminidase release by antigen-stimulated RBL-2H3 cells at a dose of 300 μ g/ml. The degranulation of β -hexosaminidase was inhibited by inhibiting the initial activation reaction, Lyn phosphorylation, in immunoglobulin E stimulated RBL-2H3. Picryl chloride-induced delayed type hypersensitivity reaction in mice was significantly inhibited by valencene and nootkatone when administered orally at 50–300 mg/kg. This showed that sesquiterpenes isolated from *C. rotundus* rhizome, but not monoterpenes contribute to prevent the allergic reaction in mice.

Anti-malarial activity

Weenen et al. (1990) isolated pure compounds from the tubers of *C. rotundus*, the root bark of *Zanthoxylum gillettii*, and the root bark of *Margaritaria discoidea* to demonstrate the anti-malarial activity. The most active compounds to exhibit strong anti-malarial activity were alpha-cyperone from *C. rotundus*, N-isobutyldeca-2,4-dienamide from *Z. gillettii* and securinine from *M. discoidea*. β -selinene autoxidation products obtained from *C. rotundus* was found to be the most potential anti-malarial substance.

Activity-guided investigation of *C. rotundus* tubers by Thebtaranonth et al. (1995), led to the isolation of sesquiterpenes such as patchoulone, caryophyllene alpha-oxide, 10,12-peroxycalamenene and 4,7-dimethyl-1-tetralone. These compounds exhibited anti-malarial activity. The strongest effect was seen in 10,12-peroxycalamenene with EC50 at 2.33×10^{-6} M.

Anti-plasmodial potential of *C. rotundus* was studied by Kaushik et al. (2013). Ethyl acetate extract of *C. rotundus* was used to assay the growth inhibition of asexual erythrocytic stages of chloroquine (CQ)-sensitive (3D7) and (CQ)-resistant (INDO) strains of *P. falciparum* in culture. The assay was carried out using fluorescence-based SYBR Green I. *C. rotundus* ethyl acetate extract showed very good (IC 50 < 10–10 µg/mL) anti-plasmodial activity.

Cardioprotective and anti-hyperlipidemic

Jahan et al. (2012) reported the cardioprotective and anti-hyperlipidemic action of methanolic extract of *C. rotundus* rhizome. Male albino rabbits were used for the experiment. The animals were divided into eight groups. Myocardial infarction was induced in rabbits using 85 mg/kg bw Iso-protorenol (ISO). Group I served as normal control, group II ISO (85 mg/kg bw) control, group III, IV and V were orally fed with 100, 150, 200 mg/kg bw of *C. rotundus* for 21 days, respectively. Group VI, VII and VIII were pretreated with 100, 150, 200 mg/kg bw of *C. rotundus*, respectively, for 21 days and injected with ISO for 2 successive days. Anti-oxidant enzymes, serum lipid and cardiac marker enzymes were assessed. Significant depletion in ISO induced elevated levels of serum lipid and cardiac marker enzymes and restoration of anti-oxidant enzyme levels which was decreased due to ISO injection were observed. This showed that *C. rotundus* rhizome extract can be used as therapeutic agent in treating myocardial infarction and high serum lipid levels. Hydro-alcoholic extract of rhizome of *C. rotundus* is effective in preventing oxidative stress, protecting DNA from H₂O₂ induced damage and also exhibits acetylcholine esterase inhibitory activity and anxiolytic effect (Kumar et al. 2014).

Cytoprotective effect

Assessment of *C. rotundus* rhizome extract by Zhu et al. (1997), for its cytoprotective effect against gastric damage induced by ethanol revealed dose dependent ulcer inhibitory effect. The decoction of rhizome (1.25, 2.5, 4.0 g/kg bw) was given to rats orally 30 min before the administration of ethanol. Inhibitory activity was also found when the decoction of rhizome was injected subcutaneously (0.3–0.6 g/kg bw) suggesting the systemic effect. Gastric motility was significantly delayed in ethanol treated rats when compared to

control group. The gastric protective action of *C. rotundus* reduced significantly in rats pretreated with indomethacin (5 mg/kg bw).

Hypotensive activity

Antihypertensive activity of *C. rotundus* aqueous extract was studied by Mansoor et al. (2013), on Sprague–Dawley rats. Significant fall in the mean arterial blood pressure was observed in rats administered with 3 mg/kg bw of aqueous *C. rotundus* extract.

Anti-arthritic activity

Biradar et al. (2010), reported the anti-arthritic activity of essential oils of *Cyperus* species in male wistar albino rats. Group I served as Arthritis control, group II as standard treated with Diclofenac sodium, group III and IV were treated with 250, 500 mg, respectively, with *Cyperus esculentus* essential oil and group V and VI treated with essential oil of *C. rotundus* respectively with 250 and 500 mg/kg. Arthritis was induced by injecting 0.1 ml formaldehyde 2% v/v in normal saline to the left hind paw after measuring the basal paw volume using plethysmometer. The treatment was done for 10 days with paw volume measured every day. The swelling of left hind paw was significantly reduced in rats treated with 500 mg of essential oil of *C. esculentus* and *C. rotundus* than in diclofenac treated rats. 75.54 and 76.58% inhibition in paw edema was exhibited by *C. rotundus* and *C. esculentus* respectively on 10th day when compared to 81.37% inhibition shown in diclofenac treated rats on 21st day. This shows that essential oils of *Cyperus* species possess anti-arthritic activity.

Anti-emetic activity

Anti-emetic activity of *C. rotundus* roots was reported by Shinde et al. (1988). The pigeons weighing between 200 and 300 g were divided into 4 groups of 10 birds in each group. Group I was treated with 0.5 mg/kg, im reserpine, group II treated with reserpine 30 min after receiving 4 mg/kg, im of triflupromazine, group III treated with 80 mg/kg, im *C. rotundus* followed by reserpine after 45 min and group IV administered with 80 mg/kg, im *C. rotundus* 24 h prior to reserpine treatment. The incidence and time of onset of vomiting was observed for 4 h and results were analyzed using Chi square test. It was observed that group that received anti emetic drug, triflupromazine, were completely protected against the emetic effect of reserpine, while 100% vomiting incidence was observed in group I treated with reserpine, the average time for the onset of vomiting being 63 ± 99 min. 83% birds treated with *C. rotundus* 45 min prior to reserpine were protected from the emetic effect of reserpine, whereas

group treated with *C. rotundus* 24 h prior to administration of reserpine failed to protect the birds from the emetic effect of reserpine. The study revealed that *C. rotundus* given 45 min before administration of reserpine was more effective in antagonizing the emetic effect of reserpine.

Neuroprotective effect

Kumar et al. (2013), studied the neuroprotective effect of *C. rotundus* rhizome extract on SIN-1 induced nitric oxide generation and protein nitration. 500 μ M nitric oxide donor SIN-1 (3-morpholiniosydnonimine hydrochloride). Nitric oxide generated reactive nitrosative species, such as peroxynitrite (ONOO(-)) mediate protein tyrosine nitration which causes structural changes of affected proteins and leads to their inactivation. The study revealed that pre treatment of human neuroblastoma SH-SY5Y cells with *C. rotundus* rhizome extract ameliorated the SIN-1 induced damage of mitochondrial and plasma membrane to 80 and 24% which was verified by MTT and LDH assays. Depletion of SOD and CAT enzymes activity induced by SIN-1 was also replenished by the rhizome extract of *C. rotundus* which was evidenced by immunoblot analysis. Pre-treatment with *C. rotundus* rhizome extract efficiently enhanced the SIN-1 induced apoptotic biomarkers such as bcl-2 and caspase-3 which manage the proteolytic damage of the cell. The cellular, nuclear and mitochondrial integrity damaged by peroxynitrite was restored by *C. rotundus* rhizome extract. This shows that *C. rotundus* rhizome extract through its oxidonitrosative and anti-apoptotic effect can prevent neuronal damage.

Inhibition of brain Na⁺ K⁺ ATPase activity

Ngamrojanavanish et al. (2006), studied the effect of 10 medicinal plants of Thai origin on Na⁺ K⁺ ATPase activity of rat brain and found that the hexane extract of *C. rotundus* showed strong inhibitory effect on Na⁺ K⁺ ATPase activity of rat brain.

Cytotoxic effect

In vitro cytotoxic assay using MTT (3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide) was carried out by Kilani et al. (2008), to investigate the effect of essential oils of *C. rotundus*. L1210 leukaemia cells line was used for the assay. Essential oil of *C. rotundus* was found to be very effective against L1210 leukaemia cells line which correlates with significantly increased apoptotic DNA fragmentation.

Investigation of methanolic extract of *C. rotundus* rhizome for its cytotoxic effect on different human cancer cell lines was carried out by Mannarreddy et al. (2017). IC50 of cancer cell lines of breast (MCF-7), cervical (HeLa), liver

(Hep G2), prostate (PC-3), colorectal (HT-29) and normal cell line (MCF-12A) was evaluated by MTT assay. Annexin V-Fluorescein isothiocyanate conjugate (AF) and propidium iodide (PI) stains were used to analyze apoptotic cells by flow cytometry. The methanolic extract of *C. rotundus* rhizome showed significant protection against non-cancerous cells and also anticancer activity against cancer cell lines.

Anti-candida activity

Duarte et al. (2005) screened 35 Brazilian medicinal plants for anti-candida activity. Essential oils of *C. rotundus* exhibited good anti-candida activity whereas ethanolic extract was found to be ineffective at any concentrations tested.

Anti-viral activity

Hydro-alcoholic extract of *C. rotundus* along with 41 Egyptian medicinal plants were screened for anti-viral activity by Soltan and Zaki (2009). The extract was tested on three viruses—HSV (herpes simplex-1 virus), POLIO (poliomyelitis-1 virus) and VSV (vesicular stomatitis virus). Determination of anti-viral activity was done by end point titration technique. *C. rotundus* showed virucidal activity against HSV.

Anti-cariogenic property

Yu et al. (2007), investigated the effect of *C. rotundus* tuber extract on the growth, adhesion, acid production and glucan synthesis of *Streptococcus mutans*, a causative bacteria in the formation of dental caries and plaques. Dose-dependent reduction in growth and acid production was observed. Adherence of *S. mutans* to saliva-coated hydroxyapatite beads was remarkably inhibited by the extract of *C. rotundus*. 0.50% repression of adherence and complete inhibition was observed at concentration of 0.5 mg/ml of the extract and 4 mg/ml of the extract, respectively. Glucosyltransferase activity responsible for synthesis of glucan from sucrose was more than 10% inhibited at a concentration of 2 mg/ml. Thus, the study suggests that the cariogenic activity of *S. mutans* may be inhibited by *C. rotundus* tuber extract.

Conclusion

This review attempts to gather all the published literature on *C. rotundus* and the attempts were made to focus on recently published data. *C. rotundus* rhizomes, and extracts have been used widely in the folk medicine of ancient cultures or ayurvedha for diverse medicinal properties. It is regarded as one of the best drug in Ayurveda. The information presented in the review is obtained from in vitro, in vivo and clinical trial

investigations, which has shown the pharmacological mechanisms and properties of *C. rotundus*. Most of the articles indicate that the various medicinal properties is due to presence of phytochemicals. These medicinal properties include anti-cariogenic, anti-viral activity, anti-Candida, cytotoxic effect, inhibition of Brain Na⁺ K⁺ ATPase, neuroprotective effect, anti-emetic, anti-arthritis, hypotensive, cytoprotective, cardioprotective, anti-hyperlipidemic, anti-malarial, anti-allergic, hepatoprotective, anti-histamine, ovidical and larvicidal effect, gastroprotective, anti-helminthic, analgesic, anti-ulcer anti-platelet, anti-obesity, anti-convulsant, anti-microbial, anti-hyperglycemic, anti-diarrheal, anti-inflammatory, anti-pyretic, wound healing, anti-oxidant property. Several chemical constituents have been established from different plant parts, however, the exact effects and involved mechanisms for the pharmacological effects of many of these chemicals identified and purified from *C. rotundus* remain unclear. In the present times, the use of medicinal plants has vastly increased due to their safety and efficiency in the prevention and treatment of numerous chronic diseases. The herbal plants and ayurvedic formulations are being extensively investigated worldwide. Because of its extensive pharmacological potential there is a need for further research to attain greater clarity of mechanism of action.

Compliance with ethical standards

Conflict of interest Authors declare no conflict of interest.

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