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Original Article

A REVIEW ON IMMENSE POSSIBILITIES WITH CYPERUS GENUS BOTANICALS

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Abstract- Cyperaceae is a very diverse family, Cyperus articulatus is one of them. This plant is found in wet lands areas. Roots/rhizomes of this plant has many ethno-medicinal use in various countries like Australia, India, America and some others too. C. articulatus is a very rich in many phytochemicals viz. essential oils (cyclocolorinone, mustakone, pogosterol, α-pipene, caryophyllene and α- copaene), volatile oils (Isocorimbolone, Corymbolone, Aristolone and Mandassidione), sesquiterpines (copa-3-en-2α-ol, caryophyllene oxide, humulene epoxide-II, kobusone, cyperotundone), phenolic acid, terpenoids and amino acids. It is beneficial for the betterment of various ailments such as in inflammation, malarial, helminthic infection, various bacterial infections, cancer, tuberculosis, epilepsy and other CNS activities like sedative effect, reduce motor activity and analgesic. There is no acute toxic effect on lower dose of either essential oil (EO) or of methanolic extract (ME) on mice, but at 1000-2000 mg/kg intra peritoneal (i.p.) dose of ME leads to ataxia at 1 hour after administration.

Keywords- *C. articulatus*, phytochemistry, pharmacological activities and acute toxicity.

Introduction

Natural products are an important source of new drugs for a wide range of diseases. In the latest review of natural medicines published by DJ Newman and GM Cragg of the National Institutes of Health (United States of America), they reported that 76.4% of all new drugs approved by the FDA from 1981 to 2019 (n = 1881) are natural products or natural-based components [1]. In impoverished nations, plants for medicinal purposes have been employed as an alternative to conventional medical care. Research on conventional medicine that concentrated on the characterization of these plants' antibacterial activity was validated by the discovery that numerous plant extracts and essential oils obtained from plants demonstrate biological activity both in vitro and in vivo [2].

Sedges, or Cyperaceae, are a diverse family of monocotyledons with over 3700 species spread across 70 genera. Even though it makes up more than 1% of all known species of plants, only few of its species have been chemically studied. Australia has 36 genera and roughly 530 species, with Cyperus (112 species) as one of the four being the largest [3]. The rhizomes of the tropical sedge Cyperus genus (Figure 1) are utilized as a fumigant and fragrance in West Africa. There have been some preliminary studies on the method of extraction of an essential oil using rhizomes [4].

Despite being used by some cultures for food and medicine, Cyperus spp. are primarily recognised as weeds **().**). Around the world, Cyperus spp. are primarily found in wetlands in tropical areas and serve as a source of primary productivity. This species produces more tubers, shoots, and fruits, which serve as a food source for amphibians and aquatic creatures [6]. The traditional usage of Cyperus plants as a cure for a variety of human maladies, including the treatment of stomach and intestinal disorders, as well as for diuretic medication, digestant, and lactodepurant purposes, has been documented from all over the world. Additionally, the plant extracts function as a targeted medication for the treatment of inflammatory diseases, bronchitis, blood problems, irregular menstruation, amenorrhea, diarrhoea, and dysentery [7,8].

An Old perennial grass-like plant called *Cyperus esculentus* L. is used as food item. It is commonly farmed for its edible tubers, known as tigernuts or earth almonds [9 & 10]. In numerous nations, notably India, China, Iran, and Japan, *Cyperus rotundus* rhizomes and tubers are referenced in Oriental medical literature to cure fever, stomach issues, and irregular menstruation [11,12]. *Cyperus compressu*s L., *Cyperus javanicus* Houtt., & *Cyperus monocephalus* Roxb. (*Cyperus cephalotes*) are further species of the Cyperus genus. For instance, the grass-like plant C. compressus is found all across the world's tropical and subtropical climates. The Santhal tribes of India have long treated intestinal helminthic illnesses with the pulverised roots of C. compressus in traditional medicine [13].

Table 1: Examples of traditional medical applications for a number of Cyperus species.

S. No.	Plant species	Country/region	Plant part (s)	Traditional use	Instruction	Reference
1	*C. rotundus* L.	India	Entire plant	Menstrual cycle problem	Juice of the Citrus maxima fruit (100 ml) and 30 g dried powder of C. rotundus is taken once daily for a week.	[14]
		India	Tubers	Urinary trouble-stone removal	Decoction of the plant is used.	[15&16]

India	Whole plant	Epilepsy	To cure epilepsy, a plant decoction (10 ml) and 5 ml of honey are taken orally.	[17]
India.	Roots	Cholera	To treat cholera, roots are cooked with an equal amount of mint.	[18]
India	Roots	Pimples	A paste made from roots, turmeric, and curd is applied to the face to treat acne and enhance beauty.	[18]
India	Roots	Increase lactation	To stimulate lactation, breasts are covered in root paste.	[18]
India	Tubers	Dermatitis	Dermatitis can be treated orally with a decoction made from the tuberous roots of C. rotundus and the leaves of Trichosanthesa anguina.	[19]
India	Tubers	Dysentery	For the treatment of dysentery, three doses containing the tuberous root of C. rotundus and other plants are administered orally.	[19]
India	Tubers	Indigestion disorders, stomachache	After being sun dried, 10 g of C. rotundus tuber, 10 g of Holarrhena antidysenterica stem bark, and 10 g of Zingiber officinalis were combined to create a powder. 250 ml of buttermilk and 30 g of powder are taken internally twice daily till the condition is resolved.	[20]
India	Tubers	Vaginal discharge	Tubers were mashed adding Abutilon indicum leaves and enough Cuminum cyminum seeds, and the extract was taken twice daily for three days.	[21&22]
India	Entire plant	Loss of libido in men	To extract juice, leaves from Psidium guajava, Punica granatum, and complete plants of C. rotundus are mixed together, warmed, and macerated. For three days, a half cup of the juice is consumed twice daily adding 10–15 drops of honey.	[22]
India	Tubers	Constipation	Three times a day, a half cup of the macerated tubers' juice is consumed.	[22]
India	Whole plant	Bone fracture	C. rotundus plant in its entirety and seven slices of ginger have been crushed and combined to form a paste. Fractures are treated with warmed paste.	[23]
India	Tubers	Bronchitis	Ground C. rotundus tubers, Tinospora cordifolia leaves, and Pergularia daemia fruits are used. For 30 days, take 2 spoons of a honey paste orally twice every day.	[24]
India	Bark	Malaria	200 g of rhizome from Costus speciosus, 200 g of bark from Costus rotundus, and 200 g of bark from Azadirachta indica are combined to create the decoction. For 15 days, 2-4 spoons of the decoction were to be taken after meals.	[25]
India	Tubers	Jaundice	Phyllanthus emblica fruits and fresh rhizomes with tuberous roots from C. rotundus are taken in equal amounts and ground. For 8 days, 2 spoonfuls of the paste diluted in one glass of water is	[26]

					consumed every day.	
		Rarotonga	Tubers	Sore throat	Four green coconuts' water is added to with 20 to 30 C. rotundus tubers and a small amount of crushed Pandanus tectorius bark. A portion of the mixture is consumed hot and a portion cold. The three-day course of treatment.	[27]
		North-West Himalaya	Roots	Intermittent fevers	Use is made of the decoction made from 5 g of fresh ginger and 10 g of C. rotundus roots.	[28&19]
		Tamil Nadu/India	Tubers	Snake bite	Heat up a paste made of Albizia amara leaf and root bark, Jasminum angustifolium root bark, and C. rotundus tubers before applying it topically for 10 days to affected areas.	[29]
		North-West Himalaya/India	Roots	Skin diseases	A. baccifera fresh leaves (10 g), C. rotundus roots (10 g), and fresh ginger (5 g) were burned and added to a decoction made with sesame oil.	[8]
2.	*Cyperus javanicus* Houtt.	Rarotonga	Leaves	Fractures/sprains	A. baccifera fresh leaves (10 g), C. rotundus roots (10 g), and fresh ginger (5 g) were burned and added to a decoction made with sesame oil.	[17]
		Rarotonga	Leaves	Irregular menstrual	alongside the leaves of numerous additional herbs.	[17]
3.	*Cyperus monocephalus* Roxb.	Philippines	Tubers	Dermatosis	Tuberous roots are used to make decoction.	[17]
		Tami Islands	Tubers	Ringworm	Tuber decoction made by adding lime.	[17]
4.	*Cyperus esculentus* L.	Oaxaca, Santa María Tecomavaca	Roots	Depression	Extract of the root.	[30]
5.	*Cyperus erectus* (Schumach.) Mattf. & Kük.	South Africa	—	Reduces foot swelling	For therapeutic purposes, ground plants are used.	[31]
6.	*Cyperus maculatus* Boeck.	West Africa	Tubers	Cattle worms	—	[32]
7.	*Cyperus flavescens* L.	Oaxaca, Santa María Tecomavaca	Roots	Depression	Root extracts	[30]
8.	*Cyperus mundii* (Nees) Kunth	Madagascar	—	Treatment of evacuation of the placenta, tuberculosis, and paludism	Extract of entire plant	[33]
9.	*Cyperus natalensis* Hochst.	South Africa	Roots	Treatment of gynaecology and obstetric complaints	The roots are used to make the decoction.	[34]

10.	*Cyperus latifolius* Poir.	East Africa	Roots	Tuberculosis and related ailments	The roots are used to make extract.	[35]
11.	*Cyperus kilimandscharicus* Kük.	East Africa	Roots	Various animal diseases	Roots are used to produce extract.	[36]
12.	*Cyperus sexangularis* Nees	South Africa	—	Asthma, fatigue, fever, pneumonia, and TB	—	[37]
13.	*Cyperus pedunculatus*(R.Br.) J.Kern	West Africa	Stem and leaves	Diarrhea, kidney disease, fever, pain, and inflammations	Whole plants are used to create the extract.	[38]
14.	*Cyperus compressus* L.	India	Roots	Helminthiasis	Oral administration of powdered roots.	[13]
15.	*Cyperus kyllingia* Endl.	Rarotonga	Tubers	Oral thrush	Four Aleurites moluccana inner nuts, a handful of Ficus prolixa aerial roots, and C. kyllingia tubers are crushed and then squeezed into a litre of water via a cloth.	[17]
16.	*Cyperus brevifolius* (Rottb.) Hassk.	Malaysia	Tubers	Sore legs	—	[17]
17.	*Cyperus articulatus* L.	Central Africa Republic	Tubers	Headache, migraine	Tuberous roots are used to make decoction.	[39]
18.	*Cyperus nitidus* Lam.	South Africa	Rhizomes	Respiratory and digestive disorders	The rhizomes are used to make extract.	[40]
19.	*Cyperus sexangularis* Nees	South Africa	Roots	Antimicrobial, emollient, diuretic, stimulant, anthelmintic, and analgesic treatment	The roots are used to make extract.	[41]

Figure 1: Inflorescence of one of the Cyperus species: *Cyperus compressus*.

Phytochemistry

One of the largest groups of flowering plants, the Cyperaceae is the third-largest monocot family after the Orchidaceae and Poaceae [42]. A growing number of studies have shown that the existence of various bioactive elements is what accounts for the diverse medical potentialities of the species in this family [43]**.** Other Cyperus species, including C. articulatus L., C. rotundus, and *Cyperus maculatus* Boeckeler, also contain essential oil [44]. Table 2 provides a summary of the phytochemicals found in the key six species of the Cyperus genus. The following subsections also provide a brief overview of the most prevalent phytochemicals found in the recently studied Cyperus spp.

Table 2: Various Cyperus species contain various phytochemicals.

SPECIES OF CYPERUS GENUS	PLANT PART	PHYTOCHEMICALS	REFERENCE
Cyperus *rotundus* L.	-	25,26-dihydroxy-vitamin D3, β-nootkatol, α-copaen11-ol, β-vatirenene, cis-10-nonadecenoic acid, trans-p-mentha-2,8-dienol, thiazol-4(5H)-one.5-(4-nitrobenzylidenol)-2-phenyl, Isobutyl lactate, cis-pinen-3-ol, pyranone, β-santalol, elema-1,3-dien6a-ol cis-13,16-docasadienoic acid	[45]
Cyperus articulatus L.	Thick rhizomes	α-Campholenal, , α-cyperone, cyperol, , βcopaen-4-α-ol, caryophyllene oxide, cyperotundone, thuja-2,4(10)-diene, , p-mentha-1,5-dien-8-ol, mustakone, α-corymbolol, α-pinene, , cyclocolorenone, p-cymene, corybolane, limonene, trans-pinocarveol, myrtenal	[46&47]
Cyperus esculentus L.	Rhizomes	cymene, coumaran, p-vinylguaiacol, cyprotundone, β-Pinene, cyperene, cyperotundone, vanillin	[42]
Cyperus conglomeratus Rottb.	Rhizomes	Saponins, tannins, steroids, triterpenes	[48]
Cyperus longus L.	Entire Plant	α-Caryophyllene oxide, β-caryophyllene oxide, humulene oxide, longiverbenone, β-himachalene, aristolone, irisone, viridiflorol	[49]

The essential oil recovered from C. articulatus rhizome was 0.58±0.04% (w/w), with terpenoids predominating in the composition viz, monoterpenes hold 22.88% and sesquiterpenes holds 56.47% of fractions and some diterpenes in trace amounts were reported to be procured. The most typical chemicals of the essential oil were cyclocolorenone, mustakone, pogosterol, α-pipene, caryophyllene and α- copaene [50]. Alpha-bulnesene, canedale, cyperotundone, cis-thujopsenal, 9,12-octadecanoic acid ethyl ester, 9-octadecenoic acid ethyl ester, and cholesta-3,5-diene were the main compounds identified by the phytochemical analysis of the ethanolic extract of C. articulatus. These substances made up more than 60% of the sample as a whole [51]. The n-hexane extract also has the linoleic acid [52]. Mandassidione, and isopatchoul-4(5) en-3-one were all discovered in the C. articulutus rhizomes along with a brand-new monocyclic sesquiterpenic diketone, some of the phytoconstituents isolated from C. articulatus are enlisted in table 3. Chemical and spectroscopic data were used to determine the structures [53]. Various amino acids are also detected as shown in table 4 [55]. Also some of the chemicals structures are illustrated with their respective biological activities in table 5.

Table 3: List chemical classes reported to be present in *c. articulatus* [54].

CHEMICAL CLASS	CONSTITUENTS
Sesquiterpenes	copa-3-en-2α-ol, caryophyllene oxide, humulene epoxide-II, kobusone, cyperotundone, humulene dioxide, (-)-guaia-1(10),11-dien-9-one
Phenolic acids	p-hydroxybenzoic acid and trans-p-hydroxycinnamic acid
Terpenoids	4R/5S-4-hydroxy-1,10-seco-muurol-5-ene-1.10-dione and trans-sobrerol. Stilbenes: piceatannol, trans-scirpusin B and cyperusphenol B
Volatile constituents	7-isopropenil-1,4a-dimetil-4,4a,5,6,7,8-hexahidro-2(3H)-naftalenona, Isocorimbolone, Corymbolone, Aristolone, Mandassidione, Cyperontundone, Undecan

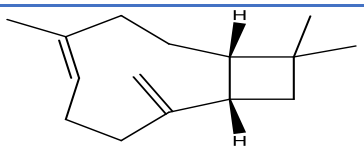
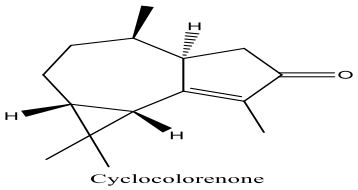
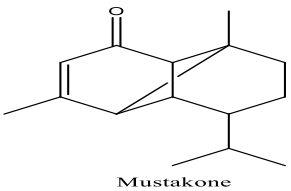
Table 4: Concentration of free various amino acids present in various extracts of *Cyperus articulatus*.

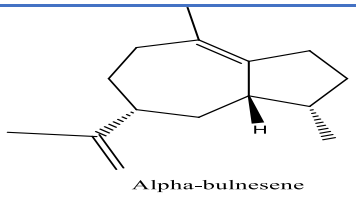
AMINO ACID	QUANTITY OF FREE AMINO ACID (NMOL)/ MG OF PLANT EXTRACT			
	METHANOLIC EXTRACT	AQUEOUS EXTRACT	ETHYL ACETATE EXTRACT	DECOCTION
Alanine	0.52	4.08	0.09	0.57
Arginine	2.10	108.41	2.71	0.13
Aspartate	5.87	76.56	2.15	1.20
Cystine	0.50	4.18	0.16	0.35
GABA	1.23	19.76	0.30	0.21

Glutamate	1.33	1.51	0.04	0.49
Glycine	0.27	1.95	0.12	0.26
Histidine	n.d.	4.00	0.07	0.21
Isoleucine	n.d.	n.d.	n.d.	0.12
Leucine	n.d.	n.d.	n.d.	0.16
Lysine	n.d.	1.68	0.05	n.d.
Methionine	n.d.	0.51	n.d.	n.d.
Phenylalanine	n.d.	n.d.	n.d.	n.d.
Proline	n.d.	n.d.	n.d.	0.17
Serine	0.34	2.65	0.12	v
Threonine	n.d.	n.d.	n.d.	0.20
Threoninol	–	–	–	0.21
Tryptophan	–	–	–	n.d.
Tyrosine	n.d.	n.d.	n.d.	n.d.
Valine	n.d.	0.74	n.d.	0.24

Nmol: nano mole, n.d.: not found and '–': not tested.

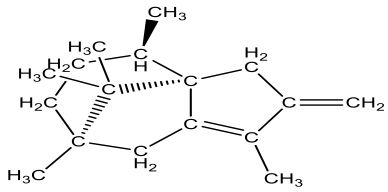
Table 5: Some common chemical structures with their biological activity.

S. NO.	CHEMICAL STRUCTURE	BIOLOGICAL ACTIVITY
1.	 Caryophyllene	Anticancer and Anti-inflammatory [56]
2.	 Cyclocolorenone	Antileishmanial [57]
3.	 Mustakone	Anti Onchocerca ochengi [52] and Anti-Plasmodic [58]

4. 

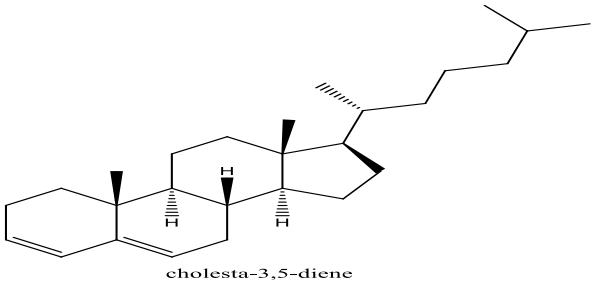
Alpha-bulnesene

PAF Receptor Inhibitor [59]

5. 

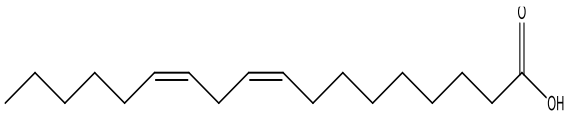
Cyperotundone

Anticancer [60]

6. 

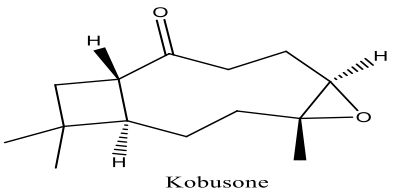
cholesta-3,5-diene

Wound Healing Effect [61]

7. 

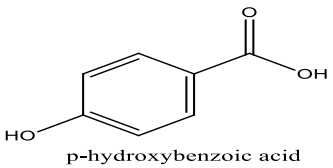
Linoleic acid

Gastroprotective [62] and Anti-tumour activity [63]

8. 

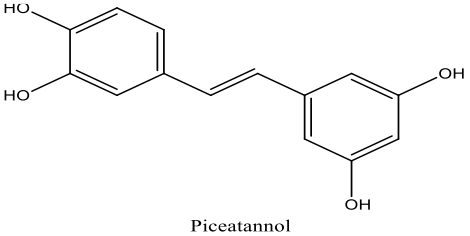
Kobusone

Anti-Diabetic agent [64]

9. 

p-hydroxybenzoic acid

Prevention and Treatment of IBD [65], Antimelanogenesis and Antioxidant [66]

10. 

Piceatannol

Anticancer [67]

PAF: Platelet activating factor, IBD: inflammatory bowel disease,

Pharmacological Activities

C. articulatus has a diverse range of activities. The anticonvulsant, antimalarial, antibacterial, antiproliferative, and antioxidant properties of rhizome essential oils are highly praised [45].

A). Haemolytic activity

The test substance was diluted in 1% DMSO and evaluated in triplicate at concentrations ranging from 1000 to 15.6 g/mL in seven sequential dilutions (1:2). Additionally, 100 µL of the 1% red blood cell suspension were added (v/v) in each well. Similar to the 0.9% saline control, the EECA did not exhibit haemolysis at the tested doses [51].

B). Anticancer

Extracts from C. rotundus have also been tested for their anticancer properties, and their mechanism of action explains how they affect the expression of genes. For instance, HeLa cell lines from people with cervical cancer showed morphological changes and variations in the extent of chromatin condensation after being exposed to various concentrations of C. rotundus extract. Additionally, a microarray study revealed that the extract increased the expression of 449 genes and decreased the expression of 484 genes, which were categorised into various interaction pathways. Gene expression induction was linked to apoptosis and arrest of the cell cycle [68].

Mateus L. N., tested the essential oil (EO) obtained from rhizomes, for cytotoxic activity against one non-cancerous cell line (MRC-5) and five cancer cell lines (HepG2, HCT116, MCF-7, HL-60, and B16-F10) adopting the Alamar blue assay. The EO showed low selectivity with a selectivity indexes (SI) below 2-fold for all cancer cells tested. The results of this screening are shown in table 6 [50].

Table 6: In vitro cytotoxicity of *Cyperus articulatus* rhizome essential oil (EO).

CELL LINE	HISTOLOGICAL TYPE	IC_{50} (95% CI) (µG/ML)		
		EO	5-FU	DOX
Non-cancerous cell				
MRC-5	Human lung fibroblast	46.0	7.5	0.2
Cancerous cells				
HepG2	Human hepatocellular carcinoma	28.5	0.2	0.03
HCT116	Human colon carcinoma	>50	0.5	0.1
MCF-7	Human breast adenocarcinoma	36.7	1.8	0.3
HL-60	Human promyelocytic leukemia	33.51	1.6	0.04
B16-F10	Mouse melanoma	39.7	0.5	0.2

The data are shown as IC50 values, in g/mL, with their corresponding 95% confidence intervals (95% CI), as determined by the Alamar blue assay after 72 hours of incubation and calculated using nonlinear regression following three independent experiments conducted in duplicate. Positive controls included the drugs 5-fluorouracil (5-FU) and doxorubicin (DOX).

The proliferation of the various cell lines was significantly reduced by the EECA of rhizomes at the applied concentrations ($p<0.0001$). There was no discernible difference between the different cell lines' inhibition of cell proliferation at the least concentration, or 0.001 g/mL of EECA. In turn, just for lineage NCI-H460 when subjected to the same concentration of extract as the HaCat cell line, there was a substantial decrease in proliferation of cells in the 0.250 and 2.5 g/mL of EECA ($p<0.0001$). There was a substantial decrease in proliferation of cells in all examined cell types (NCI-H460, U251 and MCF7) when treated with the same concentrations of extract at the highest doses tested, which equate to 25 and 250 g/mL of EECA (0.0001)) shown in table 7 [54].

Table 7: GI50 and TGI values for *c. articulatus* essential oil extracts.

Cell Lines	EECA GI_{50} Value (µg/ml)	EECA TGI Value (µg/ml)
MCF7 (human breast adenocarcinoma)	36.78	100
NCI-H460 (human lung carcinoma)	41.51	135
U251 (human tumor cell lines)	37.29	627
HaCat (human normal skin cell)	26.72	>250

TGI (concentration that resulted in complete cellular growth inhibition) and GI50 (concentration that induces 50% growth of cells inhibition or cytostatic action).

Cyperus articulatus Essential Oils (CPEOs') radical-scavenging abilities were greater than those of Chitosan Nanoparticles (CSNPs) and CPEO-CSNPs. The response was left unchecked, and after 25 hours, CPEO's scavenging activity stabilized. Even after 75 hours, the CSNPs' scavenging activity had not reached a stable state. This indicates how CSNP scavenging abilities have improved over time. The CPEO-CSNPs' strong scavenging abilities were also demonstrated by the results. approaching the conclusion of the storage time, CPEOs and free CPEOs.

It is possible to attribute this differentiation to the cooperative action of CPEOs and CPEO-CSNPs nanoparticles. When CPEOs were administered to MDA-MB-231 cells after 48 hours, the Trypan Blue Exclusion Assay demonstrated substantial toxicity (P > 0.05) when compared to CSNPs. When MDA-MB-231 cells being administered with CPEO-CSNPs, a greater cytotoxicity impact was seen (p 0.08, n = 3). The gradual release of CPEO molecules contained in the nanoparticles of chitosan is thought to be the cause of the significant cytotoxicity of CPEO-CSNPs affecting the cells. Anticancer properties of seaweeds were also studied in a study by Gutiérrez-Rodrguez et al. The production and anticancer properties of okra methanol extract were also studied by Jana et al. The study also shown a high level of toxicity to cancer cells at a high concentration of 350 g/mL extract [69].

Mechanism of action

Treatment with EO from rhizome resulted in morphological alterations linked to apoptotic cell death, including decreased cell size and/or chromatin condensation. After 24, 48, and 72 hours of incubation, the amount of intracellular DNA in HepG2 cells exposes to EO at concentrations of 12.5, 25 and 50 g/mL was also determined by flow cytometry to assess the distribution of cell cycle (phases G0/G1, S, and G2/M) and the breakdown of internucleosomal DNA (DNA that was sub-diploid dimensions [sub-G0/G1]). HepG2 cultures treated with EO showed cell cycle arrest in the G2/M phase, along with the fragmentation of internucleosomal DNA. After 24, 48, and 72 hours of incubation, the cultures injected with EO showed 24.7, 27.7, and 24.3% of cells that were in the G2/M phase in the greatest concentration, as opposed to 16.1, 10.3, and 15.4% seen for the negative control, respectively. After 72 hours of incubation, the percent of cells that had DNA fragmentation reached 22.0, 26.0, and 36.4% at doses of 12.5, 25 and 50 g/mL, respectively, compared to 9.0% for the negative control. Doxorubicin (1 g/mL) also resulted in internucleosomal DNA breakage and an arrest of the cell cycle in the G2/M phase [50].

Inhibition of Tumour Development in Genograft Model

With HepG2 cell xenografts, C.B-17 severe combined immunodeficient (SCID) mice were used to assess the in vivo anti-liver-cancer activity of EO. EO was given intraperitoneally, once daily, at dosages of 40 and 80 mg/kg for a total of 21 days. The average tumour mass weight in the EO-treated rats was 0.27 0.05 g at the lowest dose and 0.25 0.0 g at the maximum dose, compared to 0.51 0.05 g in the control group that received no treatment. The average tumour mass weight of the 5-fluorouracil (10 mg/kg) positive was 0.30 0.04 g. For EO, tumour inhibition rates ranged from 46.5 to 50.0% (p 0.05). 5-Fluorouracil resulted in a 44.2% tumour mass inhibition rate [50].

Effect on Arginase Activity in Murine Macrophages

The outcomes of this in vitro experimental model showed that the function of arginase in peritoneal macrophages triggered by LPS + IFN- (1 g/mL) was significantly decreased after treatment with EECA at doses of 12.5, 25 and 50 g/mL, (p<0.0001).

By observing that stimulation with LPS + IFN- (1 g/mL) caused an 896.7% boost in the activity values of the arginase enzyme, we were able to confirm the viability of the suggested experimental technique. The EECA treatment groups' results revealed a decrease in this activity, even at concentrations of 12.5 g/mL and 25 g/mL, where the decreases were 53.2% and 76.3%, respectively. At the highest tested concentration of 50 g/mL, the reduction in comparison to the only triggered group was 90.7% [54].

A succession of solvents with increasing polarity were used to extract the air-dried rhizomes of C. articulatus. A traditional decoction and an essential oil were also made via hydrodistillation. At their respective MTCs (maximum tolerated concentration), all extracts were tested for anti-seizure activity employing the zebrafish PTZ epilepsy model. The largest anti-seizure effects were seen with the hexane and dichloromethane extracts, which at 50 g/ml decreased PTZ-induced seizures by 93% (p<0.01) and 76%, respectively. However, dosages of 100 and 200 g/ml resulted in toxicity. Both the methanolic and the extracts made from water had a negligible effect, reducing the PTZ-induced locomotor activity by 23% and 32%, respectively, at 100 g/ml. The traditional decoction, on the other hand, exhibited no activity at any of the five concentrations examined, and the essential oil in it was discovered to be poisonous (50 to 200 g/ml). As a result, the hexane extract underwent a bioassay-guided isolation to pinpoint the substances in charge of the bioactivity [70]. With a concentration-dependent reduction in PTZ-induced seizures of up to 81% at 230 μM (p<0.0001), cyperotundone showed significant antiseizure activity. Mustakone reduced seizures by 70% at 460 μM (p<0.0001), 1,2-dehydro-α-cyperone reduced seizures by 38% at 135 μM (p<0.001), and sesquichamaenol reduced seizures by 52% at 135 μM (p<0.001). These substances were unmistakably identified by ESI-HRMS, GC-MS, and NMR [70].

Effect on Peritonial Macrophage Proliferation:

The results in percentage form demonstrate that EECA did not significantly alter the survivability of peritoneal macrophages triggered by LPS + IFN- (1 g/mL) and zymosan (1 107 particles/30 L), at doses of 12.5, 25 and 50 g/ml. The EECA-treated groups had cell viability percentages that were higher than 100%. The outcomes show that the measured EECA doses had no detrimental effects on the survival of macrophages (p<0.0001). Additionally, when exposed to the extract concentrations (EECA 25 and 50 (g/mL) + LPS + IFN- (1 g/mL)) and (EECA 50 (g/mL)), with an exception of 12.5 g/mL (p<0.0001), there is an increase in the metabolism of these cells. This is measured by the enhanced formation of formazan crystals in MTT.

We found that the applied methodology was effective in the cell viability test since the stimulus set (LPS + IFN- 1 g/mL) had a negative effect (27.8%) on the percentage of viable cells. The percentage of their viability decreased (by about 5%) in the Zymosan-treated group as well. Even in the group receiving the greatest dose of EECA, the proportion of viable cells did not significantly decline in the EECA-treated groups; the reduction was only 192% [54].

C). Anti-inflammatory Activity

In an initial screening, the NO2 inhibition properties of the resulting (petroleum ether) PE, (diethyl ether) DEE, (off-white precipitate while extraction with DEE was separated and treated as separate fraction) PRC, (ethyl acetate) EtOAc, (n-butanol) 1-BuOH, and (water)H2O fractions of methanolic extract of rhizomes were examined, release at doses of 10, 5, and 1 g mL-1 that are non-antiproliferative in LPS-stimulated J774A.1 murine macrophages. The most potent anti-inflammatory activity was found in the DEE fraction, which was chosen, along with the similarly potent PE fraction, for more traditional activity-guided isolation. In order to assess the concentration-dependent activity of the 18 sub-fractions of the DEE, (nitric oxide) NO generation, (cyclooxygenase-2) COX-2, and (inducible nitric oxide synthase) iNOS expression in LPS-stimulated macrophages were tested at less concentrations (5, 1, and 0.1 g mL1) [71].

D). Anticonvulsant Activity

In the acetic acid-induced writhing test, EECR demonstrated a dose-dependent and substantial analgesic efficacy. A dose containing 40 mg/kg administered intravenously of EECR showed a 43% protection percentage. The dose was 80 mg/kg, i.p., which caused this dose-dependent response, reached 82%. Acetyl salicylic acid (68 mg/kg, intraperitoneally), morphine sulphate (1.15 mg/kg, intraperitoneally), and paracetamol (68 mg/kg, intraperitoneally) provided 60%, 70%, and 61% protection, respectively. Additionally, it was discovered that EECR potentiated the analgesic effects of morphine and pethidine in addition to directly producing analgesia in mice [72]**.**

Cyperus articulatus water extract suppressed spontaneous epileptiform discharges generated in -Mg2+ aCSF (The Mg2+-free perfusion solution

contained (in mM): NaCl 125.3, KCl 2.2, KH2PO4 1.3, NaHCO3 24, CaCl2 2 and glucose 10) in a concentration-dependent manner. The extract decreased the rate of spontaneous epileptiform discharges by 32 9% of control at a dose of 0.5 mg/ml, but a dose of 2.2 mg/ml of the same extract resulted in a 6 minute after perfusion began, the entire block of spontaneous occurrences was completed. The extract also decreased the frequency of post-discharges per epileptiform discharge. 80±10% fewer post-discharges occurred at 0.5 mg/ml of concentration of the extract [73].

The impact of *Cyperus articulatus* water extract on AMPA-induced depolarizations is inconsistent. The AMPA-induced responses were not significantly inhibited by *Cyperus articulatus*. On the other hand, the *Cyperus articulatus* extract dramatically inhibited NMDA-induced depolarizations on the same wedge. The opposition depended on concentration. From 37.5±17.6% at a dose of 0.3 mg/ml to 83.75.8% at a dose of 3 mg/ml, NMDA gradually increased the amount of inhibition it could elicit [73].

These criteria, which were similar to those in the diazepam group in terms of the anticonvulsant effect, included start of seizures, period of seizures, score, and frequency of seizures (P<0.01). Treatment with Diazepam (1 mg/kg, i.p.) and C. articulatus (50, 150 mg/kg, p.o.) demonstrated considerable protection against PTZ-induced seizures [74].

C. articulatus demonstrated efficiency for the dose of 150 mg/kg comparable to diazepam (P 0.01; Dunnett's Test) in the biochemical assessment measured by spectrophotometry on GABA level, and lower at the dose of 300 mg/kg. MDA levels were reduced in all groups that received treatment from C. articulatus, and the effectiveness of the 150 mg/kg and 300 mg/kg doses was comparable to that of diazepam and the control group (P 0.01; Dunnett's Test) [74].

The NMDA antagonist CGP 37849 was given in a dose of 3 mg/kg i.p. to counteract the turning behaviour brought on by NMDA (75 mg/kg). Additionally, the ME stopped mice from turning. This impact was dose-dependent; at doses of 500, 1000, and 2000 mg/kg i.p., respectively, 20%, 60%, and 90% of the animals did not exhibit turning behaviour. The protection offered by the plant extract was superior to that offered by CGP 37849 at the highest dose. The ME also delayed the beginning of the turning behaviour in non-protected animals (control group: 1016290 s; ME 500 mg/kg: 1403283 s). The ED50 for preventing turning behaviour in animals was 875 (623- 1123) mg/kg i.p.. While not delaying the start of seizures in unprotected mice, the ME dose-dependently prevented animals against the clonic seizures brought on by PTZ. 40% of mice were protected from seizures by the ME at a dosage of 100 mg/kg intravenously. 90% of mice were protected at a dosage of 2000 mg/kg. The results demonstrate the dose-response correlation of the action of the ME with an ED50 of 306 (154- 541) mg/kg i.p. [75].

ME, given intravenously at a dose of 1000 mg/kg, prevented 54% of mice from dying during tonic seizures and STR 2.5 mg/kg, which is 69% of the efficacy of clonazepam, 3 mg/kg (78% protection). In non-protected animals, the same dose only marginally but significantly shifted the beginning of these seizures from 4.8 mm to 6.5 mm. On administration of 2000 mg/kg, the ME had no discernible impact on seizures brought on by bicuculline (BIC) and picrotoxin (PIC). The ME prevented seizures brought on by the MES. 1000 and 2000 mg/kg i.p. dosages of ME provided protection to 55% and 95% of mice, respectively. This impact was equivalent to that of the common antiepileptic medication carbamazepine (30 mg/kg). The ME had an ED50 of 1005 (797-1200) mg/kg i.p. [75].

E). Sedative Activity

Consequences for motor activity

Mice given an aqueous extract of the rhizome of *Cyperus articulatus* exhibited palpebral ptosis and were motionless and quiet. But when the auricle was mechanically stimulated, they reacted by leaping. C. articulatus considerably decreased the frequency of spontaneous movement by 43% at a dose of 2×10^{-2} g/kg. At 2 g/kg, a single oscillation per minute as opposed to 36 oscillations per minute in the untreated group, the highest reduction of 97% was seen. In the treated group, the amplitude decreased by 97% at this dose, going through 7.4 mm in the untreated group to 0.2 mm. After the extract was administered, there was a noticeable decrease in spontaneous motor activity, which persisted for the whole 25 min analysis. The voluntary motor activity was completely eliminated by the dosage of 2 g/kg [76].

Muscle relaxant activity

C. articulatus aqueous maceration extract did not significantly reduce muscular tonicity, whereas diazepam (5 mg/kg) reduced the muscle tone by 97.5% [76].

Analgesics activity

From 10 minutes before to 240 minutes after treatment, C. articulatus aqueous maceration extract (2 g/kg, i.p.) had no significant effects on the time needed to hold the tail in hot water (around 7 s) [76].

F). Anti Plasmodial Activity

In the in vitro anti plasmodial test, the EECA provided IC50 values of 1.21±0.01 for the W2 strain (chloroquine-resistant) and 1.10±0.06 for the 3D7 strain (chloroquine-sensitive) based on dose-response curves for P. falciparum culture. The EECA displayed an LC50 value of greater than 100 in the cytotoxicity test utilising the WI cell line conducted using the MTT-based colorimetric technique. P. falciparum proved that the EECA is a safe substance by showing selectivity index (SI) values > 91 for the 3D7 strain and 83 for the strain W2 in the calculation of the SI based on the proportion between the hazardous dose and its antimalarial properties [51].

With IC50s less than 2 g/ml, sesquiterpenes corymbolone and mustakone exhibit anti-plasmodial effects. In comparison to compound corymbolone, compound mus is over ten times more effective towards P. falciparum strain NF54. Since other sesquiterpenes obtained from the closely associated species *Cyperus rotundus* also exhibit this effect, the presence of the, α,β-unsaturated ketone function may have contributed to the high activity that was reported as in table 8 [58]. The aqueous aqueous extract of the same plant also has the significant anti-plasmodial activity against NF54 and ENT30 strains, with IC_{50} value of 7.87 ± 1.78 and 8.59 ± 1.89 respectively [77].

Table 8: Corymbolone, mustakone, and chloroform fractions from c. articulatus have anti-plasmodial efficacy against the NF54 and ENT30 strains of p. falciparum.

	NF54	**ENT30**
	IC 50s (µg/ml)	IC 50s (µg/ml)
ME	4.84 ± 0.56	8.59 ± 1.89
CL	2.11 ± 0.05	3. 27 ± 0.10
W	>50	>50

Corymbolone	1.07 ± 0.08	1.92 ± 0.06	
Mustakone	0.14 ± 0.03	0.25 ± 0.01	
Chloroquine phosphate	0.03 ± 0.005	0.08 ± 0.016	

ME: Methanol, W: water and CL: chloroform

G). Anti-Onchocerca Activity

Roundworms (Ascaris lumbricoides), whipworms (Trichuris trichiura), and hookworms (Ancylostoma duodenale and Nector americanus) are the most frequent causes of intestinal helminthiases. Helminthiases infections can produce symptoms such abdominal pain, diarrhoea, anaemia, and cognitive delays in children due to blood loss, even if the illness is not fatal [78].

Table 9 displays the concentrations that inhibit growth by 50% (IC50) and 100% (IC100) in O. ochengi microfilariae and adult worms, as well as the selectivity indices against monkey epithelial cells from kidneys (LLC-MK2) in secondary screens. Also displays the effects of isolated secondary metabolites (AMJ1 and linoleic acid) on O. ochengi microfilariae and adult worms, as well as monkey kidney epithelial cells (LLC-MK2) in secondary screens.

Compared to linoleic acid, AMJ1 is more effective against worms that are adults (lower IC50 values) Table 9. On adult male worms as opposed to adult female worms, both metabolites are more active [52].

Table 9: Mustakone and octadeca-9,12-dienoic acid's IC50, IC100, and selectivity indices (si) on O. ochengi microfilariae & adult worms, as well as monkey renal epithelial cells (LLC-MK2) during subsequent screens.

	AMJ1- MUSTAKONE				**LINOLEIC ACID**			
	Microfilariae	Adult male worm	Adult female worm	Monkey kidney cells (LLC-MK2)	Microfilariae	Adult male worm	Adult female worm	Monkey kidney cells (LLC-MK2)
IC_{50} (lg/ mL)	15.65	17.41	21.89	93.7	15.62	31.03	44.16	125
IC_{100} (µg/ mL)	31.25	62.5	62.5		62.5	62.5	125	
SI	5.98	5.38	4.28		8.0	4.02	2.83	

SI: selectivity index and IC_{50}: concentration at which half of the population is inhibited.

Apparently the EO was effective against adult worms and microfilariae at 500 µg/ml. After 24 hours of incubation, the oil totally inhibited microfilariae (Mfs) and adult male worm motility. After 120 hours of incubation, the oil induced a 100% suppression of adult female worm formazan production. The positive control was NYBC01, which was a gold conjugated molecule at 10 µM. In a dose-dependent way, the essential oil reduced the motility of O. ochengi Mfs along with adult male worms as well as the production of formazan by adult female worms [79].

F). Antimicrobial Activity

Numerous investigations have proven that C. rotundus extract has antibacterial properties [8&80]. Gram-positive bacteria were often found to be more susceptible to cyperus extract than Gram-negative bacteria. However, due to the wide range of microbiological evaluations, microbial families and species, the existence of saccharides, herb culture conditions, extraction procedures, etc., direct comparison of various research proved challenging [81].

The antibacterial activities of EOs against foodborne microorganisms like E. coli, S. typhimurium, and Listeria monocytogenes have been confirmed by prior investigations. CSNPs' antimicrobial mode of activity is still not fully understood, but some theories have been put forth. Most likely, the antimicrobial action is caused by modifications in cell porosity due to interactions among the electromagnetic charges upon the microbial cell wall as well as the NH2 group in CS. Leakage of intracellular electrolytes results from this interaction. According to studies, CSNP nanoparticles have a stronger antibacterial effect than the free CSNP polymer against both Gram-positive and Gram-negative microorganisms. The nanoparticle is responsible for the CSNPs' enhanced antibacterial activity. Surface area allowing for simple penetration of the bacterial cell wall and ultimately causing the bacterial death due to cell membrane disruption [69].

The pure essential oil of C. articulatus significantly decreased the growth of the S. sanguis biofilm by 63.96%. The crude oil from C. articulatus had the highest levels of antibacterial activity and biofilm inhibition shown in table 10. SEM images demonstrated a decline in biofilm generation. The results of this investigation suggest that the plants being investigated hold great promise as potential fresh sources of antibiotics [82].

Table 10: Antimicrobial activity of the crude EO and their fractions against oral pathogens (MIC/MBC/MFC – MG/ML).

Medicinal plant	**% yield fraction**	**Microorganism**								
		C. albicans CBS 562 F.		nucleatum ATCC 25586		P. gingivalis ATCC 33277		S. sanguis ATCC 10556	S. mitis ATCC 903	
		MIC	MFC	MIC	MBC	MIC	MBC	MBC	MIC	MIC	MBC
EO C. articulatus	0.50% yield	0.125	0.500	0.250	0.250	0.250	0.250	0.250	0.500	0.250	0.500

F1CA	9.20	0.250	1.000	0.250	*	0.125	0.250	*	*	0.500	*
F2CA	9.41	0.250	*	0.250	0.250	0.500	1.000	1.000	*	0.500	*
F3CA	24.51	0.250	*	0.250	0.250	0.250	1.000	0.500	1.000	0.250	0.500
F4CA	26.16	0.250	1.000	0.125	0.250	0.250	0.250	0.250	0.500	0.250	0.250

EO: essential oil, CA: C. articulatus, F1: fraction 1, F2: fraction 2, F3: fraction 3, F4: fraction 4 and *: Fungicidal/bactericidal action: MIC > 1 mg/ml.

Candida albicans is a pathogenic opportunistic microbe that is capable of infecting susceptible individuals locally and systemically, frequently harming those with immune impairments and those on protracted antibiotic therapy. However, until recently, there were no formulations for use by humans or animals based on the information currently available on plants, particularly medicinal herbs, active towards this yeast species [83]. Although *Cyperus articulatus*'s essential oils (EO) alongside bioactive fractions (BF) have been shown to have potent antibacterial activity against planktonic microbes, nothing is known about how these compounds can affect the morphology or survival of oral biofilms. We previously identified the EO/fractions having the best antibacterial activity against Candida species and Streptococcus mutans species. Although *Cyperus articulatus* essential oils (EO) alongside bioactive fractions (BF) have been shown to have potent antibacterial activity against planktonic microbes, nothing is known about how these compounds can affect the morphology or survival of oral biofilms. We previously identified the EO/fractions having the best antibacterial activity against Candida species and Streptococcus mutans species. confocal analysis to look into how these EO and BF affect the physical characteristics of S. mutans bacterial biofilms in terms of thickness, biovolume & architecture and how they impact the metabolic viability of C. albicans biofilms. There were no statistically significant differences for thickness in any of the groups compared with the untreated control in the study of complete treated S. mutans biofilms [84].

G). Anti-Tubercular Activity

The search for novel sources of lead antimycobacterial chemicals has become necessary due to the global issue posed by the increase in TB strains that are multidrug resistant. The goal of this research was to catalogue the antimycobacterial herbs Ghanaian people have historically used to cure tuberculosis. C. articulatus represents one of the 15 plant species that were identified, which were divided among 13 different genera and 13 families [85].

Acute Toxicity

Six Balb/c mice were given a limit dose of the essential oil via gavage (2000 mg/kg body weight), and the impact on the mice's mean weight was assessed. Only one of the six mice given the oil dose experienced rough fur, lost a little weight at first before gaining it back four days after receiving the extract. Every other mouse given the essential oil dose was healthy, active, and continued to gain weight. Individual cage-side inspections revealed no more anomalies. For 14 days, no mouse perished while being monitored. All of the mice in the control group, which received 2% DMSO in distilled water, gained weight steadily [79]. Mice given doses of 1000 and 2000 mg/kg i.p. of ME developed ataxia one hour after treatment. No obvious adverse effects were seen at lower doses [75].

Cyperus Species: Improving Health

Around the years, Cyperus species have been utilised in folk medicine across the world to both prevent and even treat a variety of medical conditions. The most frequently utilised and exploited species in this genus is C. rotundus [86&87), whose metabolites are currently well understood as well as its bioactive effects, which have been examined through a number of experiments [88].

It has also been suggested that C. rotundus may be used to treat neurocognitive problems. C. rotundus, Crocus sativus, and Astragalus membranaceus together the effectiveness of honey in treating a serious neurocognitive condition was examined. A double-blind clinical experiment was conducted on 60 patients who had already received a diagnosis. For three months, the intervention group had two 500 mg capsules per day from each combination. According to the findings, the combination may help to raise the cognitive and depressive scores. The preparation process, however, was not specified, and neither was the extract that was employed [89].

Conclusion and Future Perspective-

Cyperus species contains various chemicals compounds of various class viz, volatile oils, terpenoids, quinones, sesquiterpenes, etc. the various active phytochemicals include mustakone, α-cyperone, α-amyrine, trans-pinocarveol, corymbolone and many more.

From the various invitro performed assays, it has been reported that the extracts procured by the different methods of extraction have showed the significant activities towards many of the ailments such as anticancer activity (against HepG2, HCT116, MCF-7, HL-60, B16-F10, MRC-5, NCI-H460, U251, MCF7 and HaCat), the C. articulatus essential oil- chitosan nanoparticles (CPEO-CSNPs) has higher toxicity towards the cancer cells and one more advantage of this formulation is the regulated release of the CPEO. On treatment with the EO the cells of the HepG2 show morphological changes leading to the cellular death, it is very effective at G2/M phase. The DEE fraction of the extract has the high anti-inflammatory activity by inhibiting the COX-2, NO2 production and iNOS expression. The convulsion induced by chemical methods or by electro-convulsive therapy all are effectively controlled and the frequency & duration of convulsion is lowered in the in vivo estimation, also the extracts of this plant significantly sedative in nature as the reduce the motor activity in mice, show analgesic activity and also are muscle relaxant in nature.

It is also active against various microorganisms such as plasmodium (NF54 and ENT 30 cell lines), onchocerca [Microfilariae, Adult male worm, Adult female worm, Monkey kidney cells (LLC-MK2)]. The antimicrobial studies were carried out on C. albicans, CBS 562 F., nucleatum ATCC 25586, P. gingivalis ATCC 33277, S. sanguis ATCC 10556 and S. mitis ATCC 903. Also, it has anti-tubercular activity.

Detailed studies on the pharmacological efficacies of isolated substances still need to be done. Longevity of Cellular and Oxidative Medicine 11 The understanding of the fundamental cellular mechanisms of action of its bioactive extracts and/or phytochemicals has also been revealed by structure-activity investigations on the acquired phytoconstituents. On the other hand, despite toxicological data showing that Cyperus spp. use is safe and effective, there are still few conclusive research examining its clinical, toxicological, and safety aspects. Further research is required to determine the precise active ingredients because herbal combinations comprising Cyperus spp. have not been characterised in reported clinical

trials. Additionally, the researchers need to focus more on the subchronic toxicities as well as how it interacts with commonly used conventional medications to ensure a safe and long-term intake by human subjects. The last and most intriguing point to make is that additional research is required to clarify the mechanism of action of Cyperus spp. given their broad pharmacological potential.

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Conflict of Interest: None

References

1. David JM and Gordon MC. (2020) Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019 Journal of Natural Products 83, 770−803.
2. Duarte MCT, Figueria GM, Sartotatto A, Rehder VLG and Delarmelina C. (2005) Anti-candida activity of Brazilian medicinal plants Journal of Ethnopharmaclogy 97, 305–11.
3. Allan RD, Wells RJ, Correll RL and Macleod JK. (1978) The presence of quinones in the genus Cyperus as an aid to classification Phytochemistry 17, 263-66.
4. Couchman LFM, Pinder AR and Bromham NH (1964) Studies of the essential oil of Cyperus articulatus Tetrahedron 20, 2037-45.
5. Dwyer J. *Cyperus Rotundus* L. (2016) An ancient food staple but now designated the world's worst weed In Proceedings of 20th Australasian Weeds Conference 251-254.
6. Reznicek A, Kearns D, Simpson D, Tucker G, Camelbeke K, González-Elizondo M, Strong M, Goetghebeur P, Kral R, Thomas W. (2008) Cyperaceae. Encyclopedia Britannica.
7. Udari LM. (2018) Medicinal properties of Cyperus species (sedge family, Cyperaceae), 4314.
8. Peerzada AM, Ali HH, Naeem M, Latif M, Bukhari AH, Tanveer A. (2015) *Cyperus rotundus* L.: Traditional uses, phytochemistry, and pharmacological activities Journal of ethnopharmacology 174, 540-60.
9. Coşkuner Y, Ercan R, Karababa E, Nazlıcan AN. (2002) Physical and chemical properties of chufa (*Cyperus esculentus* L.) tubers grown in the Çukurova region of Turkey Journal of the Science of Food and Agriculture 82 (6), 625-31.
10. Shrestha U, Rosskopf EN, Butler DM. (2018) Effect of anaerobic soil disinfestation amendment type and C:N ratio on *Cyperus esculentus* tuber sprouting, growth and reproduction Weed Research 58 (5), 379-88.
11. Srivastava RK, Singh A, Shukla SV. (2013) Chemical investigation and pharmaceutical action of *Cyperus rotundus*- a review Journal of Biologically Active Products from Nature 3 (3), 166-72.
12. Dang GK, Parekar RR, Kamat SK, Scindia AM, Rege NN. (2011) Antiinflammatory activity of *Phyllanthus emblica*, *Plumbago zeylanica* and *Cyperus rotundus* in acute models of inflammation Phytotherapy Research 25 (6), 904-8.
13. Soren AD, Yadav AK, Dhar ED. (2020) Toxological evaluation of *Cyperus compressus* Linn., a traditionally used anthelmintic plant in India Advances in Traditional Medicine 20 (3), 367-72.
14. Bora D, Mehmud S, Das KK, Medhi H. (2016) Report on folklore medicinal plants used for female health care in Assam (India) International Journal of Herbal Medicine 4 (6), 4-13.
15. Lokendrajit N, Swapana N, Singh CD, Singh CB. (2011) Herbal folk medicines used for urinary and calculi/stone cases complaints in Manipur NeBIO 2 (3), 1-5.
16. S. P. Kumar, A. Latheef, and A. Remashree, (2014) “Ethnobotanical survey of diuretic and antilithiatic medicinal plants used by the traditional practitioners of Palakkad district,” International Journal of Herbal Medicine 2, 52–56.
17. Panda D, Rathinayak SS, Palita SK. (2015) Crop weeds and its uses in the treatment of common ailments in Koraput district of Odisha India American Journal of Biological and Pharmaceutical Research 2 (1), 20-23.
18. Qureshi R, Bhatti GR, Memon RA. (2010) Ethnomedicinal uses of herbs from northern part of Nara desert, Pakistan Pakistan Journal of Botany 42 (2), 839-51.
19. Das PK, Misra MK. (1988) Some ethnomedicinal plants of Koraput district Orissa Ancient Science of Life 8 (1), 60.
20. Rao M, Varma Y. (2014) Folklore traditional knowledge on digestive disorders of domestic animals (cattle, sheep and goats) in the Medak district, Telangana India Biolife 2 (3), 858-65.
21. Reddy KN, Trimurthulu G, Reddy CS. (2010) Medicinal plants used by ethnic people of Medak district, Andhra Pradesh Indian Journal of Traditional Knowledge 9 (1), 184-190.
22. F. I. Jahan, M. R. U. Hasan, R. Jahan et al., (2011) A comparison of medicinal plant usage by folk medicinal practitioners of two adjoining villages in Lalmonirhat district, Bangladesh American Eurasian Journal of Sustainable Agriculture 5, 46–66.
23. Shahidullah M, Al-Mujahidee M, Uddin SN, Hossan MS, Hanif A, Bari S, Rahmatullah M. (2009) Medicinal plants of the Santal tribe residing in Rajshahi district, Bangladesh American-Eurasian Journal of Sustanable Agriculture 3, 220-226.
24. Kumar D, Bhat ZA, Chashoo IA, Deoda RS, Mudgade SC, Kumar V. (2011) Bronchodilator activity in traditional medicines: gift of god kingdom Bronchitis 171.
25. Paul S, Devi N, Sarma GC. (2013) Ethnobotanical utilization of some medicinal plants by Bodo people of Manas biosphere reserve in the treatment of malaria International Research Journal of Pharmacy 4 (6), 102-5.
26. Suneetha J, Rao JK, Rao PP, Reddi TS. (2013) Ethnomedicine for jaundice by the tribals of East Godavari district, Andhra Pradesh Journal of Natural Remedies 13 (2), 142-5.
27. Holdsworth DK. (1990) Traditional medicinal plants of Rarotonga, Cook Islands part I. International Journal of Crude Drug Research 28 (3), 209-18.
28. Dangwal LR, Sharma A, Kumar N, Rana CS, Sharma U. (2010) Ethno-medico botany of some aquatic Angiospermae from North-West Himalaya Researcher 2 (4), 49-54.
29. Ayyanar M, Ignacimuthu S. (2005) Medicinal plants used by the tribals of Tirunelveli hills, Tamil Nadu to treat poisonous bites and skin diseases Indian Journal of Traditional Knowledge 4 (3), 229-236.
30. Guzmán Gutiérrez SL, Reyes Chilpa R, Bonilla Jaime H. (2014) Medicinal plants for the treatment of “nervios”, anxiety, and depression in Mexican Traditional Medicine Revista Brasileira de Farmacognosia 24, 591-608.
31. Thornton-Barnett SR. (2013) Ancestral Pharmacopeias: A Paleoethnobotanical Assessment of Plant Use in the Western Free State, South Africa.

32. Blench R, Dendo M. (2006) Dagomba plant names Cambridge, United Kingdom.

33. Razafindraibe M, Kuhlman AR, Rabarison H, Rakotoarimanana V, Rajeriarison C, Rakotoarivelo N, Randrianarivony T, Rakotoarivony F, Ludovic R, Randrianasolo A, Bussmann RW. (2013) Medicinal plants used by women from Agnalazaha littoral forest (Southeastern Madagascar) Journal of Ethnobiology and Ethnomedicine 9 (1), 1-3.

34. De Wet H, Ngubane SC. (2014) Traditional herbal remedies used by women in a rural community in northern Maputaland (South Africa) for the treatment of gynaecology and obstetric complaints South African Journal of Botany 94, 129-39.

35. Tabuti JR, Kukunda CB, Waako PJ. (2010) Medicinal plants used by traditional medicine practitioners in the treatment of tuberculosis and related ailments in Uganda Journal of ethnopharmacology 127 (1), 130-6.

36. Taheri Y, Herrera-Bravo J, Huala L, Salazar LA, Sharifi-Rad J, Akram M, Shahzad K, Melgar-Lalanne G, Baghalpour N, Tamimi K, Mahroo-Bakhtiyari J. (2020) Cyperus spp.: a review on phytochemical composition, biological activity, and health-promoting effects. Oxidative Medicine and Cellular Longevity. 2021 Sep 7;2021. Semenya SS, Maroyi A Ethnobotanical survey of plants used to treat respiratory infections and related symptoms in the Limpopo province, South Africa. Journal of Herbal Medicine, 24, 100390.

37. Rabelo AS, Oliveira ID, Guimarães AG, Quintans JS, Prata AP, Gelain DP, Venceslau EM, Santos JP, Quintans-Júnior LJ, Bonjardim LR, Barison A. (2013) Antinociceptive, anti-inflammatory and antioxidant activities of aqueous extract from Remirea maritima (Cyperaceae) Journal of Ethnopharmacology 145 (1), 11-7.

38. Shamkuwar PB, Hoshamani AH, Gonjari ID. (2012) Antispasmodic effect of *Cyperus rotundus* L. (Cyperaceae) in diarrhoea Der Pharmacia Lettre 4 (2), 522-4.

39. Moteetee A, Moffett RO, Seleteng-Kose L. (2019) A review of the ethnobotany of the Basotho of Lesotho and the Free State Province of South Africa (South Sotho). South African Journal of Botany 122, 21-56.

40. Fakhry AM, Aljedaani GS. (2020) Impact of disturbance on species diversity and composition of *Cyperus conglomeratus* plant community in southern Jeddah, Saudi Arabia Journal of King Saud University-Science 32 (1), 600-5.

41. Gugsa T, Yaya EE. (2018) Chemical constituents of the traditional skin care and fragrance nut, *Cyperus esculentus* (Tigernut) American Journal of Essential Oils and Natural Products, 6 (4), 04-12.

42. Kumar A, Niranjan A, Lehri A, Srivastava RK, Tewari SK. (2016) Effect of geographical climatic conditions on yield, chemical composition and carbon isotope composition of nagarmotha (*Cyperus scariosus* R. Br.) essential oil Journal of Essential Oil Bearing Plants 19 (2), 368-73.

43. Zhou Z, Zhang H. (2013) Phenolic and iridoid glycosides from the rhizomes of *Cyperus rotundus* L. Medicinal Chemistry Research 22, 4830-5.

44. El-Wakil EA, Morsi EA, Abel-Hady H. (2019) Phytochemical screening, antimicrobial evaluation and gc-ms analysis of *Cyperus rotundus* World J. Pharm. Pharm. Sci. 8 (9), 129-39.

45. Dikwa MA, Abdullahi UA, Sadiq SI, Yahya SA, Eghobor S, Idris A, Sa'adatu Abba Yusuf MR, Isa L. (2019) Comparative assessment of antibacterial activities of Syzygium aromaticum and *Cyperus articulatus* against Staphylococcus aureus and Escherichia coli Journal of Pharmacy & Bioresources 16 (2), 139-44.

46. Silva NC, Goncalves SF, Araújo LS, Kasper AA, Fonseca AL, Sartoratto A, Castro KC, Moraes TM, Baratto LC, Varotti FD, Barata LE. (2019) In vitro and in vivo antimalarial activity of the volatile oil of *Cyperus articulatus* (Cyperaceae) Acta Amazonica 49. 334-42.

47. Jyoti P, Hemali P, Nilam R, Sumitra C. (2018) *Cyperus conglomeratus* (Cyperaceae) a halophyte from Gujarat: Physicochemical, Phytochemical and Pharmacognostic studies The Journal of Phtopharmacology 7 (3), 334-340.

48. Memariani T, Hosseini T, Kamali H, Mohammadi A, Ghorbani M, Shakeri A, Spandidos DA, Tsatsakis AM, Shahsavand S. (2016) Evaluation of the cytotoxic effects of *Cyperus longus* extract, fractions and its essential oil on the PC3 and MCF7 cancer cell lines Oncology letters 11 (2), 1353-60.

49. Nogueria ML, Lima EJSPD, Adriao AAX, Fontes SS, Silva VR, Santos LDS, Soares MPB, Dias RB, Rocha CAG, Costa EV, Silva FMAD, Santos V, Cardozo NMD, Koolen HHF and Bezerra DP. (2020) *Cyperus articulatus* L. (Cyperaceae) rhizome essential oil causes cell cycle arrest in the G2/M Phase and cell death in HepG2 cells and inhibits the development of tumors in a xenograft model Molecules 25 (11), 2687.

50. Assis FFVD, Silva NCD, Moraes WP, Barata LES and Minervino AHH. (2020) Chemical composition and in vitro antiplasmodial activity of the ethanolic extract of *Cyperus articulatus* var. nodosus residue francisco Pathogens 9, 889.

51. Metuge JA, Babiaka SB, Mbah JA, Ntie-Kang F, Ayimele GA and Cho-Ngwa F. (2014) Anti-onchocerca metabolites from *Cyperus articulatus*: isolation, in vitro activity and in silico 'drug-likeness' Natural Products Bioprospect, 4, 243–249.

52. Nyasse B, Ghogomu TIH, Sondengam BL, Martin MT and Bodo B. (1988) Mandassidione and other sesquiterpenic ketones from *Cyperus articulatus* Phytochemistry 27 (10), 3319-3321.

53. da Silva ÉB, Barata LE, Arévalo MR, Vieira LQ, Castro W, Ruiz AL, Della Torre A, Castro KC, Sartoratto A, Baratto LC, de Santana MB. (2021) Chemical composition and antiproliferative activity of the ethanolic extract of *Cyperus articulatus* I. (Cyperaceae) Plants 10, 2084.

54. Bum EN, Lingenhoehl K, Rakotonirina A, Olpe HR, Schmutz M, Rakotonirina S. (2004) Ions and amino acid analysis of *Cyperus articulatus* L. (Cyperaceae) extracts and the effects of the latter on oocytes expressing some receptors Journal of Ethnopharmacology 95, 303-9.

55. Fidyt K, Fiedorowicz A, Strządała L and Szumny A. (2016) β-caryophyllene and β-caryophyllene oxide—natural compounds of anticancer and analgesic properties Cancer Medicine 5 (10), 3007-17.

56. Monteiro J, Passero LF, Jesus JA, Laurenti MD, Lago JH, Soares MG, Batista AN, Batista JM and Sartorelli P. (2022) Absolute configuration and antileishmanial activity of (–)-cyclocolorenone isolated from *Duguetia lanceolata* (Annonaceae) Current Topics in Medicinal Chemistry 22 (19), 1626-33.

57. Rukunga GM, Muregi FW, Omar SA, Gathirwa JW, Muthaura CN, Peter MG, Heydenreich M and Mungai GM. (2008) Anti-plasmodial activity of the extracts and two sesquiterpenes from *Cyperus articulatus* Fitoterapia 79 (3), 188-90.
58. Hsu HC, Yang WC, Tsai WJ, Chen CC, Huang HY and Tsai YC. (2006) α-Bulnesene, a novel PAF receptor antagonist isolated from pogostemon cablin Biochemical and Biophysical Research Communications 345 (3), 1033-8.
59. 60. Taheri Y, Herrera-Bravo J, Huala L, Salazar LA, Sharifi-Rad J, Akram M, Shahzad K, Melgar-Lalanne G, Baghalpour N, Tamimi K, Mahroo-Bakhtiyari J. Cyperus spp. (2021) A review on phytochemical composition, biological activity, and health-promoting effects Oxidative Medicine and Cellular Longevity 4014867.
60. Al-Hassan JM, Hinek A, Renno WM, Wang Y, Liu YF, Guan R, Wen XY, Litvack ML, Lindenmaier A, Afzal M and Paul B. (2020) Potential mechanism of dermal wound treatment with preparations from the skin gel of Arabian Gulf catfish: a unique furan fatty acid (F6) and cholesta-3, 5-diene (S5) Recruit neutrophils and fibroblasts to promote wound healing Frontiers in Pharmacology 11, 899.
61. Martins JL, Silva DM, Gomes EH, Fava SA, Carvalho MF, Macedo IY, Gil ES, Ghedini PC, Rocha FF, Silva ON and Fajemiroye JO. (2022) Evaluation of gastroprotective activity of linoleic acid on gastric ulcer in a mice model. Current Pharmaceutical Design 28 (8), 655-60.
62. Fang B, Zhang M, Tian M, Ren FZ. (2015) Self-assembled β-lactoglobulin–oleic acid and β-lactoglobulin–linoleic acid complexes with antitumor activities Journal of Dairy Science 98 (5), 2898-907.
63. Choi JW, Joo JD, In JH, Kim D, Kim Y, Choi ST, Kim JH and Jung HS. (2021) The small molecule kobusone can stimulate islet β-cell replication in vivo Journal of International Medical Research 49 (7), 1–9.
64. Han X, Li M, Sun L, Liu X, Yin Y, Hao J and Zhang W. (2022) p-Hydroxybenzoic acid ameliorates colitis by improving the mucosal barrier in a gut microbiota-dependent manner Nutrients 14 (24), 5383.
65. Shim SY, Lee YE, Song HY and Lee M. (2020) p-Hydroxybenzoic acid β-D-glucosyl ester and cimidahurinine with antimelanogenesis and antioxidant effects from Pyracantha angustifolia via bioactivity-guided fractionation Antioxidants 9 (3), 258
66. Banik K, Ranaware AM, Harsha C, Nitesh T, Girisa S, Deshpande V, Fan LU, Nalawade SP, Sethi G and Kunnumakkara AB (2020) Piceatannol: A natural stilbene for the prevention and treatment of cancer Pharmacological Research 153, 104635.
67. Lin CH, Peng SF, Chueh FS, Cheng ZY, Kuo CL, Chung JG. (2019) The ethanol crude extraction of *Cyperus Rotundus* regulates apoptosis-associated gene expression in HeLa human cervical carcinoma cells in vitro Anticancer Research 39 (7), 3697-709.
68. Kavaz D, Idris M and Onyebuchi C (2019) Physiochemical characterization, antioxidative, anticancer cells proliferation and food pathogens antibacterial activity of chitosan nanoparticles loaded with *Cyperus articulatus* rhizome essential oils. International Journal of Biological Macromolecules 123, 837-45.
69. Nguta JM, Appiah-Opong R, Nyarko AK, Yeboah-Manu D and Addo PG. (2015) Medicinal plants used to treat TB in Ghana International Journal of Mycobacteriology 4 (2), 116-23.
70. Mittas D, Mawunu M, Magliocca G, Lautenschläger T, Schwaiger S, Stuppner H, Marzocco S. (2022) Bioassay-guided isolation of anti-inflammatory constituents of the subaerial parts of *Cyperus articulatus* (Cyperaceae) Molecules 27 (18), 5937.
71. Pal D, Dutta S, Sarkar A. (2009) Evaluation of CNS activities of ethanol extract of roots and rhizomes of *Cyperus rotundus* in mice Acta Pol Pharm 66 (5), 535-41.
72. Bum EN, Rakotonirina A, Rakotonirina SV and Herrling P. (2003) Effects of *Cyperus articulatus* compared to effects of anticonvulsant compounds on the cortical wedge Journal of Ethnopharmacology 87 (1), 27-34.
73. Herrera-Calderon O, Santiváñez-Acosta R, Pari-Olarte B, Enciso-Roca E, Montes VM and Acevedo JL. (2018) Anticonvulsant effect of ethanolic extract of *Cyperus articulatus* L. leaves on pentylenetetrazol induced seizure in mice. Journal of Traditional and Complementary Medicine 8 (1), 95-9.
74. Bum EN, Schmutz M, Meyer C, Rakotonirina A, Bopelet M, Portet C, Jeker A, Rakotonirina SV, Olpe HR and Herrling P. (2001) Anticonvulsant properties of the methanolic extract of *Cyperus articulatus* (Cyperaceae) Journal of Ethnopharmacology 76 (2), 145-50.
75. Rakotonirina VS, Bum EN, Rakotonirina A and Bopelet M. (2001) Sedative properties of the decoction of the rhizome of *Cyperus articulatus* Fitoterapia 72 (1), 22-9.
76. Rukunga GM, Gathirwa JW, Omar SA, Muregi FW, Muthaura CN, Kirira PG, Mungai GM and Kofi-Tsekpo WM. (2009) Anti-plasmodial activity of the extracts of some Kenyan medicinal plants Journal of Ethnopharmacology 121 (2), 282-5.
77. ba Ndob IB, Mengome LE, Bourobou HP, Banfora YL and Bivigou F. (2016) Ethnobotanical survey of medicinal plants used as anthelmintic remedies in Gabon Journal of Ethnopharmacology 191, 360-71.
78. Metuge JA, Nyongbela KD, Mbah JA, Samje M, Fotso G, Babiaka SB and Cho-Ngwa F: Anti-Onchocerca activity and phytochemical analysis of an essential oil from *Cyperus articulatus* L. BMC Complementary and Alternative Medicine (2014), 14 (1), 1-10.
79. Khojaste M, Yazdanian M, Tahmasebi E, Shokri M, Houshmand B, Shahbazi R. (2018) Cell toxicity and inhibitory effects of *Cyperus rotundus* extract on Streptococcus mutans, Aggregatibacter actinomycetemcomitans and *Candida albicans* European Journal of Translational Myology 28 (4), 7917.
80. Haghgoo R, Mehran M, Zadeh HF, Afshari E, Zadeh NF. (2017) Comparison between antibacterial effect of chlorhexidine 0.2% and different concentrations of *Cyperus rotundus* extract: An in vitro study Journal of International Society of Preventive & Community Dentistry 7 (5), 242.
81. 33.Bersan SM, Galvão LC, Goes VF, Sartoratto A, Figueira GM, Rehder VL, Alencar SM, Duarte RM, Rosalen PL and Duarte MC. (2014) Action of essential oils from Brazilian native and exotic medicinal species on oral biofilms. BMC Complementary and Alternative Medicine 14 (1), 1-2.
82. Zhang Z, ElSohly HN, Jacob MR, Pasco DS, Walker LA and Clark AM. (2002) Natural products inhibiting Candida albicans secreted aspartic proteases from Lycopodium cernuum Journal of Natural Products 65 (7), 979-85.
83. Freires IA, Bueno-Silva B, Galvão LC, Duarte MC, Sartoratto A, Figueira GM, Alencar SM and Rosalen PL. (2015) The effect of essential oils and bioactive fractions on Streptococcus mutans and Candida albicans biofilms: A confocal analysis Evidence-Based Complementary and Alternative Medicine 871316, 9.
84. Brillatz T, Jacmin M, Queiroz EF, Marcourt L, Slacanin I, Petit C, Carrupt PA, Bum EN, Herrling P, Crawford AD and Wolfender JL. (2020) Zebrafish bioassay-guided isolation of antiseizure compounds from the Cameroonian medicinal plant *Cyperus articulatus* L. Phytomedicine 153175, 70.
85. Nuryana FI, Chozin MA, Guntoro D. (2019) High-Performance Liquid Chromatography analysis for α-cyperone and nootkatone

from the tuber of nutsedge (*Cyperus rotundus* L.) in the tropics Rasayan Journal of Chemistry 12 (1), 360-5.
86. Li F, Zhang Y, Wei X, Song C, Qiao M, and Zhang H. (2016) "Metabolic profiling of Shu-Yu capsule in rat serum based on metabolic fingerprinting analysis using HPLC-ESIMSn" Molecular Medicine Reports 4191–4204.
87. Kamala A, Middha SK, Karigar CS. (2018) Plants in traditional medicine with special reference to *Cyperus rotundus* L.: a review 3 Biotech 8, 309.
88. Akouchekian S, Omranifard V, Maracy MR, Pedram A, Zefreh AA. (2018) Efficacy of herbal combination of sedge, saffron, and astragalus honey on major neurocognitive disorder Journal of Research in Medical Sciences 23.