Medical, Therapeutic and Pharmaceutical Use of *Cyperus articulatus* L. – a Review

Inês Ribeiro Machado[1], Keila Rêgo Mendes[2], Michel Rios Arévalo[3], Aline Aparecida Munchen Kasper[3], Kelly Christina Ferreira Castro[3], Homero de Giorge Cerqueira[2], Amanda Souza Silva[3] & Lauro Euclides Soares Barata[3]

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[1] Universidade Estadual do Norte Fluminense Darcy Ribeiro/UENF, Avenida Alberto Lamego 2000, Parque Califórnia, Campos dos Goytacazes/RJ, Brasil. CEP: 28.013-600. <inesuenf@yahoo.com.br>.

[2] Instituto Chico Mendes de Conservação da Biodiversidade/ICMBio, EQSW 103/104, Bloco "B", Complexo Administrativo, Setor Sudoeste, Brasília/DF, Brasil. CEP: 70.670-350. <keilastm@hotmail.com, homero.cerqueira@icmbio.gov.br>.

[3] Universidade Federal do Oeste do Pará/UFOPA, Rua Vera Paz s/n (Unidade Tapajós), Bairro Salé, Santarém/PA, Brasil. CEP: 68.040-255. <michrios76@yahoo.com.br, aliny_@msn.com, kelly_quimica@yahoo.com.br, amanda_silvasousa@hotmail.com, lauroesbbarata@gmail.com>.

ABSTRACT – *Cyperus articulatus* L., belonging to the Cyperaceae family, is a plant species that has almost insignificant flowers at its ends. The stalks of the species produce tubers that, when cut, give off a fresh, woody and spicy smell; they are traditionally used in baths and in the manufacture of artisanal colonies in northern Brazil. In addition to use in cosmetics and perfumery, the plant also has medicinal and pharmacological properties. Among the pharmacological properties are the antimalarial, sedative, hepatoprotective, contraceptive effects on the central nervous system (CNS), insecticide, antimicrobial, anticancer, antioxidant, anticonvulsant, anthococcosis. The metabolites found related to the mentioned activities were cyperotundone, alpha-cyperone, mustacone for antimalarial activity in the chloroform extract of the priprioca rhizomes. In the decoction of rhizomes of *C. articulatus* flavonoids, saponins, sugars, triterpenes and polyuronides were found for sedative properties. Metabolites involved in hepatoprotective function, contraceptive effect and central nervous system effect were not found in the literature. The aromatic metabolites of mono- and sesquiterpenes have been related to insecticidal properties in the rhizome methanolic extract. In the ethanolic and chloroform extracts of rhizomes, the metabolites α and β-pinene were related to antimicrobial activity. The compounds sesquiterpenes and monoterpenes found in the essential oil of *C. articulatus* were related to anticancer properties. The phenolic compounds of the essential oil of *C. articulatus* were related to the antioxidant properties. The alkaloid compounds found in the extract of the rhizome of *C. articulatus* showed anticonvulsant activity. The mustakona metabolites and linoleic acid found in the rhizome extract of *C. articulatus* were directly related to the antioncocercal properties. The present work reviewed the medical, therapeutic and pharmacological properties of *Cyperus articulatus*.

Keywords: *Cyperus articulatus* activity; Cyperaceae properties, priprioca pharmacological properties; *Cyperus articulatus* medical and therapeutic activity.

Uso Médico, Terapêutico e Farmacêutico do *Cyperus articulatus* L. – uma Revisão

RESUMO – *Cyperus articulatus* L., pertencente à família Cyperaceae, é uma espécie vegetal que tem, em suas extremidades, flores, quase insignificantes. Os talos da espécie produzem tubérculos que, quando cortados, exalam um cheiro fresco, amadeirado e picante; são tradicionalmente usados em banhos e na manufatura de colônias artesanais na região norte do Brasil. Além do uso em cosméticos e perfumaria, a planta também possui propriedades medicinais e farmacológicas. Entre as propriedades farmacológicas estão os efeitos antimalárico, sedativo, hepatoprotetor, contraceptivo, no sistema

nervoso central (SNC), insecticida, antimicrobiano, anticancerígeno, antioxidante, anticonvulsante, antioncocercose. Os metabólitos encontrados relacionados às atividades mencionadas foram ciperotundona, alfa-ciperona, mustacona para atividade antimalárica no extrato de clorofórmio dos rizomas da priprioca. Na decocção dos rizomas de *C. articulatus* foram encontrados flavonóides, saponinas, açúcares, triterpenos e poliuronídeos para propriedades sedativas. Não foram encontrados na literatura metabólitos envolvidos na função hepatoprotetora, no efeito contraceptivo e no efeito do sistema nervoso central. Os metabólitos aromáticos de mono- e sesquiterpenos foram relacionados a propriedades inseticidas no extrato metanólico de rizoma. Nos extratos etanólicos e clorofórmicos dos rizomas, os metabólitos α e β-pineno estavam relacionados à atividade antimicrobiana. Os compostos sesquiterpenos e monoterpenos encontrados no óleo essencial de *C. articulatus* foram relacionados às propriedades anticâncer. Os compostos fenólicos do óleo essencial de *C. articulatus* foram relacionados às propriedades antioxidantes. Os compostos alcalóides achados no extrato do rizoma de *C. articulatus* apresentaram atividade anticonvulsivante. Os metabólitos mustakona e o ácido linoléico encontrados no extrato de rizomas de *C. articulatus* estavam diretamente relacionados às propriedades antioncocercais. O presente trabalho revisou as propriedades médicas, terapêuticas e farmacológicas de *Cyperus articulatus*.

Palavras-chave: Atividade de *Cyperus articulatus*; propriedades da Cyperaceae; propriedades farmacológicas da priprioca; atividade médica e terapêutica de *Cyperus articulatus*.

Uso Médico, Terapéutico y Farmacéutico de *Cyperus articulatus* L. – una Revisión

RESUMEN – *Cyperus articulatus* L., perteneciente a la familia Cyperaceae, es una especie vegetal que presenta flores casi insignificantes en sus extremos. Los tallos de la especie producen tubérculos que al cortarse desprenden un olor fresco, amaderado y especiado; se utilizan tradicionalmente en baños y en la fabricación de colonias artesanales en el norte de Brasil. Además de su uso en cosmética y perfumería, la planta también tiene propiedades medicinales y farmacológicas. Entre las propiedades farmacológicas se encuentran los efectos antimaláricos, sedantes, hepatoprotectores, anticonceptivos sobre el sistema nervioso central (SNC), insecticidas, antimicrobianos, anticancerígenos, antioxidantes, anticonvulsivos, antococosis. Los metabolitos encontrados relacionados con las actividades mencionadas fueron ciperotundona, alfa-ciperona, mustacona para la actividad antimalárica en el extracto clorofórmico de los rizomas de priprioca. En la decocción de rizomas de *C. articulatus* se encontraron flavonoides, saponinas, azúcares, triterpenos y poliuronidas con propiedades sedantes. Los metabolitos implicados en la función hepatoprotectora, el efecto anticonceptivo y el efecto del sistema nervioso central no se encontraron en la literatura. Los metabolitos aromáticos de mono y sesquiterpenos se han relacionado con las propiedades insecticidas en el extracto metanólico de rizoma. En los extractos etanólicos y clorofórmicos de rizomas, los metabolitos α y β-pineno estaban relacionados con la actividad antimicrobiana. Los compuestos sesquiterpenos y monoterpenos que se encuentran en el aceite esencial de *C. articulatus* estaban relacionados con propiedades anticancerígenas. Los compuestos fenólicos del aceite esencial de *C. articulatus* se relacionaron con las propiedades antioxidantes. Los compuestos alcaloides que se encuentran en el extracto del rizoma de *C. articulatus* mostraron actividad anticonvulsiva. Los metabolitos de mustakona y el ácido linoleico que se encuentran en el extracto de rizoma de *C. articulatus* estaban directamente relacionados con las propiedades antioncocercales. El presente trabajo revisó las propiedades médicas, terapéuticas y farmacológicas de *Cyperus articulatus*.

Palabras clave: Actividad de *Cyperus articulatus*; propiedades de Cyperaceae; propiedades farmacológicas de priprioca; actividad médica y terapéutica de *Cyperus articulatus*.

Introduction

Plant materials are used in whole world, such as home remedies, medicines and raw materials for the pharmaceutical industry, and represent a substantial part of the world medicine market (Sivapalan 2013).

Several species of Cyperaceae family present great importance in the local pharmacopoeia used, mainly, as contraceptive, analgesic and in the treatment of the diarrheas. In this context, we highlight the priprioca – plant of the Cyperaceae

family, whose scientific name is *Cyperus articulatus* L. – which is a species of tall grass found mainly along the rivers and tropical streams. At its end, there are sprout small flowers, almost insignificant. The stalks of this specie produce small rhizomes that, when cut, exude a fresh, woody and spicy scent, traditionally used in baths of smell and in the manufacture of artisanal colonies in the North region of Brazil, mainly in the state of Pará (Nicoli *et al*. 2006). Species of *Cyperus* genus belongs to the Cyperaceae family. Its class is Liliopsida, and it is in the Cyperales order. Cyperaceae is the third largest family in monocotyledons and comprises 104 genera and 5,000 species (Eniola *et al.* 2011). This species is grown in backyards, for its own comsuption, and in a consortium system with other crops for sale (Zoghbi *et al.* 2006).

In Brazil, *priprioca* has aroused a great and growing scientific and economic interest, thanks to the pleasant aroma of the essential oil obtained from its rhizomes. The essential oils of these species are composed mainly of sesquiterpenes belonging to the classes of cyperene, caryophyllene, eudesmane, patchoulane and rotunda (Couchman *et al.* 1964, Zoghbi *et al.* 2006). Plants derivatives containing natural products such as flavonoids, terpenoids and steroids have received considerable attention in recent years due to their diverse biological and pharmacological properties, including antioxidant and hepato-protective activity (Feuids *et al.* 2003, Banskota *et al.* 2000, Takeoka & Dao 2003). Thus, the objective of this review was to report the medicinal, therapeutic and pharmacological properties of *Cyperus articulatus* rhizomes. For this review about *C. articulatus* databases such as Google, Scielo, Periódicos Capes and CAPES thesis database were consulted, based on the plant's pharmaceutical and medicinal attributions.

Medicinal and Therapeutic Properties

The plant can cause miscarriage (Duke & Vasquez 1994), has carminative properties combating gas formation and it is also sedative (Botanical 2003). Moreover, it can be used as an analgesic, contraceptive, in the treatment of diarrhea (Zoghbi *et al.* 2003), rheumatism, swelling, ovulation problems, migraine (Ngo Bum *et al.* 1996) and in nausea cases during pregnancy (Chopra *et al.* 1969) (Table 1).

The Zapoteca Indians of Mexico use the subterranean parts in the treatment of "culture-linked syndromes." Such ´disease´ is found only in certain cultures and often corresponds to old indigenous concepts that are difficult to translate into Western medicine. It is characterized by ethnic psychoses, ethnic neuroses, hysterical, exotic or atypical psychoses and culture-reactive syndromes (Table 1). Various symptoms are observed during such disease and may vary from one patient to another. Diseases such as *dzieeb* (scare), *stu* (shame), *guelereza'ga* (fatigue), *gueleraaj'qui* (indigestion) and *blow* (flatulence) may be mentioned (Frei *et al.* 1998).

Underground parts of the plant are also used in diseases related to the bone-muscular system (rheumatism, arthritis, fractures, contusions, twisting) (Table 1). The rhizome is used as diaphoretic and stimulant, against amenorrhea, bladder affections, gastralgias (Table 1) (Peckolt & Peckolt 1890), in the malaria treatment, toothache, headache and epilepsy. In decoction form, the rhizomes are used for stomach pains, constipation, respiratory infection and against verminosis (Ngo Bum *et al*. 2001) (Table 1). In the form of powder is used in frictions in the skin as aphrodisiac, for migraine treatment, fever in children, rheumatism, edema and ovulation problems (Table 1). The dry powder is also inhaled to treat migraine (Ngo Bum *et al.* 1996). The *Sacoya* Indians of Ecuador and the *Tiriyó* and *Yanomami* Indians of Brazil use the infusion of the rhizome in fever cases, which can be drunk or placed on the head and body (Milliken & Albert 1996). The rhizome is also used among the Secoya Indians ground and mixed with water to heal 'bad wind', a psychological distress of fear; it has also used to treat flu or fever (Schultes & Raffauf 1990). Indians of America wiped the branches on their noses to avoid snoring (Duke & Vasquez 1994). In Congo, root juice is used as a febrifuge (Corrêa 1984).

As diaphoretic and stimulant the rhizome is used in infusion of 10g to 180g of boiled water, taken in the dose of some calices per day; against bladder and gastralgia in alcoholic form, prepared with a part of the fresh rhizome for 2 alcohol at 40°C, used in the dose of 20 drops a few times a day (Table 1). Against amenorrhea in an alcoholic extract form, in 1-decigram pills three times a day (Peckolt & Peckolt 1890).

C. articulatus (Cyperaceae), commonly known as *Piri piri*, is a useful Indian medicinal plant that has been credited with therapeutic properties for the treatment of various diseases such as headaches, migraines and epilepsy (Bum *et al.* 2003). The rhizomes extract has been used as carminative, antiemetic and sedative (Table 1). People in the countryside take the aqueous extract for treatment of various enteric diseases and also for physical and mental well-being (Datta *et al.* 2013).

Table 1 – Medicinal and therapeutic properties of *Cyperus articulatus*

MEDICINAL AND THERAPEUTIC PROPERTIES			
Activity	**Related metabolite**	**Part of the plant used**	**Source**
Carminative, analgesic, diarrhea, rheumatism, swelling, ovulation problems, migraine	unknown metabolite	whole plant	Botanical (2003), Zoghbi *et al.* (2003) Ngo Bum *et al.* (1996), Chopra *et al.* (1969)
Rheumatism, arthritis, fractures, contusions, twisting	unknown metabolite	subterranean parts	Peckolt & Peckolt (1890)
Ethnic psychoses, ethnic neuroses, hysterical, exotic or atypical psychoses and culture-reactive syndromes	unknown metabolite	subterranean parts	Frei *et al.* (1998)
Diaphoretic and stimulant, against amenorrhea, bladder affections, gastralgias	unknown metabolite	rhizomes	Peckolt & Peckolt (1890)
Stomach pains, constipation, respiratory infection and against verminosis	unknown metabolite	rhizomes decoction	Ngo Bum *et al.* (2001)
Aphrodisiac, for migraine treatment, fever in children, rheumatism, edema and ovulation problems	unknown metabolite	rhizomes powder	Ngo Bum *et al.* (1996)
Fever, diaphoretic and stimulant	unknown metabolite	rhizomes infusion	Peckolt & Peckolt (1890)

Pharmacological Properties

Anti-malaria and sedative properties

Cyperus articulatus contains flavonoids, polyphenols, saponins, tannins, terpenes and sugars. Many of its biological aspects are attributed to several sesquiterpenes called ciperone. The rizhomes contain a sesquiterpene, articulone ketone, which is identical to ciperone. Two of these chemicals, called cyperotundone and alpha – ciperone have been reported to have anti-malarial actions and the ability to inhibit the synthesis of nitric oxide (a pro-oxidant) (Table 2) (Rakotonirina *et al.* 2001, Ohshima *et al.* 1998).

According to Rukanga *et al.* (2008), two sesquiterpenes, corimbolones and mustacones isolated from the chloroform extract of *C. articulatus* rhizomes exhibited significant plasmodial properties (Table 2). Mustacone was approximately ten times more active than corimbolone against sensitive *Plasmodium falciparum* lineages.

The decoction of *Cyperus articulatus* rhizomes has been shown to have sedative properties in mice (Rakotonirina *et al.* 2001). Rakotonirina *et al.* (2001) demonstrated that the total extract of *C. articulatus* rhizomes does not seem to possess anesthetic or paralyzing effects. In contrast, spontaneous motor activity is significantly

reduced by the extract. These authors' observations suggest that the rhizome of *C. articulatus* has pharmacological properties similar to sedatives with metabolite as flavonoids, saponins, sugars, triterpenes and polyuronides (Table 2).

Hepatoprotective effect

Datta *et al.* (2013) studied the possible hepato-protective role of the methanolic extract of *Cyperus articulatus* rhizomes (Table 2). Sections obtained from rats poisoned with paracetamol and treated with methanolic extract from this plant showed that the cellular architecture was maintained normal in comparison to the control rats.

Contraceptive properties

Priprioca has also been traditionally used as a contraceptive. Since there are no clinical studies to support this traditional use, women seeking pregnancy should probably avoid using this plant (Raintree Nutrition 2006). This plant is used as an abortifacient, contraceptive and to induce premature labor (Ayahuasca 2004). Some other properties and actions documented by traditional users include anthelmintic, anticonvulsants, anti-epileptic, antidote and carminative (Raintree Nutrition 2006).

Eniola *et al.* (2011) investigated the effects of the aqueous extract of *Cyperus articulatus* rhizome on the follicle stimulating and luteinizing hormones, which control the reproductive functions of the ovary in rats (Table 2). The researchers concluded that the plant increases levels of luteinizing hormone (LH) which regulates ovarian functions, and also causes distortions in the cellular architecture of the pituitary gland. There must therefore be a great need for caution in the use of these herbs, especially in women who wish to become pregnant. It is used in Peru as abortive, anticonvulsive, anti-epileptic, antidote, carminative, contraceptive, hemostatic, stomach, tonic, for baldness and for childbirth (Arvigo & Balick 2004).

Effect on the central nervous system

For the treatment of epilepsy, the rhizome powder is boiled in water for 30 min and then drunk by the patient (Ngo Bum *et al.* 2001) (Table 2). Several diseases treated with *C. articulatus* are related to the nervous system. Therefore, studies were carried out to verify the interaction of the plant with this system. Studies have shown that decoction of the rhizomes has depressive activity in the central nervous system. Ngo Bum *et al.* (1996) suggested in their work that one or several components contained in the rhizome of *C. articulatus* interact with the NMDA receptor complex (N-methyl-D-aspartate), thus resulting in the anti-epileptic effect. The NMDA receptor is involved in epileptiform activity and in initiation and spread of seizures. Since NMDA receptor antagonists are known to have anti-convulsive properties *in vivo* but further experiments have to be carried out and rhizome extract has been found to have anti-convulsive properties in animals, which may explain, at least in part, its use in epilepsy (Ngo Bum *et al.* 2001).

Rakotonirina *et al.* (2001) carried out experiments and observed that the extract of the rhizome of *C. articulatus* did not show any analgesic or paralyzing effect, but it significantly reduced the spontaneous motor activity in mice, confirming the presence of pharmacological properties similar to sedatives. When compared to diazepam, it appears that the plant extract has no muscle relaxant effect and when associated with thiopental sodium or diazepam, the extract facilitated the induction of sleep and increased sleeping time without any concomitant analgesic effect.

According to Ngo Bum *et al.* (2004), extracts of *Cyperus articulatus* L. (Cyperaceae) rhizomes in Africa and Amazon have been used to treat many diseases since it has been shown to present sedative and anticonvulsant properties. The authors determined the mechanism of action of *Cyperus articulatus* extracts on *Xenopus* oocytes expressing receptors by using electrophysiological measurement. They concluded that the *Cyperus articulatus* rhizomes could contain compounds antagonistic to NMDA receptors and agonist for the $GABA_B$ receptors, thus increasing the inhibition of nervous system activity. These pharmacological properties confirm the effect of *C. articulatus* on the nervous system and justify its use in traditional medicine. The authors in our laboratory are still investigating determinations of the active compounds.

Insecticidal properties

Cyperus articulatus is traditionally used for pest control in Nigeria. In a study by Abubakar *et al.* (2000) the authors observed that the methanolic extract of the plant rhizome presented repellent action against the beetle *Tribolium casteneum* Herbst. Plants of the Cyperaceae family contains terpenoid compounds and *Cyperus rotundus* has been reported to possess the same insecticidal actions (Akatsuka *et al.* 1994) (Table 2).

Antimicrobial properties

Mongelli *et al.* (1995) in their studies observed that the decoction of *C. articulatus* completely inhibited the microorganism *Staphylococcus aureus* and partially inhibited the growth of *Pseudomonas aeruginosa*. According to Yusuf *et al.* (2012), the ethanolic and chloroform extracts of *C. articulatus* exhibited a significant antibacterial activity in all concentrations against the production of AMP_C enzyme that is responsible for antibiotic resistance to *Echerichia coli*, *K. pneumoniae* and *P. mirabilis* (Table 2). Bersan (2012), studying the antimicrobial activity of essential oils against oral pathogens, observed that *C. articulatus* inhibited the formation of *Candida albicans* biofilm in 28.08%, confirming that the essential oils have anti-Candida activity (Duarte *et al.* 2005).

According to Freires *et al.* (2015), *C. articulatus* essential oil presents compounds as α and β-pinene that inhibited yeast biofilm adherence onto a polystyrene substrate in *Candida albicans* (Table 2). In addition, Martins *et al.* (2003) reported that *C. articulatus* exerted a considerable antibacterial effect, especially on methicillin-resistant *Staphylococcus aureus* and Gram-positive and Gram-negative bacteria. The evaluation of the antimicrobial activity of *Cyperus articulatus* extracts showed antifungal activity against *Cladosporium sphaerospermum* in 333 K and 13 MPa and antibacterial activity against *Staphylococcus aureus* in 333 K - 25 MPa (Silva *et al.* 2014).

Anticancer properties

C. articulatus is a plant that has been used extensively in traditional medicine for the treatment of different diseases worldwide (Paula *et al.* 2011). *Cyperus* sp. it has activities against gram-positive and gram-negative microorganisms among these organisms are E. coli, *Klebsiella pneumonia*, *Haemophilus influenza*, *Staphylococcus aureus*, *Bacillus cereus* and *Streptococcus pyogenes* (Oladosu *et al.* 2011). In addition, the anti-malarial and anti-inflammatory activities of the essential oil have also been reported with a positive result (Oladosu *et al.* 2011). Chitosan is one of the first polysaccharides most present in nature. It comes from crustacean shells made up of N-acetyl-D-glucosamine and D-glucosamine units connected by b-(1-4) glycosidic bonds (Kavaz *et al.* 2012). Among all the numerous materials for nanoencapsulation, chitosan is widely recognized for being biodegradable, biocompatible and safe (Kavaz *et al.* 2010).

In addition to the aforementioned advantages, chitosan has often been adopted for the preservation of compounds sensitive to high temperatures and pH (Erdal *et al.* 2012) and allows the reformulation of a substantial amount of pharmaceutical and food items (Akbal *et al.* 2017). Thus, chitosan has been considered a reliable substance in the encapsulation of essential oils (Ulkowsky *et al.* 2005). However, the use of chitosan nanoparticles to serve as a transport vehicle for bioactive compounds such as the essential oils of *C. articulatus* has not been reported in any study.

According to Andrade *et al.* (2006) there are variations in the chemical compositions of *Cyperus* species and depending on the country of origin. In line with the studies by Sotelo-Boyás *et al.* (2017) the majority of bioactive compounds associated with essential oils of *Cyperus* species include oxygenated hydrocarbon derivatives, a sesquiterpene and a monoterpene (Kavaz *et al.* 2019) (Table 2). According to Kavaz, Idris and Onyebuchi (2019) there is a high level of toxicity of cancer cells in high concentration of the extract of *C. articulatus* at a concentration of 350 μg/mL. *C. articulatus* essential oil encapsulated with chitosan nanoparticles showed more cytotoxicity in vitro against MDAMB-231 breast cancer cells after 40h compared to the chitosan nanoparticles and the free *C. articulatus* essential oil.

Antioxidant properties

The concept of antioxidants relates them to substances that slow the rate of oxidation, when excessive production of oxygen radicals occurs during pathophysiological processes or

due to environmental factors (Huang *et al*. 2006). Through one or more mechanisms, antioxidants have the main function of reducing oxidation, for example, by inhibiting free radicals and complexing metals (Duarte-Almeida *et al*. 2006).

In nature, free radicals are produced endogenously or acquired exogenously, and their excess produces oxidative stress (Núñez-Sellés 2005). There are many antioxidant substances, which stimulates a greater interest for use in food, cosmetics and pharmaceutical products. The interest is that these substances are able to replace synthetic antioxidants that are suspected of inducing cancer (Sasaki *et al*. 2002; Djeridane *et al*. 2006). There is great interest in natural antioxidants derived from plant extracts (Wolfe *et al*. 2003), especially from aromatic and medicinal plants, considered sources of natural antioxidants. Secondary metabolites, such as phenolic compounds have antioxidant action, which act by inhibiting the generation of free radicals (Singer *et al*. 2003, Lapornik *et al*. 2005) (Table 2). For this reason, essential oils and their constituents have provided acceptance due to their wide range of biological activities, including antioxidant action (Batish *et al*. 2008).

Halvose *et al*. (2002) found that due to the oxidation kinetics of compounds is unpredictable. According to the aforementioned authors, the reaction is likely to continue for longer than normally recommended. Many compounds also demonstrate complex kinetics and reach end points in a few hours or days, some of the more complex compounds never seem to reach steady state conditions within a reasonable time (Ozgen *et al*. 2006).

The kinetics of the free antioxidant activity of *C. articulatus* essential oil were analyzed by Kavaz *et al*. (2019) in comparison with the essential oil loaded with chitosan nanoparticles. The free radical scavenging properties of *C. articulatus* essential oil were higher in the initial moment compared to chitosan nanoparticles and with essential oil loaded with chitosan nanoparticles.

Anticonvulsant properties

Epilepsy is a disease characterized by recurrent seizures and other complications. Such complications have been shown to cause oxidative stress by reactive oxygen species in the brain (Xu *et al*. 2016). Approximately more than 50 million people worldwide have already been diagnosed with epilepsy, representing a public health problem of all ages, genders and social groups. Medical reports have shown an incidence rate of epilepsy in developed countries of 50 per 100,000 inhabitants. In developing countries, this rate increases from 100 per 100,000 people (Gupta *et al.* 2014). The modern concept of epilepsy according to the International League Against Epilepsy (ILAE) involves the occurrence of at least one or more epileptic seizures (Coimbra *et al*., 2015). There are several drugs used by doctors to control epilepsy. However, these drugs, like so many others, have side effects that are serious, such as ischemia, liver toxicity, cognitive disorders and motor disability (Ngo *et al*. 2003). In addition, approximately 20% to 30% of these patients are resistant to synthetic drug treatments. Thus, it is necessary to discover other treatments using natural medication to reduce complications or side effects of antiepileptic drugs. *C. articulatus* (Cyperaceae) also known as "piri-piri" in Peru is a rhizome herb found in Africa, Latin America, Asia and Oceania.

In Cameroon, Central African Republic, Gabon and Senegal it is very common to use the decoction of your rhizome to treat headaches, migraines, etc. In addition, Amazonian Indians use the plant in a similar way (Abubakar *et al*. 2000). However, Herrera-Calderon *et al*. (2017) proposed to study the leaves of this plant in order to find an anticonvulsant effect of *C. articulatus* from its extract. In the study by the aforementioned authors, pentylenetetrazole was used as a seizure-inducing chemical in mice and gamma amino-butyric acid (GABA) and malondialdehyde (MDA) were evaluated in the brain of rats.

In the Rakotonirina *et al*. (2001) works established 300 mg/kg efficacy doses of rhizome extract of *C. articulatus* administered in mice. Herrera-Calderon *et al*. (2017) showed efficacy in the test group of *C. articulatus* leaf extract that received a single dose of 150 mg/kg orally. Possibly these differences could be linked to the alkaloids that were reported in the study or the rhizome extract would not have this metabolite (Table 2). Still, other aspects could be involved, such as solvent, solubility, origin of the studied species. Previous studies indicated that the mechanism of the rhizome extract anticonvulsant effect was related to the selective inhibition of NMDA receptors. According to Ngo *et al*. (2001), the leaf extract of *C. articulatus* may have a direct modification in the production

of GABA and protection against lipid peroxidation (MDA) generated in the brain. It is known that lipid peroxidation disturbs the membranes and is particularly destructive to the structure and function of the extract component of *C. articulatus* leaves. In conclusion, Herrera-Calderon *et al*. (2017) were able to note that the leaf extract exerted MDA inhibition in the mice's brain, protecting against neuronal damage. The authors also concluded that although the anticonvulsant mechanism of the extract is unknown, the ethanolic extract of the leaves of *C. articulatus* could be useful in the treatment of epileptic seizures in the future.

Anti-onchocercal properties

Onchocerciasis, also known as "river blindness" and "garimpeiro's disease", is a filariasis caused by *Onchocerca volvulus*, parasite of the phylum Nematoda, order Spirurida, family Onchocercidae. This disease is transmitted by several species of dipterans of the genus *Simuliidae*, which are known as black and "rubbery flies" (Blanks *et al.* 1998). The first record of onchocerciasis in Brazil was when two nodules were removed containing adult parasites present on the head of an American missionary child, who lived in the Yanomami indigenous area, in northern Brazil (Bearzoti *et al*. 1967). According to the World Health Organization, in 2007, 37 million people were infected with the parasite and about 300,000 are blinded with onchocerciasis (WHO 2007). The disease is transmitted through the bites of black flies of the *Simulium* species in infected people. These flies carry immature larval forms of the parasite and are responsible for endemic transmissions. In the human body, the larvae form nodules in the subcutaneous tissue, where they mature to adult worms. After mating, the adult female worm can release up to 1000 microfilariae a day. They move around the body and, when they die, they cause a variety of conditions, including blindness, skin rashes, injuries, intense itching and depigmentation of the skin (WHO 2014).

According to WHO (1991) ivermectin has been shown to be safe and effective in the treatment of onchocerciasis and has become the most used drug for control by the strategy of mass drug administration (WHO 1991). However, ivermectin is effective only against the microfilarial effect and not against the adult form. Based on this information, there is a need to search for a medication that kills the adult worm a priority area of research (Osei-Atweneboana *et al*. 2001). In addition, during mass treatment of onchocerciasis with ivermectin in forested areas of Central Africa, several side effects have occurred, including encephalopathy and deaths have been reported (Gardon *et al*. 1997). There is also the possibility of the potential development of strains resistant to ivermectin. Thus, it is necessary to identify alternative drugs that are candidates for the control of onchocerciasis (Lizotte-Waniewski *et al*. 2000).

Natural products have demonstrated great potential in the treatment of infectious diseases in humans (Oliver-Bever 1986). Studies have shown that natural products of plant origin can provide a good alternative source as antifilarial drugs precisely because they are cheap, readily available, and have few side effects (Ebigwai *et al*. 2012, Comley 1990). Studies on the chemical composition and biological activity of *C. articulatus* suggest that the rhizomes of the plant have antispasmodial, antibacterial, anti-fungal and anticonvulsant actions (Rukunga *et al*. 2008, Bum *et al*. 2001). In this way, Metuge *et al*. (2014a) investigated the activity of extracts from the *C. articulatus* rhizomes of in the traditional treatment of onchocerciasis in northeastern Cameroon. Crude extracts were prepared from the dry parts of the plant, using hexane, methylene chloride and methanol. The authors tested the antifilarial activity in vitro on microfilariae and adult worms through their viability and also based on reduced motility. As a result, only the hexane extract, an essential oil, showed anti-cancer activity. The oil killed *O. ochengi* adult microfilariae and worms in a dose-dependent manner, with IC50s of 23.4 μg/ml in Mfs, 23.4 μg/ml in adult male worms and 31.25 μg/ml in adult females. Thus, the results obtained show that the use of *C. articulatus* in traditional medicine is extremely important for the treatment of human onchocerciasis. Still promoting the same line of studies, Metuge *et al*. (2014b) isolated the active ingredients from the roots / rhizomes of *Cyperus articulatus* used as a herbal medicine in Cameroon for the treatment of human onchocerciasis. They also assessed the effectiveness of metabolites in *Onchocerca* worms. Two secondary metabolites, AMJ1, con-taining mustakona as the main component and linoleic acid or (9Z, 12Z) -octadeca-9, 12-dienoic acid were isolated (Table 2). According to the same authors, both compounds were found to kill both the microfilariae and adult worms of *O. ochengi* in a dose-dependent manner.

Thus, it is possible that compounds active against the bovine parasite will also affect the human parasite, *O. volvulus*. Further studies are being done to identify the real compound that transmits high activity to AMJ1. In addition, these metabolites may provide a guide for the design and development of new drugs that can act as antifilarial agents.

Table 2 – Pharmacological properties of *Cyperus articulatus*

PHARMACOLOGICAL PROPERTIES			
Activity	**Related metabolite**	**Part of the plant used**	**Source**
Anti-malarial activity	cyperotundone, alpha-ciperone, mustacones	rizhomes chloroform extract	Rakotonirina *et al.* (2001), Ohshima *et al.* (1998)
Sedative properties	flavonoids, saponins, sugars, triterpenes and polyuronides.	rizhomes decoction	Rukanga *et al.* (2008), Rakotonirina *et al.* (2001)
Hepato-protective role	unknown metabolite	rizhomes methanolic extract	Datta *et al.* (2013)
Contraceptive effect	unknown metabolite	rizhomes aqueous extract	Eniola *et al.* (2011)
Central nervous system effect	unknown metabolite	rhizomes powder	Ngo Bum *et al.* (2001)
Insecticidal properties	aromatic mono- and sesquiterpenes	rizhomes methanolic extract	Abubakar *et al.* (2000)
Antimicrobial activity	α and β-pinene compounds	rhizomes ethanolic and chloroform extracts	Yusuf *et al.* (2012), Freires *et al.* (2015)
Anticancer properties	sesquiterpene and a monoterpene compounds	essential oil	Kavaz *et al.* (2019)
Antioxidant properties	phenolic compounds	essential oil	Singer *et al.* (2003), Lapornik *et al.* (2005)
Anticonvulsant activity	Alkaloids compounds	rhizome extract	Herrera-Calderon *et al.* (2017)
Anti-onchocercal properties	Mustakona and linoleic acid compounds	rhizome extract	Metuge *et al.* (2014b)

Conclusion

Despite scientific studies demonstrating the anti-malarial, sedative, hepato-protective, contraceptive, anticancer, antioxidant, anticonvulsant, anti-onchocercal properties, effects in the central nervous system as well as insecticide and antimicrobial of the rhizome of *Cyperus articulatus* that could be useful in the treatment of several human diseases, more clinical studies in humans are necessary. There is a need for these studies is precisely to confirm all plant properties and to avoid possible side effects in humans. In addition, protocols for the use of the plant are necessary in relation to the quantities and concentrations of the formulations presented.

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