Popular use, phytochemical composition and biological activities of *Chenopodium ambrosioides* L. (Chenopodiaceae)

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Abstract—*Chenopodium ambrosioides* is a plant used in folk medicine. The therapeutic and biological effects of its extracts and those of its essential oil (antimicrobials, antiparasiths, insecticides, antioxidants and anti-inflammatory drugs ...) have been documented. This review is an analysis of published data on the plant ranging from its use in traditional medicine to laboratory work. Search engines such as Science Direct, Google and PubMed were used with keywords to dispose of the results of previous work. The results confirm popular uses and prove that the plant has biological activities that can be very useful to humans in the field of health and agriculture. However, its use must be controlled in order to avoid side effects.

Index Terms— Biological activities, Chemical composition, *Chenopodium ambrosioides*, Essential oil.

1 Introduction

Chenopodium ambrosioides is a plant native to Central and South America, probably Mexico. The plant grows spontaneously and is also cultivated in the tropics and subtropics mainly in America and Africa as well as in temperate zones, from the Mediterranean to central Europe **[65]** . It is an aromatic medicinal plant about a meter high, branched, erect or ascending. The stems are angled, smooth or glandular-pubescent. The leaves are 3 to 10 centimeters oblong, with lobed edges. The flowers are small, white and thorny, regular. The stamens are as numerous as the sepals, the filaments are distinct. The plant is also known as worming wormseed in English." It is a member of the *Chenopodiaceae* composed of 120 species **[46]** . It has long been used as an anthelmintic, dewormer and has many other medicinal properties used in folk medicine **[4]** . Today, this herbaceous plant is widely distributed in Africa and is widely used in health care, to treat parasitic diseases, bacterial infections, to deworm livestock, it is also used in agriculture as an agricultural input **[1], [40]**. The results of the research work confirmed the many pharmaceutical activities of the plant such as antibacterial, antifungal, anticancer activities, etc. **[14] [73].**

This paper is a review of the results of 95 articles on Chenopodium ambrosioides from 1965 to 2019. The article reviews the popular uses, phytochemistry , biological activities of extracts of Chenopodium ambrosioides and its essential oil .

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2 Methodology

Search engines such as internet, google , pubmed , libgen , sci hub, hinari were used with the following keywords*: Chenopodium ambrosioides* , biological activities, popular use, chemical composition and essential oil. In all, 129 articles were found and 95 were selected on the basis of their scientific quality, materials and methods used.

3 Results

6.1 Botany

This annual or perennial herb from the Chenopodiaceae family can reach a height of one meter. In the axils of its fragrant leaves stand panicles of yellowish flowers.

3.2 vernacular names of Chenopodium ambrosioides

Togo :

Ewé-Watchi : Magbezôde, Agbalisakô, Agbalissakon, Agometutumakpa, Emigbe, Magbezôli, Magbézonli, Matruzu, Megbezôdhoe, Yovoma, Agonetutumakpa
Mina-Guin : Emigbé
Bassar : Gbanssoukou
Kabye : Doma Koyé, Domgnèou

Bénin

Adja : Duba yovome
Fon-Goun : Goto, Matruzu, Azogbidiwa, Amahun kokwe, Mawanwan, Amatluzu, Gogo, Gboswaluukun
Mina-gen : Matruzu, Emigbe
Watchi : Magbezonde
Yorouba-Nago : Ma-ntulusi, Lakure

France

French : chénopode ambroisie, thé du Mexique

3.3 Popular use of *Chenopodium ambrosioides* around the world

Chenopodium ambrosioides is a plant known and used by many peoples around the world. Table 1 summarizes the dif-

ferent uses in the regions where the plant grows. The data in the table shows that the use of the plant is very diverse depending on the regions. The pathologies cited concern both infectious diseases and metabolic disorders. In Benin, for example, the plant is especially cited for the treatment of abscesses, epilepsy, vomiting, dermatoses, and intercostal neuralgia. However, prescriptions against inflammation and parasitic diseases are recurrent in use in traditional medicine. The method of preparation is often decoction, infusion or in the form of tea. The route of administration is almost exclusively the oral route, except in a few rare cases such as abscesses where the route of administration is external.

Table 1. Popular uses of Chenopodium ambrosioides

Regions	Parts used	Method of preparation and routes of administration	Purposes of use	References
Togo	Leaves, Pulp, Leafy stem, Roots and Whole plant	Decoction and Infusion (oral route), poultice and Bath (external application)	Abscess, Epilepsy, Edema, Child vermifuge, Psychosis, Nervous disorders.	**[28]**
Benin	Leaves	Decoction (oral route), poultice (external application)	Abscess, epilepsy, vomiting, skin dermatosis, intercostal neuralgia	**[4]**
United States of America	Young leaves, seeds	Decoction, ground seeds into a porridge (oral use)	Intestinal worms, Ascaris anthelmintic, dewormer, emmenagogue digestive, respiratory problems, urogenital, vascular and nervous disorders, metabolism disorders such as diabetes and hypercholesterolemia, sedative, antipyretic and antirheumatic	**[20]**
Peru	Leaves, roots, inflorescences	Infusion, decoction (oral)	Vermifuge	**[33]**
Korea	Whole plant	Infusion (oral route), poultice (external application)	Painkillers, anti-inflammatory drugs, diabetes	**[85]**
Brazil	Leaves, Whole plant	Tea, infusion (oral route), poultice (external application)	antiparasitic, anti-inflammatory antibiotic, diuretic, anthelmintic, treatment of wounds and, respiratory problems such as, bronchitis, tuberculosis and flu, rheumatism, ulcers.	**[48], [65]**
Mexico	Whole plant	Decoction (oral)	anthelmintic	**[45]**
China	Aerial parts	Condiment (oral)	Purgative, rheumatism	**[39]**
Ghana	Leaves	Decoction (oral)	Tuberculosis	**[69]**
Cameroon	Leaves	Infusion (oral), powder	Intestinal worms ; conservator of agricultural products	**[70], [88]**
Trinidad	Leaves	Infusion (oral)	Flu, pneumonia, typhoid fever, vermicide	**[15]**
Congo	Whole plant	Powder	conservator of agricultural products	**[23]**
Nigeria	Leaves	Hanging on doors	insecticide	**[24]**
Morocco	Whole plant	Infusion, juice (oral) local application	gastrointestinal ailments, typhoid, dysentery and galactogen. against oral abscesses, ulcerations and purulent wounds.	**[25]**
Madagascar	Stems, leaves	Infusion (oral)	antispasmodic, dewormer, acaricide syphilis,	**[13]**
Rwanda	Whole plant	-	Veterinary dewormer	**[67]**

3.4 CHEMICAL COMPOSITION OF *CHENOPODIUM AMBROSIOIDES* EXTRACTS

Several research studies have been carried out to determine the chemical composition of *Chenopodium ambrosioides* . The results obtained showed that C. ambrosioides contains phenolic compounds. Indeed, **[52]** found that an acetone extract of C. ambrosioides contained gallic tannins and tannic acid. HPLC-DAD analysis identified rutin in the crude extract, while quercetin and chrysin were quantified in the chloroform fraction **[38]** . In an ethanolic extract of the plant collected in Mexico, it has been identified in addition, kaempferol 3-O rutinoside , kaempferol O- rhamnosyl - pentoside , quercetin dirhamnoside **[54]** . Other phenolic substances identified in extracts are isorhamnetine , luteolin **[47]** . Terpene alcohols are also found in a hydroalcoholic extract. One of these terpene alcohols found is phytol **[57]** . The 2-methyl-5- (1-methylethenyl) - Cyclohexanol and 5-Isopropenyl-2-methyl-7-oxabicyclo [4.1.0] heptan-2-ol monoterpenes were also found in the same extract. In addition, some authors have reported the presence of alkaloids **[38]**.

The difference observed in the composition of the extracts can be explained by the difference between the polarity of the extraction solvents, the edaphic and climatic conditions in which the plant was grown, the time of harvest and also the experimental conditions. These different results obtained can also be due to the performance of the detection and identification equipment. Some of these molecules isolated from the extracts are shown in Figure 1. These molecules would be partly involved in the biological and pharmaceutical activities of *Chenopodium ambrosioides* .

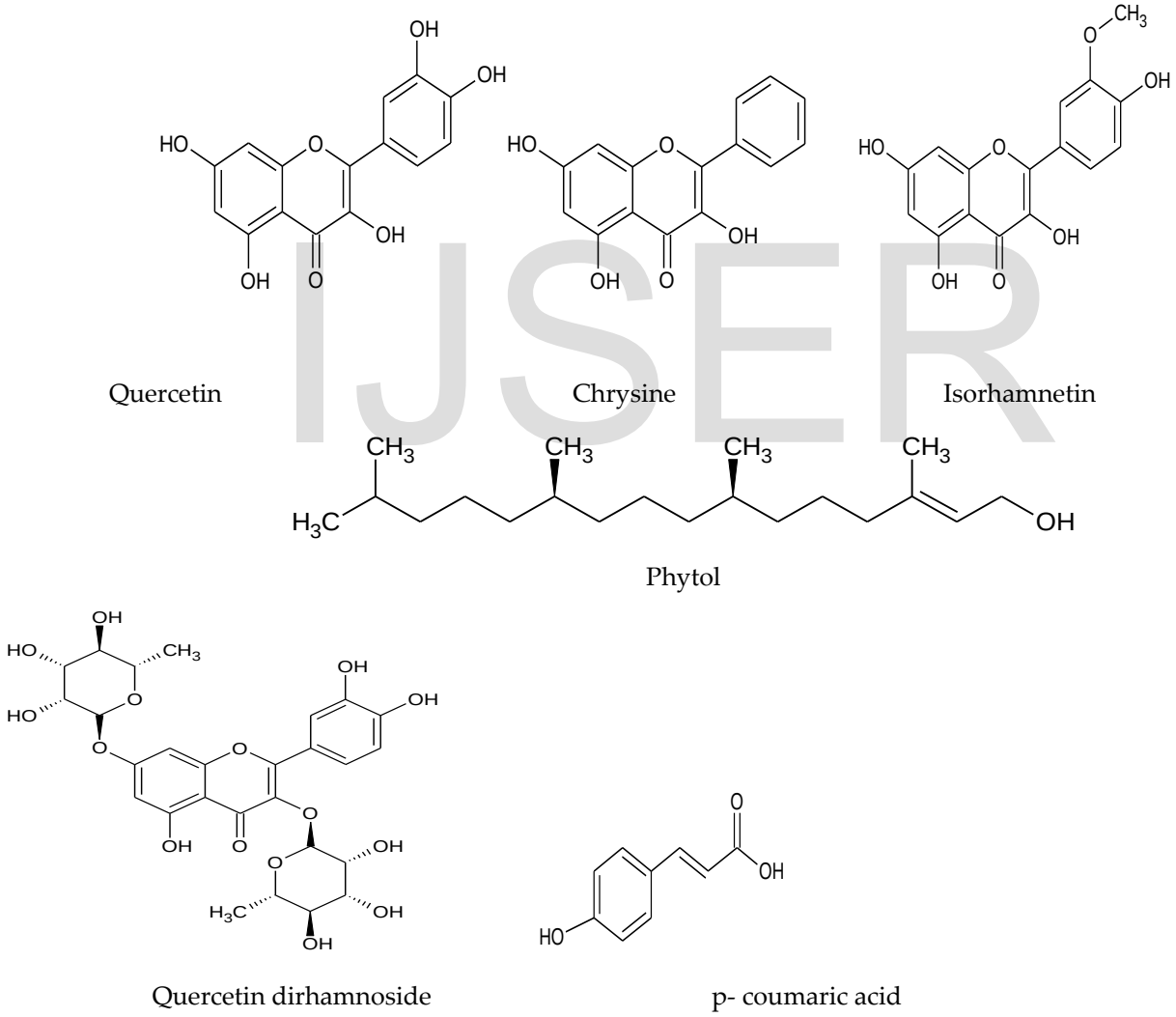

Fig. 1. Structures of some phenolic compounds and phytol isolated from Chenopodium ambrosioides

3.5 ANTIMICROBIAL AND ANTIPARASITIC ACTIVITIES OF *CHENOPODIUM AMBROSIOIDES* EXTRACTS

The results of research work have revealed that Chenopodium

a*mbrosioides* exhibited several therapeutic virtues, also as a preservative of agricultural products; however, toxic effects have been pointed out by some authors. Indeed, extracts of C. ambrosioides have been studied for their antimicrobial activities. Several plant extracts were studied using the liquid microdilution method in order to inhibit the growth of strains of Escherichia , Staphylococcus aureus , Candida , Klebsiella pneumoniae and Pseudomonas aeruginosa **[97]** . Thus, with the ethanolic extract, no inhibition of the growth of the germs was noted at 100 µg / mL ; However, the hexane extract at 200 µg / mL inhibited the growth of C. krusei ATCC 6258. This antibacterial activity of the hexane extract was also approved by **[79]** who administered 5mg / kg body weight of three types of extracts to male Swiss mice after inducing polymicrobial sepsis. Twelve hours after the treatment, the animals were sacrificed and the count of the microorganisms in colony forming units was carried out. The results showed that only hexane treatment inhibited bacterial growth in the peritoneum. In the same context, **[77]** . used the disk diffusion and microdilution technique against ten bacterial strains. At the end of the work, they did not obtain any inhibitory activity with the methanolic extract . In Nigeria, the phenolic fractions of acetone extracts were tested by the disk method against Escherichia coli , Staphylococcus aureus , Salmonella typhi , Candida albicans . The results of this work showed that the phenols inhibited the growth of all the germs tested with inhibition diameters ranging from 16.00 ± 1 to 27.90 ± 0.5 mm at 250 mg / mL **[52]** . Another team studied the antimicrobial potential of the bark and fruits of C. ambrosioides against several microorganisms using the disc method coupled to the microdilution . It emerged from this work that the peel and fruits macerated in petroleum ether have the best antimicrobial potentials against B. subtilis (33 ± 1.5 mm) and A. niger (16 ± 1.5 mm, respectively).), the aqueous extracts showing no activity against the selected organisms. The Minimum Inhibitory Concentration (MIC) of the fruit extract against S. aureus was 0.7 mg / mL ((Muhammad *et al*., 2016). The literature also reports that the methanolic extract of the fruits of the plant inhibits the growth of Enterococcus faecalis (MIC = 4375 μ g / mL), E. coli (MIC = 1094 μ g / mL) and Salmonella typhimurium (MIC = 137 μ g / mL) **[77]** . Similarly, a decoction of *C. ambrosioides* harvested in Argentina obtained by soaking 5.0 g of the aerial parts in 100 ml of water inhibited the larvae of Paenibacillus after 72 hours of incubation **[31]**. The leaves of *C. ambrosioides* were extracted with 70% ethanol and fractionated with chloroform, ethyl acetate, and n-butanol. The extracts were evaporated in a rotary evaporator and then diluted in DMSO for testing against microorganisms. The authors reported that the crude extract and all other fractions at the concentrations tested were active against B. cereus (ATCC 9634), L. monocytogenes (ATCC 7644), E. faecalis (ATCC 29212), S. aureus (ATCC 25923)), E. coli (ATCC 35218), P. aeruginosa (ATCC 340), S. choleraesuis (ATCC 10708), C. albicans (ATCC 90028). However, the most promising results were obtained with the ethyl acetate fraction, which obtained the lowest MIC values ranging from (4.29 to 34.37 mg / mL) against S. aureus, P . aeruginosa , E. faecalis , Paenibacillus apiarus and P. thiaminolyticus . The samples were also tested against the genus Mycobacterium . For this test, the techniques of microplates in the presence of alamar blue , of disks diffusion and of microdilution were used. At the end, the best MICs were obtained with the chloroform fraction against M. tuberculosis , M. smegmatis and M. avium (MIC ranging from 156.25 to 625 µg / ml), respectively **[38]** .

There is evidence that these sample activities are probably due to the action of phenolic compounds present in plants and responsible for their antimicrobial activities **[42]** . Phenolic compounds are substances used as disinfectants, they cause the inactivation of the enzymatic system and the loss of essential metabolites of microorganisms through the cell wall with bactericidal, fungicidal, virucidal and even anti-tuberculosis properties **[32]**. The antimicrobial potential of *C. ambrosioides* phenolic compounds such as rutin, quercetin and chrysin has been documented. These compounds can by destabilization of the bacterial membrane, cause a disturbance of the driving force of the protons, the flow of electrons, the coagulation and the leakage of the cellular contents, thus causing a bactericidal effect **[21], [82]**. Particulary, tannins have the ability to disrupt the metabolic process of the microorganism by depriving it of iron and other metal ions through the restriction of oxidative phosphorylation **[52]**.

The low activity of crude extracts of *C ambrosioides* could be due to the antagonism of the chemical components present in the extract, thus reducing their activities on organisms **[52]** . This low activity can also be caused by other factors including the sensitivity of the microorganism tested, the method used and the organ of the plant extracted.

Chenopodium . ambrosioides is also known for its antiparasitic and insecticidal activity. To this end, tests were carried out in Benin; the study used fifteen West African goats (Capra hircus) naturally infected with nematodes, the scientists **[80]** administered an infusion of 50mg / L to three experimental groups respectively 1, 2 and 4ml / kg of body weight for 3 days of treatment. Their results showed a significant decrease in parasite eggs in the experimental groups. The reduction in egg excretion rate was greater than 70% in animals treated with *C. ambrosioides* . Egg reduction rates reached almost 100% within 5-6 days. In addition, the helminthological autopsy performed on the study animals after treatment showed a complete absence of the worms. The authors found that a dosage of 1 ml / kg of body weight for a three-day treatment was appropriate and prescriptive.

Two research teams **[27]** and **[8]** studied the anti Leishmania activity of C. ambrosioides by oral and intralesional route. At the end of their work, they concluded, firstly, that intralesional treatment is more effective than oral treatment, secondly, that treatment with the hydroalcoholic crude extract and the aqueous extract of *C. ambrosioides* have an activity against the extracellular forms at 100 μ g / mL thus inhibiting the growth of the parasites at 87.4%. In the same context, the nematicidal effect of the n-hexane extract was evaluated in vitro against Haemonchus contortus parasites and helminths and then in vivo by experimentally infesting gerbils (rodents) with 20 parasites. The results of this test showed that the most lethal effect in vitro was obtained 72 hours after treatment at 40 mg / ml and made it possible to reduce the parasites to

96.3%. The same plant in vivo at 40mg / kg body weight reduced the parasite load in gerbils by 45.8% **[96]** . Cats and dogs, are also prime targets of the parasites Rhipicephalus (Boophilus) microplus and Toxocara canis respectively. To fight against these parasites, hydroalcoholic and hexane extracts of *C. ambrosioides* were used to treat cats experimentally infected with R. microplus for 19 days and dogs infected with T. canis treated for 7 days. The results obtained from this work show that the 40% and 60% hydro-alcoholic extract is effective against cat parasites and that the hexane extract dosed at 30 mg / kg is toxic for T. canis larvae **[72] [78].**

Chenopodium ambrosioides has also been studied against schistosomiasis resistant to praziquantel. Thus, the researchers conducted an experiment in which a methanolic extract of C. ambrosioides at 1250 mg / kg was combined with an antimalarial drug to treat mice infected with S. mansoni for two days. The authors mentioned that the treatment eliminated 95.5% of the parasites. The S. mansoni parasite uses Biomphalaria glabrata as an intermediate vector. Some work has therefore focused on the activity of extracts of *C. ambrosioides* against B. glabrata . At the end of this work, the plant was shown to be effective with a lethal concentration (LC 50) of 13.51 mg / mL **[61]**. Other scientists have studied the antiparasitic activity of *C. ambrosioides* . Thus, a methanolic extract at 1250 mg / kg was tested. The results mention that the plant eliminated the parasite S. mansoni at 53.7%. Likewise, four monoterpene hydroperoxides extracted from C. ambrosioides in 2001 were tested and the results revealed that these compounds have anti- Trypanosoma cruzi activity at concentrations ranging from 0.8 to 3.1 µM. The authors conclude that this plant has anthelmintic and anti trypanosomal activity. **[92]** studied the anti Giardia activity of *C. ambrosioides* leaves using a cell quantification method. The results showed strong anti Giardia activity in vitro . The authors indicated that their activity was between (199 <IC 50 <215 µg / mL). This activity has been attributed to the phenolic compounds of the plant. A combination of the methanolic extracts of C. ambrosioides at 1250 mg / kg and Sesbania sesban was also administered to male mice infected with the parasite *S. mansoni* . But this test only reduced 24% of the parasites **[61]**. However, a decoction of C. ambrosioides at a therapeutic dose of 6000 mg / Kg of powdered plant had no significant anti-helminthic effect on adults of Necator Trichuris **[59]** . The ethanolic extract of C. ambrosioides has been tested against Amblyomma cajennense , a fever vector tick in Central America. The authors used the " Fingertip bioassay". At the end of the test, they reported that concentrations of (2.2-0.275 mg / cm 2) showed a good repellency index (66%). Also, the *C. ambrosioides* extract was tested against A. cajennense nymphs , at the two highest concentrations (1.1 and 2.2mg / cm 2), but with a longer repulsion time. short (10 min) after treatment **[84]** .

In addition, this plant is also toxic to insect pests of legume and grain crops stored after harvest. To help the agricultural sector, researchers studied the effectiveness of powders and *C. ambrosioides* extracts on insects in fields and during grain storage. Thus, tomato plantations have been sprayed with extracts of the plant. In Brazil, researchers sprayed the 5% alcoholic extract of C. ambrosioides in a tomato field. Insect counts were performed within 24 to 72 hours and compared with untreated control plots. This work showed that C. ambrosioides is effective against Tuta absoluta , insects of the Eulophidae family and on the eggs of Trichogramma sp **[9]** . The powder of the plant was applied for 6 days at doses ranging from 1.25% to 10% (m / m) on cowpea seeds. infested with the cowpea weevil , C*allosobruchus maculatus* Fab . The powder from the leaves of C. ambrosioides showed insecticidal and repellent properties against C. maculatus and the LD 50 obtained was 2.8 g / kg **[88]**.

Several other scientists have studied the insecticidal activity of *C. ambrosioides* ; Thus, larvae of Anopheles gambiae to each developmental stage were exposed to several concentrations of extract of C. ambrosioides and the number of dead larvae was recorded 24 and 48 hours after exposure. The results showed that the tested extract is toxic to all larval stages and adults of A. gambiae . The values of the LC 50 found are the most toxic for the larvae of the first instar (LC 50 14.89 mg / mL) followed by stage 4 (LC 50 18.90 mg / mL) and stage 3 (LC 50 183.77 mg / mL) **[3]** . The insecticidal effect of *C. ambrosioides* powder was evaluated against non-sexual adults of *C. maculatus* . The insects were infested for seven days in containers with 0.3 g of C. ambrosioides powder mixed with 10 g of cowpea. Results showed that *C. ambrosioides* powder reduced both egg laying and adult emergence of C. maculatus (Pannuti *et al.*, 2012). The same study was carried out by **[16]**; the insecticidal effect of powdered leaves of *C. ambrosioides* was compared with the effect of seeds of Aframomum melegueta against cowpea weevils, *C. maculatus* . 5 g of the two powders were used in several proportions. Vegetable powders were added to 20 g of cowpea seeds. Insect mortality was assessed 24 to 144 hours after treatment. The results indicate that the vegetable powders are toxic to the insects tested and cause a significant mortality of C. *maculatus* . The highest mortality rate (83.33 ± 20.81%) was obtained by the jar treated with *C. ambrosioides* 100%. A fourth team of scientists evaluated the insecticidal activities of leaf powders of C. ambrosioides against *C. maculatus* infested with stored cowpea **[60]** . Three doses were tested : 0.1 ; 1 and 3g of powder / 10g of cowpea seeds. The authors evaluated the mortality and emergence of adults, the reduction in laying and the percentage of damaged seeds. The results showed that the powder of the plant offer complete protection of the seeds and an inhibition of the emergence of adults using the three doses of foliar powders of *C. ambrosioides* . 100% insect mortality was obtained on the fourth day of contact. These results were also confirmed by the work of **[8].** Another team, **[83]** also evaluated the effect of C. ambrosioide s powder against Sitophilus zeamais . The powder was evaluated at proportions of 0.1 ; 0.5 ; 1.0 and 2.0% on corn kernels experimentally infested with insects for 24 hours, 30, 60 and 90 days. The results showed that the percentage of insect mortality was obtained respectively 65.8% and 90.3% at 1 and 2% proportion. Likewise, the insecticidal activity of 4 other plants was tested against Zabrotes subfasciatus , a major pest of bean seeds, and compared to *C. ambrosioides* powder. The results of this experiment demonstrated that C. ambrosioides was more toxic with mortality rates of 74.28 ± 2.41% and 87.22 ± 3.85% at 1% and 2% (w / w) respectively **[11]** . The

insecticidal efficacy of crude aqueous extracts of *C. ambrosioides* was also tested to determine their ability to control Clavigralla tomentosicollis Stâl , a cowpea pod sucking bug. The aqueous extracts were sprayed to the field at 10% (v / w) for four weeks. The results showed that the extracts of the plant reduced the insect population **[37]** . The sweet potato white fly, Bemisia tabaci (Gennadius), is a pest of crops. Thus, plant extracts, have been used to overcome this parasite. Ethanolic extract of C. ambrosioides was evaluated. Researchers reported that extract 6% killed 93% of this pest **[93]** . It should be noted that the extracts of *C. ambrosioides* were active regardless of the parasite tested; these results justify its popular use to control intestinal parasites. The results presented above are not all the same. To do this, the sensitivity of the parasites tested must be taken into account in the variability of the results since it has been reported that the field strain develops more resistance than the strain bred in the laboratory **[87]** . Wild strains are genetically more heterogeneous than those bred in the laboratory **[41]**. They are also regularly exposed to various insecticides and therefore have a greater tolerance to toxic compounds. Likewise, the powders of the plant have been shown to be very active against insects which destroy agricultural products. The insecticidal effect of this plant could be due to a physical action since the particles of the powder can block the respiratory system of insects and cause their death by asphyxiation. In this vein, Ofuya et al,. 2002 have shown that there is a direct relationship between the size of the particles of plant powders and the mortality of insects. In addition, fine particles promote an even distribution of powders on the surface of the seeds and on the walls of the storage container, thus increasing their possibility of coming into contact with insects and killing them. Moreover, vegetable powders cause abrasion of the cuticle of insects and lead to a loss of water from it **[86]**.

3.6 ACTIVITY ANTIOXIDANT , ANTI-INFLAMMATORY, ANTI NOCEPTION AND ANALGESIC EXTRACTS OF *CHENOPODIUM AMBROSIOIDES*

Few works have been interested in the antioxidant , anti-inflammatory, anti- noceptive and analgesic activity of the extracts of C. ambrosioides . In this regard, the literature reports that **[36]** tested the anti-inflammatory activity of C. ambrosioides extracts using carrageenin to induce acute inflammation and cotton balls to induce chronic inflammation in rats. To test for analgesic activity, they used both hot plate device and formaldehyde tests. They tested 300, 500, 700mg / kg. They observed that the edema of the rat paw induced by carrageenan was markedly inhibited by the methanolic extract. They mentioned that the results of the extract at 700mg / kg was more interesting than indomethacin, 16.22% and 14.53% inhibition respectively. With cotton pellet-induced granuloma inhibition from 27.90 to 60.04%. They also found that the extract has analgesic activity by causing it to prolong latency during the hot plate test. The ethanolic extract (EE) was also tested for its anti-inflammatory and anti- noceptive effect induced by several phlogistic agents and its wound healing effect in rats. Thus, after performing these experiments, **[50]** found that the treatment of animals with a cream containing the EE of *C. ambrosioides* at 1%, 3% and 5% produced a significant decrease in edema finger from 70.85% to 78.08%. EE (500 mg / kg.) inhibited also paw edema from 40 to 57%, induced by phlogistics. Their results also demonstrated that EE at 500mg / kg elicited a pronounced anti-nociceptive effect and inhibited phlogistic-induced pain. EE (500mg / kg) was also effective in inhibiting (68%, 53%, 32%) the nociception induced by phlogistics. To heal the wounds induced experimentally in animals, they applied 5% of EE on the wounds. The results showed that the treatment significantly reduced the wound area.

To understand *C. ambrosioides* activities , phytochemical of EE was performed and revealed the presence of two monoterpenes, ascaridole and 1, 2, 3,4-tetrahydroxy-p-menthane. These data suggest that these compounds detected in EE would be responsible for its activities. Likewise, palmitoleic acid isolated from the plant have been tested for its analgesic, antipyretic and anti-inflammatory activities. The results revealed a potential activity, 96.77% inhibition of edema significantly greater than that of aspirin (64.68%). However, the results obtained by C. ambrosioides did not differ from those of morphine used as a reference with the hot plate test (14 ± 1.41 sec, 15 ± 000 sec) respectively. To assess antipyretic and anti-inflammatory activities, they respectively induced pyrexia in rats by subcutaneous injection of 20% of aqueous suspension of yeast and induced edema by injecting egg albumin into the sub-plantar tissue of the right hind paw. They revealed that C. ambrosioides possessed not only antipyretic activity but also hypothermic activity. Palmitoleic acid at 200mg / kg inhibited 30.88% of edema, lower than indomethacin, 129.41% **[52]**. Other authors obtained a maximum inhibition of nociception activity at 89.77% by administering to mice an aqueous extract of *C. ambrosioides* at 300 mg / kg **[35]** . An analgesic effect was also observed with the hot plate device maintained at 55 ° C. In addition, the extract produced inhibition of yeast-induced pyrexia in rats. They hypothesized that the anti-inflammatory activity of palmitoleic acid isolated could imply an inhibition of prostaglandin synthesis since the effect of the compound was more pronounced in the later stages of inflammation **[53]** .

Among the biological activities *of C. ambrosioides* reported, it is also noted that this plant exhibite antioxidant activity. In this regard, an infusion of the plant containing 36 mg / L of phenolics exhibited a low antioxidant activity estimated in ORAC-fluorescein and ORAC-pyrogallol red equivalence of 395 ± 13 and 3.3 ± 0 , 2 respectively [6] . This antioxidant activity has been applied to preserve raw minced pork meat for nine days. At the end of the nine days, the extract of C. ambrosioides exhibited low antioxidant activity but that it could be used to preserve meat in a short time **[54]** . **[67]** reported that they evaluated the antioxidant potential of the fruits and the bark of *C. ambrosioides* using DPPH, ABTS and metal chelation tests. The results showed that the aqueous fruit extract has the highest value expressed as percentage of bound iron and gallic acid equivalent respectively 76.99 ± 1.7% and 1076 ± 0.3 μ gAG / mL . However, the highest content of flavonoids and the maximum value of the ABTS test were obtained by the aqueous bark extract, 1997.09 ± 1.5 μ g / mL and 10.22 ± 0.9Mm. The highest percentage of DPPH inhibition was obtained by

the bark extract, 34.1%. According to **[10]** , the antioxidant activity of C. ambrosioides extracts is due to their flavonoids as well as to their organic acids such as citric acid.

3.7 OTHER ACTIVITIES OF *CHENOPODIUM AMBROSIOIDES* EXTRACTS

Beyond the biological activities mentioned above, the literature reports that *C. ambrosioides* could relieve diabetics. For this purpose, methanolic extracts at 100, 200 and 400 mg / kg of body weight were administered for 14 days to induced diabetic mice. After the analyzes, the results showed that the blood glucose level of the animals significantly decreased **[85]** . In Togo, a team used 0.5 g of ointments made from an EE of *C. ambrosioides* leaves which they applied twice a day to heal wound induced and infected with Pseudomonas aeruginosa . The infected wounds in the control group healed in 12.6 ± 0.245 days. However, the ointment based on C. ambrosioides leaf extract reduced this time to 07.04 ± 0.245 days **[55]** . Other authors confirmed these results **[50]** . **[26]** applied 20mg / kg of the aqueous extract to repair experimentally perforated bone tissue in rats. At the end of the experiment, the authors noted that bone regeneration occurred in the group treated with the extracts of *C. ambrosioides* for 10 days of treatment. **[68]** studied the effect of treatment with a EE against the development of Ehrlich's tumor. To this end, mice were treated intraperitoneally with an extract of *C. ambrosioides* leaves at 5 mg / kg 48 hours before or 48 hours after implantation of the Ehrlich tumor. The tumor cells were implanted on the left paw (solid tumor) or in the peritoneal cavity (sciatica tumor). The development of the tumor was evaluated after 8 days of implantation by quantifying the volume of sciatic fluid and the number of tumor cells. The results of the experiment showed that the Ehrlich tumor implanted in mice before or after administration of the extract was significantly inhibited compared to untreated control mice. The treatment also increased the survival of the tumor-bearing mice. It should be remembered that *Chenopodium ambrosioides* is an aromatic plant. Its two components, extracts and its essential oil would be used in its activities.

3.8 CHEMICAL COMPOSITION OF THE ESSENTIAL OIL OF *CHENOPODIUM AMBROSIOIDES*

The chemical composition of an essential oil (EO) depends on several biotic factors but also on the extraction method. It should be noted that terpene compounds are the main molecular components of EO **[8]** . Some of these terpene molecules identified in the EO of *C. ambrosioides* in various regions are listed below: cymol , α - terpinene, ascaridole, carvacrol , cis β - farnesene , p- cymene , 4-carene, trans-2-caren-4-ol, carveol , myrcene , α pinene, phellandrene , α -terpineol, limonene, p- cresol, p-mentha-1, 3, 8-triene, p - cimen-8-ol, piperitone, piperitol acetate, (Z) acetate - carvyl , limonene diepoxide , ρ , α Dimenthylstyrene , 2-ethylcyclohexanone, α , α -4-trimethylbenzyl alcohol , 3,4 -epoxy ρ -menthan-2-one, precocene II, tiglate of geranyl , tiglate of hexyl , hexahydro farnesyl acetone, Phytol , E, E- Cosmene , benzaldehyde, n- nonanal , n- octanol **[29], [43], [49].** In general, depending on the geographic region, several chemotypes have been identified in the EO of *C. ambrosioides* . Thus, the ascaridole chemotype is found in Brazil and Yemen (Carolina *et al*., 2008) [7] ά - terpinene chemotype in Nigeria and India **[73], [34]** , p- cymene chemotypes have been reported in Cameroon **[88]** limonene-rich chemotypes have been characterized in Spain **[76]** and a pinocarvone / α -pinene chemotype originating from Japan **[91]** . The structures of some of the compounds isolated from EO from the plant are shown in Figure 2.

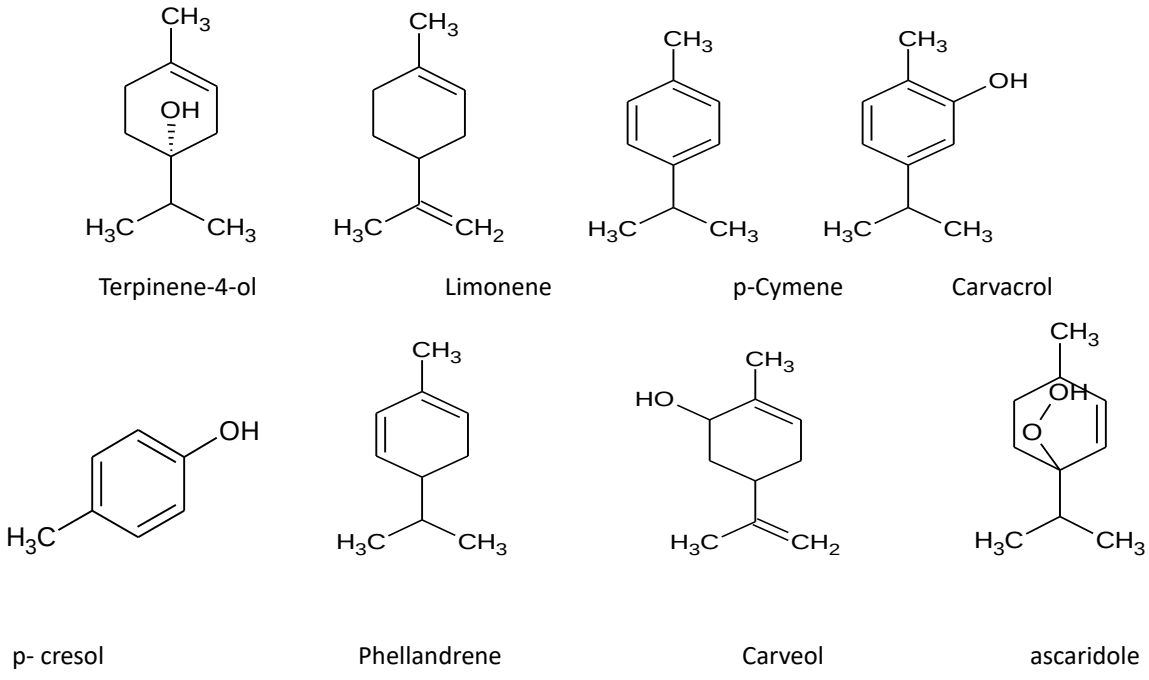

Fig. 2. Structures of some molecules isolated from the essential oils of Chenopodium ambrosioides

3.9 ANTIMICROBIAL ACTIVITY OF THE ESSENTIAL OIL OF *CHENOPODIUM AMBROSIOIDES*

Several methods have been used to evaluate the antimicrobial activity of the EO of C. ambrosioides. Thus, the antifungal activity of the EO was evaluated. Thus poisoned food test was used at concentrations of 0.3%, 0.1% and 0.05% of the oil against strains of Aspergillus , Colletotrichum and Fusarium . The results showed that the growth of all fungi was completely inhibited at 0.3% and 90 to 100% using 0.1% **[14]**. **[48]** used also poisoned food method to inhibited the growth of 10 strains of fungi using 100 µg / mL . Another team impregnated the filter paper discs with the EO of *C. ambrosioides* at various concentrations; these filter paper discs were placed 2 cm from the mycelium disc of Fusarium oxysporum f. sp . Dianthi grown on dextrose agar. The results showed that after 72 hours of incubation, the growth of the mycelium was inhibited by 97.3% using 176.5µL / L **[12]** . The literature reported that using the microdilution technique, the EO of *C. ambrosioides* inhibited up to 99% the growth of antibiotic-resistant Helicobacter pylori bacteria with 0.64 g / L after 4 hours of incubation **[51]** . Methods using agar agar and disk diffusion of C. ambrosioides EO have also been shown to be effective against the growth of several bacterial and fungal strains **[56], [81]** . In contrast, no antimicrobial activity of EO was found from *C. ambrosioides* harvested from Nigeria using dilution technique **[73]**.

3.10 ACTIVITY ANTIOXIDANT AND ANTI-INFLAMMATORY ESSENTIAL OIL OF *CHENOPODIUM AMBROSIOIDES*

The results of research and empirical practice have shown that EO of *C. ambrosioides* possesses antioxidant and anti-inflammatory activities. Thus, the antioxidant activity was determined by the method using DPPH radical and by the oxidation of β -carotene / linoleic acid. The antioxidant activity found with the β -carotene / linoleic acid was IC 50 = 455.7 µ g / ml lower than that of ascorbic acid (IC 50 = 25µg / mL). Likewise, the reduction of 11.94% and 15.79% of the DPPH radical using respectively 300 µg / mL and 500 µg /mL of EO were obtained. But the same test was used by a second team and the authors obtained 84.89% of DPPH inhibition with 25µL / mL **[81]**, [7], **[12]**. Other authors, **[56]** evaluated the antioxidant power of EO using the same methods as above in addition to the iron reducing power test. They proved that the EO of C. ambrosioides possesses a moderate antioxidant activity using with DPPH and high activity using the β -carotene / linoleic acid test (IC 50 = 3.03 µg / mL) and of iron reducing (IC 50 = 6.02 µg / mL). For the same objectives, the test using the ABTS radical was carried out. The EO of *C. ambrosioides* at 3000 µg / mL has shown potential antioxidant activity with 95.66% inhibition of the radical **[48]**. The chemical composition of essential oils is very complex and therefore it is difficult to establish a relationship between the composition and / or structures of the compounds and their antioxidant activities . But in general, essential oils which contain monoterpene compounds and / or oxygenated sesquiterpenes have more important antioxidant properties than those of oils with non-oxygenated molecules **[89]** . Other factors can influence the antioxidant activity: the concentration of the sample, temperature, light, type of substrate **[90]** . The antioxidant activity would also depend on the method used for the test.

Reports showed that the anti-inflammatory activity of C. ambrosioides is well known.Thus [5] evaluated in vitro the anti-inflammatory activity of three samples of EO of *C. ambrosioides* using the lipoxygenase inhibition technique . The results obtained with 100 ppm of EO indicated that the percentages of inhibitions of lipoxygenase are relatively low. all samples obtained an inhibition less than 50%. The EO samples tested are characterized by a high level of hydrocarbon monoterpenes , no correlation between chemical composition and anti-inflammatory activity appears clearly. But in general, the anti-inflammatory activities of plant molecules use several mechanisms such as inhibition of lipoxygenase , prevention of leukotriene synthesis, inhibition of COX-2 enzyme, inhibition of pro-inflammatory cytokines , interleukin-1 and tumor necrosis factor (TNF), as well as the repression of pro-inflammatory genes.

3.11 PEST CONTROL AND INSECTICIDE ACTIVITIES OF THE ESSENTIAL OIL OF *CHENOPODIUM AMBROSIOIDES*

In the search for new molecules to treat parasitic diseases and fight against insects harmful to man and agriculture, the EO of C. ambrosioides has been the subject of experimentation. To this end, **[62]** examined the anti-parasitic activity of the EO of *C. ambrosioides* . For the test, they infected BALB / c mice with Leishmania amazonensis. Then, the infected animals were treated by various routes of administration. The authors reported that intraperitoneal administration of EO at a dose of 30 mg / Kg prevented the development of lesions and reduced the parasite burden. Oral administration delayed infection of mice with parasites compared to control mice, although this route was less effective than the intraperitoneal route. They repeated the test in 2011 and found that the second study also showed anti leishmania activity like the one previously reported. They obtained an IC50 of 4.6 µg / mL . (Monzote *et al.*, 2011) . To help smallholder farmers to control gastrointestinal parasites, EO from *C. ambrosioides* has been used to treat kids infected with Haemonchus contortus. In addition, EO from the same plant has also been used against nematodes naturally infected in goats and kids **[44]**. The team tested several doses ranging from 0.1 to 0.4mL EO / kg of body weight. None of the treatments applied were effective. These contradictory results can be explained by the genetic diversity of the parasites, their resistance.

In Argentina, experiments were carried out to evaluate the repellent activity of the EO of *C. ambrosioides* . The sample was tested against Aedes aegypti . For the test, 60µL of EO emulsion at 90% was applied to one arm. Subjects inserted their arm treated with EO into a cage containing 25 hungry mosquito females. The time between the introduction of the arm and the first injection was recorded. The results of this test showed that the EO of *C. ambrosioides* repelled mosquitoes for 60 ± 17min **[30]**. In Ethiopia, the EOs of 11 local plants were assessed for their larvicidal activities against Anopheles arabiensis and Aedes aegypti larvae in the early fourth instar **[58]**

. This laboratory experiment was applied in the field at concentrations ranging from 6 to 333.3 ppm and from 16 to 200 ppm of EO diluted in acetone. The authors reported that *C. ambrosioides* oil induced greater larvicidal activities in the laboratory and also in the field. The researchers studied the action of EO of *C. ambrosioides* against Plutella xylostella , a parasite of agricultural plantations. The authors found that the LD50 varied with the age of the larvae. Second instar larvae (0.353µg / larva), third instar larvae (2.916µg / larva) and fourth instar (4.843µg / larva) **[94]** . The same practice was used by **[17]** to test the EO of C. ambrosioides and its compound (Z) - ascaridole against Sitophilus zeamais , the experiment lasted one week. The values of the LC50 obtained by fumigation of EO and of compound (Z) - ascaridole against *S. zeamais* were respectively 3.08 and 0.84 mg L^{-1} of air. The LD50 values by contact toxicity of crude EO and (Z) - ascaridole are respectively 2.12 and 0.86 µg g -1 body weight. In the same context, other authors have found an LC50 of 1.90µL / L against S. zeamais **[2].** To protect the stored grains from damage caused by insects, tests were carried out using the contact toxicity and repellent activities of C. ambrosioides against *Callosobruchus maculatus* Fab . In accordance with the methods used by the authors, they obtained several results. Using the contact toxicity test, the LD50 found was 0.17µL / g of grain **[95]** ; by the fumigation method, the LC50s found were 1.33, 2.07 and 43.68µL / L against adults, eggs and larvae of the insect C. maculatus respectively **[2]** . Similar work was conducted by **[74]** who studied the repellent activity of EO at 0.36 µl / mL against *C. maculatus* and *C. chinensis*. They reported that the oil showed 100% repellency against insects. The toxicity assessment on insects also helped to achieve 100% mortality on both insects tested them with 10 µ L / mL and LD50 = 2.8 µ L against *C. chinensis* and 2.5 µ L against *C. maculatus*. EOs extracted from *C. ambrosioides* (L.) from Morocco were tested against white larvae of *Melolontha melolontha* . This work included two stages: The first was carried out *in vitro* the second was carried out in an infested avocado field based on the results of the first in vitro test . Throughout the exposure period, the authors determined the LC50 and LC99. The results showed that the LC50 is 0.36% and the LC99 0.89% after 5 days of treatment in a Petri dish and in the field in small pots, the LC50 obtained is 0.44% and the LC99 3.08% **[25]**. The insecticidal activity of *C. ambrosioides* was also tested on insect pests of greenhouses by **[18]**. They sprayed 0.5% EO on greenhouse plants. After 4 days of treatment, they reported that they obtained a significant death rate on the midges. The treatment resulted in a high percentage of long-tailed mealybug mortality (55%) compared to the control. However, EO was less effective against citrus mealybug (3% mortality) and flower thrips (18-34% mortality). The insecticidal effect of plant EO is undoubtedly due to its active components. But the insect death rate is not always the same depending on the insect species and the samples tested. Other insect species are probably protected because of their waxy coating on the body, which tends to protect them against the action of aggressive agents such as insecticidal EO **[19]** . In addition, the composition of the EO tested is variable, or the constituent molecules do not have the same activity. The test with ascaridole proved that this molecule was more active than the whole oil.

3.12 OTHER BIOLOGICAL ACTIVITIES OF THE ESSENTIAL OIL OF *CHENOPODIUM AMBROSIOIDES*

The results of the above investigations have provided sufficient evidence that the EO of *C. ambrosioides* has beneficial biological activities for humans; however, the results of other experiments have shown that the essential oil can be harmful to humans if used improperly. To do this, **[46]** studied the in vitro cytotoxic activity of HE on the HaCat cell line of the human epidermis. These bioassays revealed a moderate level of EO toxicity from *C. ambrosioides* . They obtained an IC50 of 700 µ L.mL -1 . Based on the chemical composition of the EO sample used, this cytotoxicity was attributed to the neral compound present in EO in a proportion of 8.70%. Similarly, the cytotoxicity of three samples (fresh material, dried and fermented in water) of HE from Cuba was also evaluated on macrophages taken from peritoneal cavities of apparently holy BALB / c mice. The authors reported that from this study they obtained a lower cytotoxicity of EO extracted from green plant material (sample 1) than the other samples; CC50 = 335.7 ± 2.2 µg / mL for the fresh material and 265.0 ± 2.8 µg / mL , 216.8 ± 1.6 µg / mL respectively for the other two samples. The three main compounds of the samples are respectively ascaridole , ὰ - terpinene and p – cymene **[63]**. In Brazil, HE chemotypes , ascaridole (49.77%) and p- cymene (42.32%) was also tested for 48 per **[22]** on various tumor cell lines, including Myeloid leukemia (K562), acute B lymphoid leukemia (NALM6 and B15) and Burkitt's lymphoma (RAJI). The potential cytotoxicity found in the samples tested was evaluated at IC50 = 1 mg / mL on the RAJI cells. This cytotoxicity was greater than that of the doxorrubicin control (13.2 mg / ml). These oil samples were tested on the K562, NALM6 and B15 cell lines; the IC50s obtained were respectively 86.1 ± 10.6 µg / mL ; 25.3 ± 3.6 µg / mL and> 100 µg / mL . The cytotoxicity of these EOs from *C. ambrosioides* has been attributed to the predominant compound ascaridole . It also varies depending on the cell lines tested. Other experiments by **[62]** examined the activity of the EO of C. ambrosioides in BALB / c mice infected with Leishmania amazonensis using a dose of 30 mg / kg injected intra-lesionally, oral and intraperitoneal. After treatment, they assessed the in vivo toxicity produced by HE by examining damage to the peritoneum, spleen, pancreas, stomach, liver, kidneys, diaphragm, heart and lungs. . The results showed that oral and intralesional administration of HE to BALB / c mice showed no visible sign of toxicity in these animals at the dose tested. On the other hand, in the mice treated intraperitoneally, they observed small abscesses in the peritoneal cavity, as in the mice treated with the solvent, by the same route. They speculated that the damage observed could be the result of the intraperitoneal injection. Another experiment investigated the mechanism of this toxicity of EO from *C. ambrosioides* and its pure compounds (carvacrol , caryophyllene oxide and ascaridole) on mammalian cells and mitochondria. The authors reported that all of the compounds, especially caryophyllene oxide , inhibited the mitochondrial electron transport chain. This effect of the molecules was attributed by the direct inhibition of the mitochondrial complex

I. In addition, they reported that the toxicity of ascaridole on mitochondrial oxidative phosphorylation was strongly dependent on the availability of Fe 2+ electrons **[64]** . However, in Brazil the said plant has been used for decades in the diet for the treatment of helminthic infestations, but no toxic effects have been associated with its use **[45]** . These different results could be justified by the diversity of the organisms treated, the routes of administration and also by the genetic variety of the species of C. ambrosioides in several regions.

4 CONCLUSION

Chenopodium ambrosioides is a plant known in several regions. It is used mainly for therapeutic purposes against various pathologies, as evidenced by the results of previous work. These works mentioned that this plant can also help the agricultural sector in the fight against destructive insects of agricultural products. But some work, based on the chemical composition of samples of its essential oil from various backgrounds, has focused our attention on the harmful effects that its inappropriate use can cause. The composition of the essential oil of this plant is affected by the climatic and edaphic conditions of the region where the plant is grown and also by experimental conditions. Ascaridole is most implicated in the toxicity of this essential oil. The use of essential oil in agriculture is more appropriate. But work can also be done to standardize its composition for beneficial therapeutic use.

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