ORIGINAL ARTICLE

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A review on the Bioactivity and Phytochemistry of *Jatropha podagrica* Hook (Euphorbiaceae)

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ABSTRACT

Aims: to provide knowledge on the bioactivity and phytochemistry of *Jatropha podagrica* Hook.

Study Design: Advanced multidisciplinary bibliographical research, use of the ChemBioDraw software package and dissemination of the knowledge obtained.

Methodology: A literature review was conducted to obtain information on the pharmacognosy and phytochemistry of *Jatropha podagrica* Hook. from various scientific databases (SciLEO, PubMed, Google scholar, Science Direct and PubMed Central). The scientific name of this plant species was used as a keyword for the search, as well as the terms pharmacognosy and phytochemistry. ChemBioDraw Ultra 12.0 software was used to draw the structures of chemical compounds of *Jatropha podagrica* Hook. and other species of the genus *Jatropha*.

Results: The results obtained revealed that this plant is traditionally used as a stimulant or analgesic. This species possesses various biological properties such as anti-tumor, antimicrobial, molluscicidal and anti-insect. These properties are due to the presence of natural chemical compounds such as steroids, flavonoids and diterpenoids.

Conclusion: This study can therefore help guide future scientific research towards the development of new antisickling drugs from *Jatropha podagrica* Hook.

Keywords: *Jatropha podagrica*, medicinal plant, phytochemistry, pharmacology

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INTRODUCTION

Natural products have contributed extensively to the development of new drugs. Therefore, considerable importance has been placed on investigating medicinal plants and herbs for bioactive compounds.[1] A large number of plants have been screened for natural antioxidants, antibiotics and cytotoxic agents to combat various pathological events. Recent findings revealed that over 80% of the African population relies on medicinal plant species for their primary healthcare.[2] The Democratic Republic of the Congo (DRC), through its cultural diversity, the richness and diversity of its flora and fauna, constitutes a real reservoir of biodiversity as indicated by the results of recent work, which is why it has been allows it to occupy a privileged place among the countries of the Congo Basin with traditional plant-based know-how medicinal and/or animal[2] *Jatropha podagrica* Hook is an exotic ornamental grown in Democratic Republic of the Congo.[3]

The genus *Jatropha*, belonging to the family Euphorbiaceae, includes succulents, shrubs and trees,[3] distributed mainly in tropical and subtropical areas of Asia, Latin America and Africa.[4,5] The genus is a rich source of many beneficial chemicals and has been extensively studied for biological activities.[6,7] *Jatropha podagrica* Hook is a plant species of the genus *Jatropha* and is widely used for ornamental purposes and in traditional therapies to treat and prevent various diseases.[8]

Truong Ngoc Minh et *al.* (2019),[9] reported in the literature that in traditional therapies, this plant has been widely used to effectively treat skin infections, jaundice and fever.[10,11] sexually transmitted infections and/or diseases such as gonorrhea,[12] pain relief,[13] gout[14] and paralysis.[15,16] In addition, the oil from its seeds is used in African ethno-medicine as a natural remedy for rheumatism, pruritus and to relieve constipation, while its leaves are used as a hemostatic agent. In Nigeria, the indigenous people use this shrub to treat hepatitis.[17]

Research on the bioactive compounds of *J. podagrica* has led to the isolation of Japanese acid, erytrinasinate, fraxidine,[12] steroids and flavonoids,[18] podacyclin A and B.[19] Diterpenoids,

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japodagrone, japodagrine,[8] 3-acetylaleuritolic acid, japodagrol[20] n-heptyl ferulate and sitosterol,[21] tetramethylpyrazine.[10,16] Although extracts from different parts of *J. podagrica* Hook. have been reported to have various biological properties, including antiproliferative, antitumor, antioxidant and antimicrobial activities against insects,[12] the search for phytochemicals responsible for the observed activities has been conducted sporadically, except for antibacterial activity. In addition, little information has been found so far on the phytochemical data and biological activity of *J. podagrica* Hook stem bark.[22] Several secondary metabolites, including fraxidine, fraxetine, scoparone, 3-acetylaleuritolic acid, sitosterol and sitosterone, have been isolated from the stem bark of this plant, but their biological activity has not been examined.[21] However, it is important to note that *Jatropha curcas*, a plant species belonging to the same genus that *J. podagrica* has reported to possess antisickling activity *in vitro*.[23]

Sickle cell disease (SCD) is a haemoglobinopathy that occurs naturally in people of colour. Genetically, the disorder is characterized by a single base substitution in the gene coding for the human subunit β-globin and results in the replacement of the glutamic acid β6 by valine which causes an abnormal, rigid, sickle-like form of hypoxia.[24] In the Democratic Republic of the Congo (DRC), surveys have revealed that 12% of children hospitalized are sickle cell disease patients and that the annual cost of treating the disease is more than US$ 1,000 per patient.[25] As *Jatropha podagrica* Hook is thought to contain phenolic and terpenoid compounds,[3,26] it can be hypothesized by chemotaxonomy that this plant may have hemolytic inhibitory effects on sickle cell disease, thus justifying the present extensive literature review on the phytochemistry and pharmacology of this plant, with the aim of integrating this plant species into a future research program for their antisickling activity.

METHODOLOGY

A literature review was conducted to obtain information on the pharmacognosy and phytochemistry of *Jatropha podagrica* Hook. from various scientific databases (SciLEO, PubMed, Google scholar, Science Direct and PubMed Central). The scientific name of this plant species was used as a keyword for the search, as well as the terms pharmacognosy and phytochemistry. ChemBioDraw Ultra 12.0 software was used to draw the structures of chemical compounds of *Jatropha podagrica* Hook. and species of the genus *Jatropha*.

RESULTS

Ethnopharmacology

The genus *Jatropha* (Euphorbiaceae) comprises about 175 species distributed mainly in tropical and subtropical areas of Latin America, Asia, and Africa. Species of the genus *Jatropha* are used in traditional medicine for various diseases such as skin infections, sexually transmitted diseases such as gonorrhoea, jaundice and fever.[27] These species are known for their various biological activities, such as antimicrobial, anti-tumor, molluscicidal and anti-insect activities.[28] In recent years, a variety of interesting bioactive natural products, particularly diterpenes, including rhamnofolan, daphnan, tiglian and lathyrene-type diterpenoids, have been isolated from this genus.[26] Some of these diterpenoids exhibit interesting bioactivities, including cytotoxic properties, which have attracted the interest of chemists for their total synthesis. In recent studies, the new diterpenoids japodagricanones A (1) and B (2), as well as the diterpenoid biogenetically related to 15-epi-4 jatrogrossidentadion (3), have been isolated from the leaves of *Jatropha podagrica* Hook. *Jatropha podagrica* Hook is an exotic ornamental plant grown in the Democratic Republic of the Congo.[3] The stem and roots of *Jatropha podagrica* Hook. are used as chewing sticks. The plant is also used as an antipyretic, diuretic, choleretic and purgative.[29] Various pharmacological activities, including antibacterial, antitumor and anti-insecticide activities have been reported for this plant.[30]

Antibacterial and antioxidant activities

Aiyelaagbe et *al*.[30] reported in the literature the results of the antimicrobial activity of extracts against the tested organisms. Hexane extract from yellow root bark was the most active of all extracts, followed closely by its chloroform and methanol extracts. Methanol extract from red bark was the least active. Yellow bark extracts were almost twice as active as red bark extracts. Hexane extracts were generally more active than chloroform and methanol extracts. Root wood extracts were as effective as red bark extracts but were less effective than yellow bark extracts. All extracts showed broad-spectrum antibacterial activity. The antibacterial activity of the yellow and red bark extracts was similar to that of gentamycin but the hexane extract from yellow bark was more active than gentamycin with respect to two strains of *S. aureus* and *B. cereus*. Root wood extracts were more active against the different strains of *E. coli* and *B. cereus* tested. Hexane extracts from red root bark were particularly active

against three strains of *Ps. aeruginosa* which were resistant to most extracts and to ampicillin and gentamycin. Methanol extracts from yellow bark and root wood were also active against one clinical strain of *Ps. aeruginosa*. It should also be noted that all extracts, with the exception of the methanolic extract from red bark, were active against certain clinical strains of *S. aureus* and *E. coli* that are resistant to tetracycline, cotrimoxazole (septrin), ampicillin and streptomycin. Hexane extracts from yellow bark and rootwood and rootwood methanol extract (RWM) were moderately active against the yeast fungus *Candida albicans*, but less active than the tioconazole control. The antimicrobial activity of *J. podagrica* root wood extracts and yellow and red bark suggests that they may contain steroids, terpenoids, flavonoids and alkaloids such as stem and stem bark that have antimicrobial activity.[31] Hexane extract from the bark of this plant was found to be cytotoxic and a macrocyclic diterpenoid with anti-tumor activity was isolated from it.[32] All these results showed the potency of these bark extracts in the chemotherapy of various pathologies. Aiyelaagbe et al. (2007)[6] Japodagrin (1) and japodagrone (2), two macrocylic diterpenoids possessing lathyrane and jatrophane skeletons, respectively, have been isolated from the root of *Jatropha podagrica* Hook. Four other diterpenoids were also isolated from this plant. The structures of these compounds were elucidated on the basis of NMR and HRMS analysis, and by spectral comparisons. The compounds have shown antibacterial activity against some gram-positive bacteria. Bioactive compounds from the bark of the stem of *Jatropha podagrica* Hook, a well-known medicinal plant. Ethyl acetate extract from the bark of the stem had the highest antioxidant activity as assessed by the 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,20-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and ferric reducing antioxidant potency (FRAP) scavenger tests (IC_{50} = 46.7, 66.0 and 492.6, respectively). The chemical structures of the constituents have been elucidated by gas chromatography-mass spectrometry (GC-MS), electrospray-mass spectrometry (ESI-MS) and nuclear magnetic resonance (NMR), in particular methyl gallate (C1, C2, C3, C4), gallic acid (C1, C2), fraxetine (C2, C3, C4, C5) and tomentine (C3). The mixture of C2 (IC_{50} DPPH and ABTS = 2.5 g/mL) and C3 (IC_{50} FRAP = 381 g/mL) showed the highest antioxidant properties of the fractions isolated, C4 was the most likely agent to inhibit the growth of six bacterial strains, including *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Listeria monocytogenes*, *Bacillus subtilis* and *Proteus mirabilis* (MIC = 5, 20, 30, 20, 25 and 20 mg/mL, respectively). All identified compounds showed inhibitory activity on the growth of *Lactuca sativa*, whose C3 mixture revealed maximum inhibition on shoot (IC_{50} = 49.4 g/ml) and root (IC_{50} = 47.1 g/mL) growth.[9]

The antioxidant activity of *Jatropha* species has been demonstrated by *J. gaumeri*, *J. macrantha* and *J. unicostata* dosed using the DPPH radical and beta-carotene. Mothana (2011)[33] studied the methanol extract of *J. unicostata* and showed a total antioxidant activity of 43.8%. Desmarchelier et *al.*[34] reported the antioxidant activity of methanol and dichloromethane extracts from *J. macrantha* roots by extinction of light-enhanced chemiluminance. Similarly, the methanol extract from the leaves of *J. gaumeri* showed promising activity.[35] Molluscicidal activity against *Biomphalaria glabrata*, *Bulinus* and *Oncomelania hupensis* of *J. curcas* extracts which are known to contain phorbol esters. Al-Zanbagi et *al.*[36] studied extracts of fresh and dried leaves of *J. glandulifera* towards *B. pfeifferi* and found that methanol extract from fresh leaves had an LD_{50} of 21.7 ppm and an LD_{90} of 29.8 ppm, while acetone extract from fresh leaves had an LD_{50} of 6.76 ppm and an LD_{90} of 12.5 ppm. In contrast, the plant dry leaf extracts of cold water, methanol, chloroform, acetone and hexane had LD_{50}s of 73.3, 84.9, 16.5, 102.6, 96.0 ppm and LD_{90}s of 118.8, 160.7, 46.8, 129.0 and 118.0 ppm, respectively. Acetone extract from fresh leaves and chloroform extract from dry leaves of *J. glandulifera* showed the best molluscicidal activity.[36]

Immunomodulating activity

Immunomodulating activity from *Jatropha* plants were displayed by the cyclic peptides isolated from the latex. Cyclic peptides 1, 11 and 12 showed inhibition of the classical pathway of human complement activation *in vitro*.[37] Both 11 and 12 bound to aggregated and antigen-bound IgG, mostly blocked the antibody Clq acceptor site, which is restricted to IgG subclass IgGl.[38]

Anti-inflammatory activity

Carrageenan-induced paw edema in rats is reduced by the anti-inflammatory action of the extracts of *J. curcas* and *J. gossypifolia*. The anti-inflammatory activity of *J. curcas* were derived from the methanol extract of its roots[39] while the methanol and petroleum ether extracts of dried aerial parts of *J. gossypifolia* showed this activity.[40] Mothana[35] reported that the extract from *J. unicostata* reduced abdominal constriction induced by acetic acid Curcain, the protein from the seed oil of *J. curcas* were reported to exhibit wound-healing property when tested on mice at two different enzyme concentrations. Curcain powder at 0.5% and 1.0% (w/w) were mixed with washable ointment base and

wound-healingactivity by the curcain ointments was compared to the controls nitrofurazone (0.2% w/w) and propamidine isoethionate (0.15%).[41]

Protoscolicidal and antihelminthic activities

Protoscolicidal activity of *Jatropha* plants was reported from *J. curcas* and *J. unicostata* and the antihelminthic activity of *J. curcas* were reported from its leaf against *Pheretima poshtuma* (Ahirrao et *al*., 2009).[42] Barzinji et *al*. (2009)[43] investigated the aqueous and methanolic extracts of *J. unicostata* on the viability of *Echinococcus granulosus* protoscoleces *in vitro* where a concentration of 1.0 103l g/mL exhibited the highest protoscolicidal activity. Furthermore, oral and intraperitoneal administration of its extracts to white mice invoked noticeable inhibitory effects on the *in vivo* development of secondary hydatid cysts compared to albendazole sulfoxide, which is commonly used in the treatment for hydatidosis.

Insecticidal activity

Insecticidal activity of *Jatropha* plants was demonstrated by *J.curcas* and *J. gossypiifolia*. The extract of *J. gossypiifolia* leaf suggested to have compounds that are toxic to insects was tested against the larvae of three lepidopteran species, *Busseola fusca*, *Ostrinia nubilalis* and *Sesamia nonagrioides*. These lepidopterans are important pests of maize in Africa, Europe and Mediterranean countries.[44] Insecticidal activities of *J. curcas* oil containing phorbol esters have been reported against *Aphis gossypii*, *B. fusca*, *Blattella germanica, Callosobruchus chinensis, Culexsp., Empoasca biguttula, Helicoverpa armigera, Manduca sexta Oncopeltus fasciatus, Pectinophora gossypiella, Oncopeltus fasciatus, Phthorimaea operculella, Sesamia calamistis and Sitophilus zeamais*. Boateng and Kusi (2008)[45] found that the seed oil of *J. curcas* were also toxic against *Callosobruchus maculatus* and its parasite, *Dinarmus basalis*.

Inhibition of acetylcholinesterase (AChE)

Inhibition of the acetylcholinesterase (AChE) was reported from *J. gossypiifolia* species. The aqueous solutions of the leaf and stem bark of *J. gossypiifolia* were found to be active in killing fish. The toxic effect of the stem bark of the plant were time as well as dose dependent. Significant negative correlation between LC_{50} and exposure periods was also derived. The LC_{50} values of the stem bark extract of *J. gossypiifolia* were found to decrease from 4.61-106l g/L (24 h) to 4.34-106l g/L (96 h). It were suggested that the plant cannot be used directly in freshwater bodies, without detailed studies on the long-term effects on non-target organisms and their structure–activity relationship.[46] Significant alteration in total proteins, total free amino acids, nucleic acids, glycogen, pyruvate, lactate level and protease activity in different tissues (muscle, liver and gonadal) of *Channa punctatus* were shown by aqueous latex extracts of *J. gossypiifolia* after 96 h of exposition to 40% and 80% of LC_{50} (24 h).

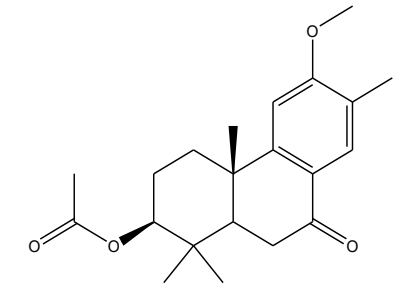
The changes in all levels of glycogen, pyruvate, lactate and nucleic acids, but almost complete recovery in total proteins, total free amino acids level and protease activity in all the three tissues of the fish after the 7th day of the withdrawal of treatment, supported the view that the plant products are safer to be used as pesticides for control of common weed in culture fish ponds.[47] The latex of *J. gossypiifolia* which were obtained by cutting the stem into pieces and draining them into a glass tube were lyophilised and the powder was used for biochemical experiment. The latex caused a significant reductionin acid/alkaline phosphatase and anti-acetylcholinesterase activities in the nervous tissue of freshwater air breathing fish *Channa marulius* and the reduction were depended on time and dose.[48]

Antiviral activity

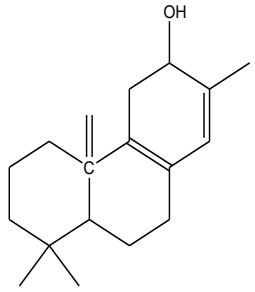
One new lathyrane diterpenoid, Jatropodagrene (1) along with three known compounds have been isolated from the root bark of *Jatropha podagrica* Hook. The structure of the new compound was established from its 1D and 2D NMR spectra and by comparison with data reported in the literature. The compound 1 was been reported highly cytotoxic (98.86% inhibition) against HCV virus, while compounds 2 (EC_{50}, EC_{90}, CC_{50} 5.8, 33.1, 22.6 μg/mL, respectively) and 3 displayed significant anti HCV activity.[49]

Toxicity activity

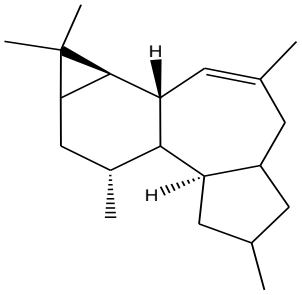
Jatropha is an inedible oleaginous plant belonging to the Euphorbiaceae family. Global awareness of sustainable and alternative energy resources has propelled research into *Jatropha* oil as a feedstock for biodiesel production. Over the past two decades, several cultivation projects have been undertaken to produce *Jatropha* oil. In the future, the increased cultivation of toxic *Jatropha* species and the use of its agro-industrial by-products may increase the frequency of contact with humans, animals and other organisms. Therefore, an attempt has been made to present known information on the toxicity of *Jatropha* species. The toxicity of *Jatropha* extracts from fruits, roots, oil, roots, latex, bark and leaves to a number of species, microorganisms, and animals is well established. In general, these extracts have moluscicidal, piscicidal, insecticidal, rodenticidal, antimicrobial, and cytotoxic properties, and have adverse effects on animals, including rats, poultry,



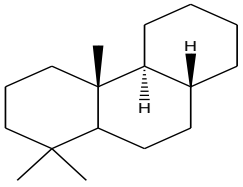
3b-Acetoxy-12-methoxy-13-methyl-podocarpa-8,11,13-triene-7-one



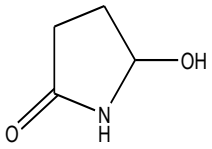
3b,12-Hydroxy-13-methyl-podocarpa-8,10,13-triene



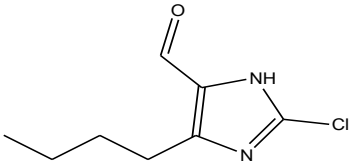
Tigliane



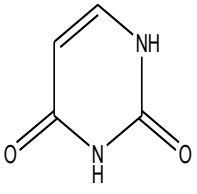
Podocarpane



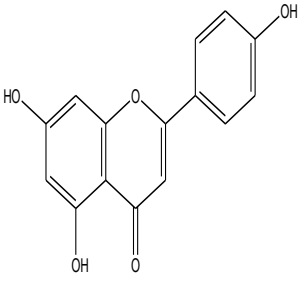
5-Hydroxypyrrolidine-2-one



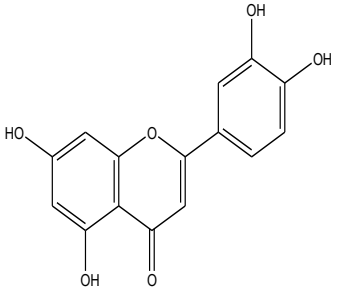
4-Butyl-2-chloro-5-formyl-1H-imidazole



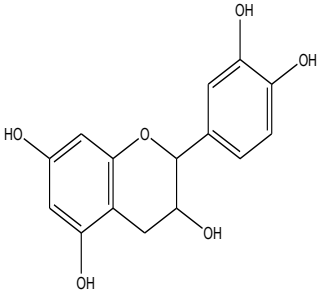
Uracil



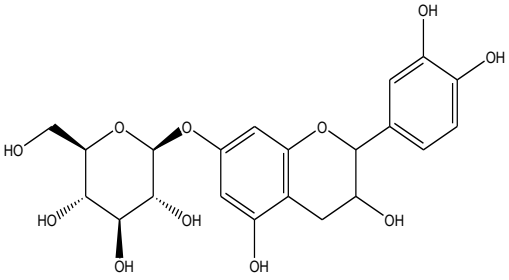
Apigenin



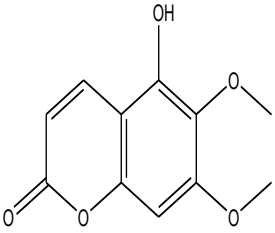
Luteolin



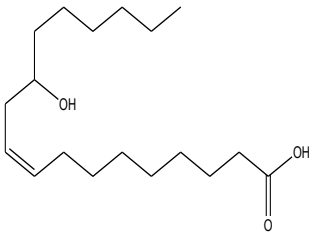
Catechin



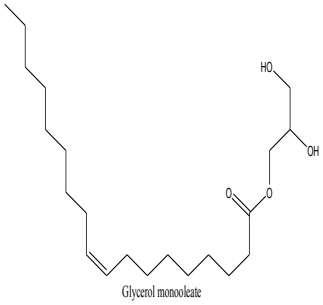
Catechin-7-O-b-glucopyranoside



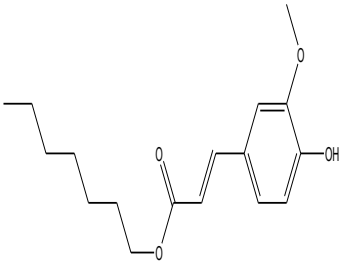
5-Hydroxy-6,7-dimethoxycoumarin



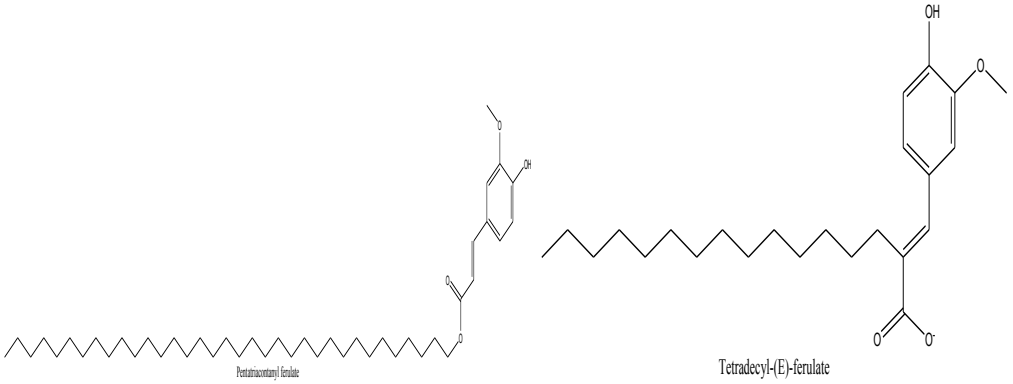
12-Hydroxyoctadec-cis-9-enoic acid

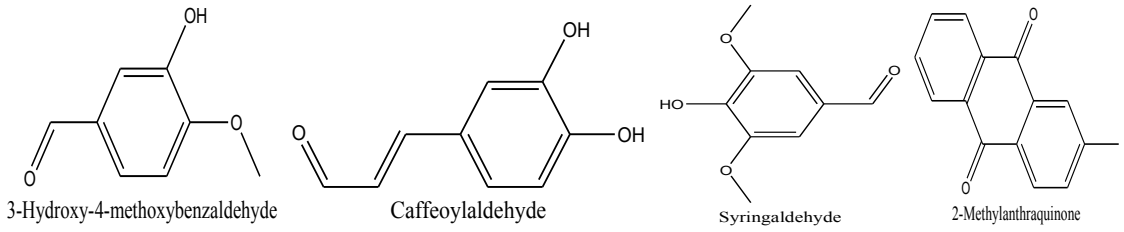


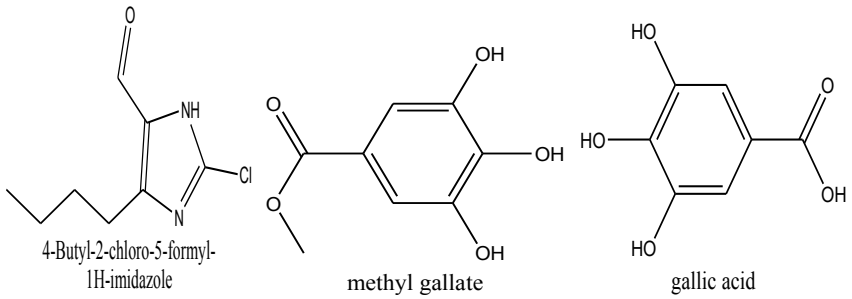
Glycerol monooleate

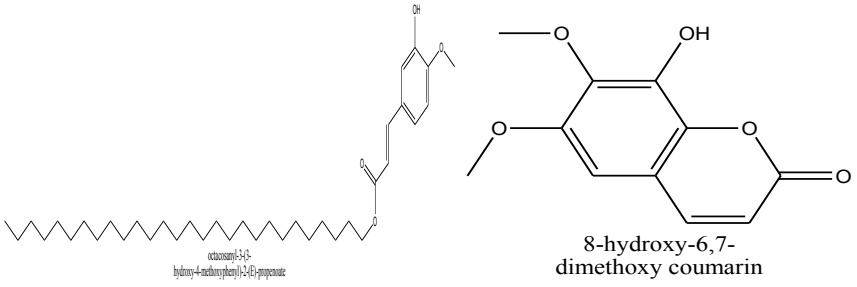


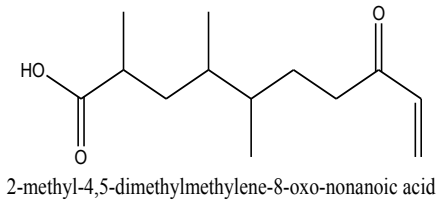
n-Heptyl ferulate


Pentatriacontanyl ferulate
Tetradecyl-(E)-ferulate


3-Hydroxy-4-methoxybenzaldehyde
Caffeoylaldehyde
Syringaldehyde
2-Methylanthraquinone


4-Butyl-2-chloro-5-formyl-1H-imidazole
methyl gallate
gallic acid


octacosanyl-3-(3-hydroxy-4-methoxyphenyl)-2-(E)-propenoate
8-hydroxy-6,7-dimethoxy coumarin


2-methyl-4,5-dimethylmethylene-8-oxo-nonanoic acid

and ruminants. The toxicity attributed to these seeds due to accidental consumption by children is also well documented. An attempt has also been made to identify areas requiring further study. The information provided in this study could help to raise awareness among agro-industries involved in the cultivation, harvesting and use of these plants and its products and, consequently, in the application and implementation of food safety measures. Data on the bioactivity of the genus *Jatropha* and its products have been identified and it is hoped that this will create new opportunities for the exploitation of these chemicals by the pharmaceutical industry to develop chemotherapeutic agents.[50]

Lioglier[51] reported that the seeds of *Jatropha* species are highly toxic and advised against their usage in herbal medicine. The toxic element in the seed is a toxalbumin named jatrophin which causes agglutination and haemolysis of red cells and also injurious to other cells.[52] The toxicological effects of *J. curcas* oil in rats reported an acute oral LD_{50} of the oil to be ion of the oil were found to have a haemolytic action at 25l and 100l g/mL of saline brine shrimp. Carp (*Cyprinus carpio*) were discovered to be highly susceptible to phorbol esters and gave antagonism effects at 15 ppm in its diet. A level higher than 311 g/mL of extract in the diet lowered its average metabolic rate, increased fecal mucus production and rejection of feed. Furthermore, Mongkolvisut et *al*.[53] reported that the latex of *J. integerrima* were known to be toxic and its leaf can cause squeamish, stomachalgia and has a strong purgative effect. Levin et *al*.[54] reported an incident of two unrelated healthy boys (9.5 and 8.5 years of age) who experienced intractable vomiting, colicky abdominal pain and watery diarrhoea after one hour of ingesting probably more than ten seeds of *J. multifida* each. Another case was reported from Sri Lanka whereby a child spontaneously vomited several times and became drowsy after ingesting the seeds of the "Kapum Kiriya" (*J. multifida*) plant which was growing near a fence.[55] B Glucanase, a protein from the seed oil of *J. curcas* was reported to be toxic to mice with an LD_{50} of 2.22 g/kg.[56] Devappa et al. 2010a, b[50,57] in their review concluded that a number of *Jatropha* species have a mixture of toxic and antinutritional compounds. They were also suggested that phorbol esters and curcin are significant toxic compounds contain in organic solvent extracts and aqueous extracts, respectively.

CONCLUSION

The literature review showed that *Jatropha podagrica* Hook. is a less studied species pharmacologically and chemically, although its diversity in secondary metabolites. As a candidate plant for disease control, it is therefore imperative to evaluate the biological activity of this plant and to set up a research program for the development of new bioactive compounds against genetic and metabolic diseases such as sickle cell disease.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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