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Research Article

Genus *Enterolobium*: Traditional uses, chemistry, and biological activities

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ABSTRACT

The chemical composition, pharmacological activity and traditional uses of 20 species attributed to the genus *Enterolobium* (Fabaceae) as used in the South and Central America, and Tropical Africa, were revised and compared. A survey of the available literature shows that these species are used mostly for their anti-inflammatory and cytotoxic activities. Additionally, some of these *Enterolobium* species showed antibacterial, antifungal, insecticidal, molluscicidal and larvicidal activities. Generally, the triterpenes or the phenolic compounds isolated from these plant extracts are assumed to be the bioactive principles.

Keywords: *Enteroobium*; traditional uses; chemical constituents; biological activities.

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1. INTRODUCTION

In recent times, interest in plant research has increased all over the world owing to its potential use in traditional systems of medicine for treating a wide variety of diseases. Various medicinal plants have been identified and modern scientific approaches have been used to study their authenticity, safety, and efficacy of their therapeutic use. The results highlight the great potential of medicinal plants in the field of pharmacology. *Enterolobium* is an important genus of family Fabaceae belongs to subfamily Mimosoideae. It comprises 12 species of flowering plants native to tropical and warm-temperate regions of the Americas. They are medium-sized to large trees. Some of these *Enterolobium sp*, including, *Enterolobium timbouva* are cultivated in Egypt **[1]**. Genus *Enterolobium* is closely related to Albizia and Samanea and is probably only maintained as a separate genus due to its widespread cultivation. The focus of this review is to provide information on the structures and biological activities of compounds isolated and identified from genus *Enterolobium.*

2. MATERIALS AND METHODS

The pharmacological activities of compounds isolated and identified from *Enterolobium* were searched through SciFinder that retrieves information in databases produced by Chemical Abstracts Service (CAS) as well as the MEDLINE database of the National Library of Medicine. The CAS databases are CAplusSM (reference database), REGISTRYSM (chemical structure database), CASREACT® (chemical reaction database), CHEMCATS® (commercial source database), and CHEMLIST® (regulatory database). The data were updated in Septemper 2016, using biological activities or chemical constituents and Enterolobiumas keywords.

3. RESULTS AND DISCUSSION

3.1. Chemical constituents

Deep reviewing of literature concerning genus Enterolobium revealed the isolation and separation of different following classes of compounds:

3.1.1 Triterpenes

Marx and Trusch, 1963, isolated lupeol (1) and lupeyl acetate (2) from the hexane fraction of *E. contortisiliquum* **[1]**. Marx and Trusch, 1967, isolated triterpene of the β-amyrin type, the lactone of machaerenic acid from the fruits of *E. contortisiliquum* **[2]**. Delgado et al., 1984, isolated the triterpenes 3β-hydroxy-21β-E-cinnamoyl-oxyolean-12-en-20-oic acid (3), 3β, 21β-dihydroxyolean-12-en-28-oic acid (machaerinic acid) (4) and its lactone (3β-hydroxyolean-12-en-21β→28-lactone) (5) from the fruits of *E. contorstisiliquum*. Methyl and ethyl esters of 3β, 21β-dihydroxyolean-12-en-oic acid was isolated and characterized as artifacts **[3]** as shown in figure **Fig. 1**

Mimaki *et al.*, 2003, isolated two triterpene bisdesmosides, designated as enterolosaponins A (6) and B (7), from the n-butanol soluble fraction of the aqueous extract of the pericarps of E. contortisiliquum as shown in **Fig. 2 [4]**.

Mimaki *et al.*, 2004, isolated seven bisdesmosidic triterpene saponins, with up to eight monosaccharides, which were given the trivial names contortisiliosides A→G (8-14) from the n-butanol soluble fraction of the aqueous extract of the pericarps of *E. contortisiliquum* **[6]** as shown in **Fig. 3**.

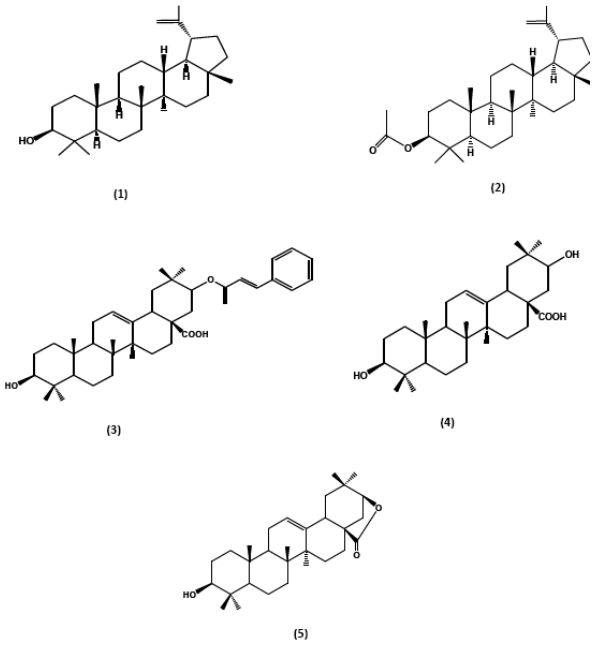
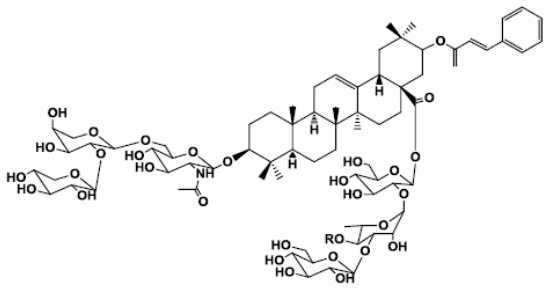
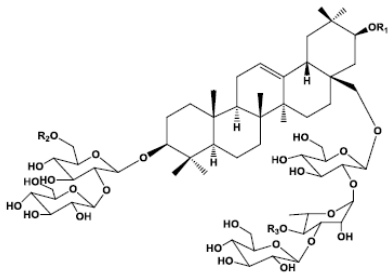


Fig. 1 Chemical structures of compounds **(1-5)** isolated from *E. contortisiliquum*



*Compound 6 (R= α-l-arabino-furanosyl group), Compound 7(R= H)

Fig. 2 Chemical structures of Enterolosaponins A **(6)** (R= α-l-arabino-furanosyl group) and Enterolosaponins B **(7)** (R= H) isolated from *E. contortisiliquum*



Compound	R1	R2	R3
8	Cinnamoyl	Xylose-(1→ 2 arabinose)	H
9	Cinnamoyl	Xylose-(1→ 2 arabinose)	α-L-arabino-furanosyl
10	Cinnamoyl	Xylose-(1→ 2 galactose)	α-L-arabino-furanosyl
11	H	Xylose-(1→ 2 arabinose)	H
12	H	Xylose-(1→ 2 arabinose)	α-L-arabino-furanosyl
13	H	Xylose-(1 →2 galactose)	α-L-arabino-furanosyl
14	H	H	α-L-arabino-furanosyl

Fig. 3 Chemical structures of compounds **(8-14)** isolated from *E. contortisiliquum*

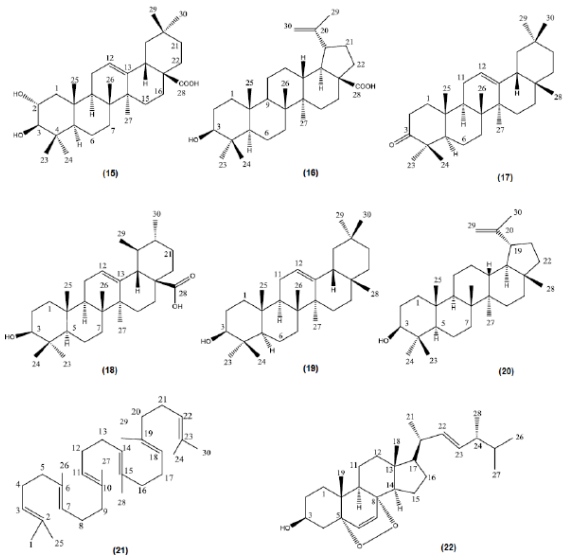


Fig. 4 Chemical structures of compounds **(15-20)** isolated from *E. contortisiliquum*

Triterpenes maslinic acid (15), betulinic acid (16), 3-oxo-β-amyrin (17), ursolic acid (18), β amyrin (18), lupeol (19) and squalene (20) **Fig. 4** were isolated from the fruits of *Enterolobium* contortisiliquum **[5]**. Hanna, 1981, identified three saponins from *E. cyclocarpum*. All have machaerenic acid aglycone, differing in their sugar moiety either glucosylgalactose or rhamno-galactoside or glucoside **[6]**.

3.1.2 Phenolics

Ten phenolic compounds were isolated for the first time from *Enterolobium contortisiliquum* leaf extract including 3,4-Dihydroxy-Cinnamic acid (Caffeic acid) (21); Quercetin-3-O-β-D-glucopyranoside (Isoquercitrin) (22); Quercetin-3-O-β-D-galactopyranoside (Hyperin) (23); Kaempferol-3-O-β-D–glucopyranoside (Astragalin) (24); Hesperetin-7-O-rutinoside (Hesperidin) (25); Quercetin 3-O-rutinoside (Rutin) (26); Quercetin (27); Kaempferol (28); 7-methoxycoumarin (Herniarin) (29); and Chrysin (30) **Fig. 5 [7]**. Gallic acid, protocatechuic acid, quercetin-7-rutinoside, catechin, isovitexin, and quercetin were isolated from *Enterolobium contortisiliquum* pods using polyamide column fractionation. Besides, HPLC analysis of the phenolic fraction revealed the presence of pyrogallol, syringic and p-coumaric acids **[8]**.

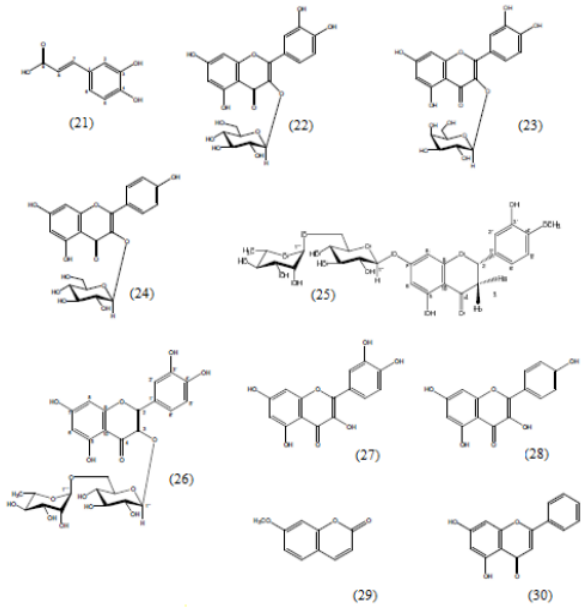


Fig. 5 Chemical structures of compounds **(21-30)** isolated from *E. contortisiliquum*

3.1.3 Fatty Acids

Ikechukwu *et al.*, 1998, studied 15 tropical seeds gathered in Nigeria including *Enterolobium cyclocarpium* seeds to determine their fat content and the fatty acid composition of their oils. The oil of *Enterolobium cyclocarpium* was found to contain high proportions of linoleic and oleic acid as well as palmitic and linolenic acid. It was assumed that some of these less familiar wild seeds could be used as sources for industrial or edible oils, provided that possible toxic constituents could be removed **[9]**. GC-MS analysis of unsaponifiable matter of *Enterolobium contortisiliquum* revealed that α- and β-amyrin and 4-methyl 2, 6-di-tert-butylphenol are the main components, while palmitic and 9, 12-octadecadienoic acids were the major fatty acids **[10]**.

3.1.4 Essential oils

Shahat *et al.*, 2006, isolated essential oils from seeds of *Enterolobium contortisiliquum*. Seeds of *Enterolobium contortisiliquum* were subjected to steam distillation to obtain a light yellow essential oil in a yield of 3 ml/kg of seeds. The major components of the oil were identified using gas chromatography/mass spectrometry (GC-MS) and were furfural, limonene, linalool, estragole, carvone, and apiole with carvone representing more than 50% of the total composition **[11]**.

3.1.5 Carbohydrates

Oliveira, Silva *et al.* 2001, investigated the composition, structure and rheological properties of *Enterolobium contortisilliquum* gum. The gum proved to contain galactose, arabinose, rhamnose and glucuronic acid as main monosaccharide components. 13C nuclear magnetic resonance spectroscopy revealed that the anomeric composition is similar to the *Enterolobium cyclocarpum* exudate; however, no 4-O-methylglucuronic acid was detected for *E. contortisilliquum* **[12]**. Nine sugar components were identified in hydrolysate of *Enterolobium contortisilliquum* mucilage with glucose (34.89%), xylose (6.78%) and rhamnose (5.98%) being the predominant sugars by GLC **[10]**. Oliva et al. 1987 carried out a structural study of the gum exudate from *Enterolobium cyclocarpum* using chemical methods and 13C NMR spectroscopy. The results revealed that the structure of this gum is essentially a beta-(1-->3)-galactan. Some galactoses are 6-O-linked and others also occur as terminal residues. There is evidence that supports the presence of alpha-L-arabinofuranose and beta-L-arabinopyranose. The beta-d-glucuronic acid may be present as terminal and internal residues, while the 4-O-methyl-alpha-D-glucuronic acid residues exist predominantly in internal positions **[13]**.

3.2 Biological activities of genus *Enterolobium*:

3.2.1 Cytotoxic activity

The aqueous alcohol extract of *Enterolobium contortisilliquum* leaves exhibited potent cytotoxic activity against different cancer cell lines with IC_{50} values of 2.67 μg/mL against MCF-7 cell line, 3.89 μg/mL against HCT116 cells, 4 μg/mL against HEp2 cells, 4.5 μg/mL against HeLa cells, 1.7 μg/mL against PC-3 cells, and 5.7 μg/mL against Huh-7 cells. *In vitro* cytotoxic assay of the isolated pure compounds against Huh-7 cell Line showed that compounds 1, 9 and 10 are the only tested compounds exhibiting potent cytotoxic activity with IC_{50} of 3 μg/mL, 0.76 μg/mL, and 18.51 μg/mL respectively. The rest of the tested compounds exhibited IC_{50} exceeding 1000 μg/mL which reflects their safety **[1]**. Mimaki et al., 2003, examined the cytotoxic activities of enterolosaponins A and B isolated from E. contortisiliquum against BAC1.2F5 mouse macrophages, EL-4 mouse lymphoma cells, and L-929 mouse fibroblasts. Although enterolosaponin B and the de-(E)-cinnamoyl derivative of enterolosaponin A did not show any apparent cytotoxic activities against all the cell lines, enterolosaponin A exhibited a highly

selective cytotoxicity against BAC1.2F5 mouse macrophages with an LD_{50} value of about 3 μM. The cinnamoyl group attached to the C-21β-hydroxyl group and the terminal α-l-arabino-furanosyl groups were considered to be essential for the selective cytotoxicity **[6]**. It should be notable that the macrophage death caused by enterolosaponin A was shown to be neither necrotic nor apoptotic from the morphology of the dead cells, whose cytosol occurred in vacuolation. Although the precise mechanism is unknown, one possibility could be raised that enterolosaponin A caused fusion of endosomal membranes to make the large vacuole structure after it internalized by macrophages. Mimaki et al., 2004, evaluated for the cytotoxic activities of the seven triterpene saponins (contortisiliosides A-G) isolated from *E. contortisiliquum* against BAC1.2F5 mouse macrophages, EL-4 mouse lymphoma cells, and L-929 mouse fibroblasts. Whereas contortisiliosides A and C were moderately cytotoxic to both BAC1.2F5 macrophages and EL-4 cells, and contortisiliosides D-G did not show any apparent cytotoxic activities against the three cell lines, contortisilioside B exhibited selective cytotoxic activity against BAC1.2F 5 mouse macrophages, with an IC_{50} value of 3.4 μM **[14]**. The above results imply that the cinnamoyl group at C-(21) of the aglycone is essential for the cytotoxicities against macrophages and lymphoma cells. The selective cytotoxicity against macrophages is particularly sensitive to the structures of the oligosaccharide moieties. It should be noted that the macrophage death caused by contortisilioside B was shown to be neither necrotic nor apoptosis-inducing according to the unique morphological change of the dead cells, whose cytosols were converted into large vacuolar structures. Oliva *et al.*, 2007, identified and characterized proteinase inhibitors from the seed of *E. contortisiliquum* that can be used to prevent proteolysis of the extracellular matrix in the treatment of cancer. The inhibitors have distinct spectra of inhibition and show different levels of effectiveness in inhibiting the growth of tumor cell lines in culture. They interacted synergistically with 5-fluorouracil in the inhibition of tumor cell growth **[15]**.

Nakahata *et al.*, 2011, stated that supplementary to the efficient inhibition of trypsin, chymotrypsin, plasma kallikrein, and plasmin already described by *E. contortisiliquum* Trypsin Inhibitor (EcTI) from *E. contortisiliquum*, it also blocks human neutrophil elastase and prevents phorbol ester (PMA)-stimulated activation of matrix metalloproteinase (MMP)-2 probably via interference with membrane-type 1(MT1)-MMP. Moreover, plasminogen-induced activation of proMMP-9 and processing of active MMP-2 was also inhibited. Furthermore, the effect of EcTI on the human cancer cell lines HCT116 and HT29 (colorectal), SkBr-3 and MCF-7 (breast), K562 and THP-1 (leukemia), as well as on human primary fibroblasts and human mesenchymal stem cells (hMSCs) was studied. EcTI inhibited rather specifically tumor cell viability without targeting primary fibroblasts and hMSCs. It was stated that the polyspecific proteinase inhibitor EcTI prevents proMMP activation and is cytotoxic against tumor cells without affecting normal tissue remodeling fibroblasts or regenerative hMSCs being an important tool in the studies of tumor cell development and dissemination. de Paula *et al.*, 2012, studied the effect of the plant proteinase inhibitor (EcTI) from *E. contortisiliquum*, on the adhesion, migration, and invasion of gastric cancer cells. EcTI showed no effect on the proliferation of gastric cancer cells or fibroblasts but inhibited the adhesion, migration and cell invasion of gastric cancer cells, however, had no effect upon the adhesion of fibroblasts. EcTI was shown to decrease the expression and to disrupt the cellular organization of molecules involved in the formation and maturation of invadopodia, such as integrin β1, cortactin, N-WASP, MT1-MMP, and MMP-2. Moreover, gastric cancer cells treated

with EcTI presented a significant decrease in intracellular phosphorylated Src and FAK, integrin-dependent cell signaling components **[16]**. Together, these results indicate that EcTI inhibits the invasion of gastric cancer cells through alterations in integrin-dependent cell signaling pathways. The aqueous alcohol extract of *Enterolobium contortisilliquum* leaves exhibited potent cytotoxic activity against different cancer cell lines with IC_{50} values of 2.67 µg/mL against MCF-7 cell line, 3.89 µg/mL against HCT116 cells, 4 µg/mL against HEpG2 cells, 4.5 µg/mL against HeLa cells, 1.7 µg/mL against PC-3 cells, and 5.7 µg/mL against Huh-7 cells. In vitro cytotoxic assay of the isolated pure compounds against Huh-7 cell Line showed that compounds 1, 9, and 10 are the only tested compounds exhibiting potent cytotoxic activity with IC_{50} of 3 µg/mL, 0.76 µg/mL, and 18.51 µg/mL, respectively. The rest of the tested compounds exhibited IC_{50} exceeding 1000 µg/mL which reflects their safety **[1]**.

The cytotoxicity of the methanolic extract of *Enterolobium cyclocarpum* leaves was investigated using the brine shrimp lethality assay, MTT assay using cervical (HeLa) and breast (MCF7) cancer cell lines, cell cycle analysis and Annexin V-FITC/PI assay. The extract showed cytotoxic activity with the LC_{50} value of 31.63 µg/mL. Significant growth inhibition was observed in both cell lines with IC_{50} values of 2.07±1.30 µg/mL and 11.84±1.18 µg/mL for HeLa and MCF7, respectively. Cell cycle analysis indicated that HeLa cells were arrested in the G2/M phase while MCF7 cells arrested in the G1/G0 phase. The Annexin V-FITC/PI assay revealed phosphatidylserine translocation in both cell lines and thus apoptosis induction upon treatment with the extract. The crude extract (70% alcohol) of *Enterolobium contortisiliquum* pods and the saponin fraction exhibited potent cytotoxic activity on HepG2 (IC_{50} 14 and 29 µg/mL) and MCF7 (IC_{50} 16 & 31 µg/mL) cell lines **[18]**. The mucilage and petroleum ether fractions showed cytotoxicity activity on HepG2 with (IC_{50} 19 & 61 µg/mL), while phenolic fraction showed cytotoxicity towards MCF7 cells with the IC_{50} value of 79 µg/mL **[12]**.

3.2.2 Inflammatory activity

Castro-Faria-Neto *et al.*, 1991, investigated the pro-inflammatory activity of enterolobin, a hemolytic protein from *E. contortisiliquum* seeds. In doses ranging from 1 to 20 µg/site, enterolobin induced a dose-dependent paw edema and pleurisy in rats. One hour after the intrathoracic injection of enterolobin, the total leukocyte content of the pleural cavity increased significantly, mainly due to mononuclear and neutrophil accumulation. At 24 h, although the no. of mononuclear and neutrophil cells tended to decrease, a great rise in eosinophil counts was noted. Intraperitoneal treatment with the dual lipoxygenase and cyclooxygenase blockers, BW 755c (25 mg/kg) and NDGA (50 mg/kg), or the corticosteroid dexamethasone (0.1 mg/kg) inhibited enterolobin-induced paw edema by 35, 38, and 47% resp., whereas indomethacin (2 mg/kg) was inactive. The H1 antagonist, meclizine (25 mg/kg), was also effective against enterolobin edema, while the PAF antagonists WEB 2086 and PCA 4248 (20 mg/kg) did not modify the reaction. It was concluded that enterolobin is a potent inducer of pleural exudation, cellular infiltration, and paw edema. Furthermore, enterolobin-induced edema is partially dependent on lipoxygenase metabolites and histamine, while PAF and prostaglandins did not seem to be important in this reaction **[19]**.

3.2.3 Insecticidal, molluscicidal and larvicidal activities

Rehr *et al.*, 1973, studied the presence of insecticidal amino acids in different legume seeds. They stated that certain legumes are free from predation on their seeds due to the presence of insecticidal amino acids in these seeds. *E. cyclocarpum* seeds proved to be one of those

seeds due to the presence of albizziine amino acid [$H_2NCONHCH_2CH(NH_2)COOH$]. Soussa *et al.*, 1993, tested for the toxic effects enterolobin, the cytolytic and inflammatory protein isolated from *E. contortisiliquum* seeds, on larvae of the coleopteran *Callosobruchus maculatus* and the *Lepidopteran Spodoptera littoralis* **[21]**. Bioassays performed with enterolobin incorporated into artificial seeds showed that the phytocytolysin was toxic to larvae of *C. maculatus*, and proved to be innocuous to *S. littoralis* larvae. In vitro proteolysis studies using larval gut enzymes, analyzed on SDS-PAGE, showed that only *S. littoralis* proteases could digest enterolobin, suggesting that the insect's digestive proteases were able to inactivate the cytolysin before it could exert any toxic effect. *C. maculatus* proteases, on the other hand, were unable to hydrolyze enterolobin. The mechanism of toxicity of enterolobin did not appear to involve any damage to the microvilli of the epithelial gut cells of *C. maculatus* as shown by electron microscopy. Some tentative hypotheses are considered in order to explain the toxic mechanism of action of enterolobin towards C. maculatus. Moura *et al.*, 2007, purified Chitin-binding vicilin from E.contortisiliquum seeds by ammonium sulfate followed by gel filtration on Sephacryl 300-SH and on Sephacryl 200-SH. The vicilin, called E.contortisiliquum vicilin (EcV), is a dimeric glycoprotein. It was tested for anti-insect activity against Callosobruchus maculatus and Zabrotes subfasciatus larvae and for phytopathogenic fungi, *Fusarium solani* and *Colletrichum lindemuntianum*. EcV was very effective against both bruchids, and also exerted an inhibitory effect on the germination of *F. solani* at concentrations of 10 and 20 μg mL-1 **[20]**. Farias *et al.*, 2010, assessed the toxicity of seed water extracts of 15 leguminous species including *E.contortisiliquum* upon *Aedes aegypti* larvae responsible for dengue and yellow fever. A partial chemical and biochemical characterization of water extracts, as well as assessment of their acute toxicity in mice, were performed. *E.contortisiliquum* extract, as well as other three leguminous species, extracts caused 100% of larval mortality after 1 to 3 h of exposure. The extracts showed low toxicity to mice (LD_{50} > 0.15 ± 0.01 g/kg body weight), but despite these promising results, further studies are necessary to understand the toxicity of these extracts and their constituents from primary and secondary metabolism upon *Aedes aegypti* [22].

3.2.4 Spermicidal activity

Elbary and Nour, 1979, investigated the spermicidal effects of saponins isolated from *E. cyclocarpum*. They showed that all saponins tested were spermicidal independent on their nature.

3.2.5 Antifungal activity

Quiñones *et al.*, 1995, tested the antifungal activity of ethanol and water extracts from the heartwood of *E. cyclocarpum*. The fungi tested were *Trametes versicolor* (white rot), Coniophora puteana (brown rot), *Chaetomium globosum* (soft rot) and the mold-fungus *Trichoderma viride*. Only the ethanol extract showed a distinct fungistatic effect, even at low concentrations. But the water extract had no impact on fungal growth **[23]**.

3.2.6 Hepatogenous photosensitization activity

Grecco *et al.*, 2002, reported three outbreaks of hepatogenous photosensitization in cattle caused by *E. contortisiliquum* pods. Clinical signs were anorexia, depression, photo-sensitization, and abortion. Most affected cattle recovered in 30-40 days. At necropsies, the liver was present, the gallbladder was enlarged and edematous, and numerous seeds of *E. contortisiliquum* were in the forestomachs and abomasum. Fruits of the plants administrated to 2 calves produced clinical signs and 2/4 died. Clinical chemistry, gross necropsies, and histopathology confirmed gastrointestinal irritation and liver degeneration. One calf dosed

with only *E. contortisiliquum* leaves did not develop clinical signs **[24]**.

3.2.7 Antimicrobial activity

The antibacterial activity of different fractions of *E. contortisiliquum* fruit extract was evaluated against seven Gram-positive and six Gram-negative microorganisms using the agar well diffusion assay method. Maximum inhibition was observed with compounds at 1 mg/mL; catechin and protocatechuic acid against Pseudomonas aeruginosa (-ve) (14.5 and 17 mm, respectively) while, the crude and petroleum ether extracts showed antimicrobial activity against Micrococcus luteus (+ve) (inhibition zone 12 and 10 mm, respectively). Whereas, polysaccharide and protein exhibited antimicrobial activity against Klebsiella pneumonia (-ve) (16 and 13 mm, respectively) **[10]**. Shahat *et al.*, 2008, evaluated for the antimicrobial activities of the essential oil isolated from seeds of *E. contortisiliquum*.

The antimicrobial activities were determined against four species of Gram-positive bacteria (Bacillus subtilis, Bacillus cereus, Staphylococcus aureus, Micrococcus luteus) and two Gram-negative bacteria (Klebsiella pneumoniae, Serratia Marcescencs). The essential oil inhibited the growth of all tested bacteria but was most effective against the gram-positive bacteria. Chemicals that are responsible for the antibacterial effect of the essential oil were determined using the bio-autography thin layer chromatography (TLC) technique. The active compounds responsible for the activity were found to be carvone and estragole.

3.2.8 Proteinase inhibitor

Oliva *et al.*, 1987, purified two types of proteinase inhibitors from *E. contortisiliquum* beans. The inhibitor of serine proteinases inhibited trypsin, chymotrypsin, and plasma kallikrein, but not tissue kallikreins. The 2nd inhibitor, with activity directed against mercaptoproteinases, was isolated by CM-papain-Sepharose. Papain and bromelain were inhibited **[24]**. Sampaio *et al.*, 1992, studied serine proteinase inhibitors, in the seeds of *E. contortisiliquum* using bovine trypsin, Factor XIIa, and human plasma kallikrein. *E. contortisiliquum* inhibitor inactivated all three enzymes. It was assumed that the trypsin inhibitor isolated from *E. contortisiliquum*, is of the Kunitz type **[25]**. Batista *et al.*, 1996, isolated a trypsin inhibitor from *E. contortisiliquum* seeds. It was found that ECTI (contortisiliquum trypsin inhibitor) strongly inhibits bovine trypsin and chymotrypsin and also some serine proteinases involved in the blood clotting cascade and fibrinogen proteolysis: human plasma kallikrein, factor XIIa and plasmin. ECTI showed no inhibitory activity on factor Xa, thrombin or tissue kallikrein or as on cysteine proteinases such as papain and bromelain. ECTI didn't affect thrombin time (TT) or prothrombin time (PT) but increased activated partial thrombin time (APTT) **[17]**.

3.3 Folk and traditional uses of genus *Enterolobium*

The wide spreading canopy of a mature *Enterolobium* makes it an ideal shade tree, whether for livestock in pasture lands, for perennial crops such as coffee, or in roadside and urban plantings **[26]**. *Enterolobium cyclocarpum* has been proposed as an alternative for rehabilitation of marginal soils, due to its ability to form a symbiotic association with nitrogen-fixing soil microorganisms **[27]**. Fruits and leaves are used as forage allowing cattle to feed directly from the tree or as a nutritional complement in combination with the fodder **[28]**. The wood *E. cyclocarpum* is resistant to attack by dry-wood termites, which makes it feasible to be used in house construction. It is also used as firewood due to its high caloric content.

Enterolobium wood may also be used for boat-building because of its durability in water; it

has been used in the past for water-troughs and dug-out canoes. Mature fruits contain a gummy-resinous juice which along with their own smashed pulp is used to produce charcoal **[29]**. Seeds of *E. cyclocarpum* are rich in protein (up to 35%), and its amino acid composition is comparable to that of wheat or fish flour. Seeds also contain iron, calcium, phosphorus and ascorbic acid. In some places, they are consumed in sauces, soups and as a coffee substitute, and several medicinal properties have been attributed to them **[30]**. The root decoction of *E. saman* is used in hot baths for stomach cancer in Venezuela. Rain Tree is a traditional remedy for colds, diarrhea, headache, intestinal ailments, and stomachache. The leaf infusion is used as a laxative In the West Indies; seeds are chewed for a sore throat. The alcoholic extract of the leaves inhibits Mycobacterium tuberculosis. In Colombia, the fruit decoction is used as a sedative **[31]**. Besides the traditional uses, several biotechnological applications have been proposed for this tree, such as the use of its gum as a fungi culture substrate or for the production of ice cream and yogurt **[32]**.

4. CONCLUSION AND RECOMMENDATIONS

The plants of the genus *Enterolobium* have long been used in folk medicine for the treatment of different pathological conditions. In recent years, the scientific interest in plants of *Enterolobium* genus has increased greatly. Substantial progress on chemistry and pharmacological properties of this genus has shown it. Some species showed antimicrobial, anti-inflammatory, antifungal, and anticancer activities. Pharmacological studies have confirmed some uses in folk medicine. Triterpenes and phenolic compounds are of particular interest as many are highly potent bioactive and perhaps responsible for most of the activities shown by the plants of this genus.

A detailed study is recommended to understand the structure-activity relationship of these constituents. Many plant extracts of *Enterolobium* showed biological activity. However, the particular constituent responsible for the activity has not always been isolated in the further process. Furthermore, some plant extracts were only preliminary studied for their in vitro activities, so, the advanced clinical trial of them deserves to be further investigated.

5. REFERENCES

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