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: Enterobium, traditional uses, chemical constituents and biological activities
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* species, 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. Material 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 September 2016, using biological activities or chemical constituents and *Enterolobium*as 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-amyрин 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 (machaerenic acid) (4) and its lactone (3β-hydroxyolean-12-en-21β→28-lactone) (5) from the fruits of *E. contortisiliquum*. Methyl and ethyl esters of 3β, 21β-dihydroxyolean-12-en-oic acid were isolated and characterized as artifacts [3] as shown in figure 1.

![Chemical structures of compounds (1-5)](image)

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

*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 figure 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 figure 3.

<table>
<thead>
<tr>
<th>Compound</th>
<th>(R_1)</th>
<th>(R_2)</th>
<th>(R_3)</th>
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<tbody>
<tr>
<td>8</td>
<td>Cinnamoyl</td>
<td>Xylose-(1(\rightarrow)2\ arabinose)</td>
<td>H</td>
</tr>
<tr>
<td>9</td>
<td>Cinnamoyl</td>
<td>Xylose-(1(\rightarrow)2\ arabinose)</td>
<td>(\alpha)-L-arabino-furanosyl</td>
</tr>
<tr>
<td>10</td>
<td>Cinnamoyl</td>
<td>Xylose-(1(\rightarrow)2\ galactose)</td>
<td>(\alpha)-L-arabino-furanosyl</td>
</tr>
<tr>
<td>11</td>
<td>H</td>
<td>Xylose-(1(\rightarrow)2\ arabinose)</td>
<td>H</td>
</tr>
<tr>
<td>12</td>
<td>H</td>
<td>Xylose-(1(\rightarrow)2\ arabinose)</td>
<td>(\alpha)-L-arabino-furanosyl</td>
</tr>
<tr>
<td>13</td>
<td>H</td>
<td>Xylose-(1(\rightarrow)2\ galactose)</td>
<td>(\alpha)-L-arabino-furanosyl</td>
</tr>
<tr>
<td>14</td>
<td>H</td>
<td>H</td>
<td>(\alpha)-L-arabino-furanosyl</td>
</tr>
</tbody>
</table>

Figure 3. Chemical structures of compounds \((8-14)\) isolated from \(E.\ contortisiliquum\)
Triterpenes maslinic acid (15), betulinic acid (16), 3-oxo-β-amin (17), ursolic acid (18), β amyrin (18), lupeol (19) and squalene (20) were isolated from the fruits of Enterolobium contortsiliquum [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].

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

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-galacto-pyranoside (Hyperin) (23); Kaempferol-3-O-β-D-glucopyranoside (Astragal) (24); Hesperetin-7-O-rutinoside (Hesperidin) (25); Quercetin 3-O-rutinoside (Rutin) (26); Quercetin (27); Kaempferol (28); 7-methoxycoumarin (Herniarin) (29); and Chrysin (30) [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].
Figure 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 apiol 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 contortisiliquum gum. The gum proved to contain galactose, arabinose, rhamnose and glucuronic acid as main monosaccharide components. $^{13}$C 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. contortisiliquum [12]. Nine sugar components were identified in hydrolysate of Enterolobium contortisiliquum 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 $^{13}$C 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. 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 contortisiliquum 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 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 at the C-21β-hydroxyl group and the terminal α-l-arabinofuranosyl group 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 morphology of the dead cells, whose cytosol occurred in vacuolation. Although the precise mechanism is unknown, one possible 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 particular 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 killed cells, whose cytosols were converted into large vacuolar structures. Oliva et al., 2007, identified and characterized proteinase inhibitors from 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 contortisiliquum* leaves exhibited potent cytotoxic activity against different cancer cell lines with IC\textsubscript{50} values of 2.67 μg/mL against MCF-7 cell line, 3.89 μg/ml against HCT\textsubscript{116} cells, 4 μg/mL against HEp\textsubscript{2} 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\textsubscript{50} of 3 μg/mL, 0.76 μg/mL, and 18.51 μg/mL respectively. The rest of tested compounds exhibited IC\textsubscript{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 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 G$_2$/M phase while MCF7 cells arrested in the G$_1$/G$_0$ 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 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 H$_1$ 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 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 [H₂NCONH₂CH(NH₂)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, analysed 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 hydrolyse 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 *Collettrichum 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 (LD50 > 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 mould-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, 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 were evaluated against seven Gram-positive and six Gram-negative microorganisms using 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 Marcescens*). 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 bioautography 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 drywood termites, which makes it feasible to be used in house construction. It is also useful 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 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 progresses on chemistry and pharmacological properties of this genus have showed 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 bioactives and perhaps responsible for most of 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 further process. Furthermore, some plant extracts were only preliminarly studied for their in vitro activities, so, the advance clinical trial of them deserves to be further investigated.
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