**Ximenia americana**: Chemistry, Pharmacology and Biological Properties, a Review

Francisco José Queiroz Monte¹, Telma Leda Gomes de Lemos¹, Mônica Regina Silva de Araújo² and Edilane de Sousa Gomes¹

Programa de Pós-Graduação em Química Universidade Federal do Ceará, Fortaleza - Ceará
Depatamento de Química, Universidade Federal do Piauí, Teresina - Piauí, Brasil

1. Introduction

The use of plants as medicinal agents to the treat of many diseases has been investigated for a long time since the antique civilizations. Several plants are used in traditional medicine against inflammatory diseases as well as various types of tumors on the base the potential of their chemical constituents. Although many compounds are extremely toxic, when we have the relation between the toxicity of a compound and its chemical pattern of substitution that can result in a more in-depth understanding of these compounds (Atta-ur-Rahman, 2005). Today, even after more than 200 years, the chemistry of natural products remains a challenge and an important field of research in several science areas (chemistry, biology, medicine, agronomy, botany and pharmacy). The reasons for it’s large use are the considerable pharmacological potential observed in natural products, in the great development in the process of detection, isolation, purification and, especially, the advances in spectrometric techniques [infrared (IR), mass spectrometry (MS) and nuclear magnetic resonance (NMR ¹H and ¹³C) for structural elucidation of new and complex compounds. These advances were outstanding in both NMR and MS spectrometry. The NMR allows the complete ¹H and ¹³C NMR spectral assignments (chemical shifts and coupling constants) which serve to build a data base to support computer assisted structure elucidation. These data are also useful in the fuller understanding of the correlations between molecular conformation and biological activity of natural substances with biological importance (Loganathan et al., 1990). Mass spectrometry has a huge application in chemistry, biochemistry, medicine, pharmacology, agriculture and food science. Although the mass spectrometric ionization techniques EI (electron impact) and CI (chemical ionization) required the analyte molecules to be present in the gas phase and were thus suitable only for volatile compounds, the development of several desorption ionization methods [FD (field desorption), FABMS (fast atom bombardment), ESIMS (electrospray), MALDI-MS (matrix assisted laser desorption ionization)] allowed the hight-precision mass spectrometric analysis of different classes of biomolecules.

The genus Ximenia belongs to the Olacaceae and comprises about 8 species (Brasileiro et al., 2008): Ximenia roiigi, Ximenia aegyptiaca, Ximenia parviflora, Ximenia coriaceae, Ximenia aculeata, Ximenia caffra, Ximenia americana and Ximenia aegyptica. X. caffra stands out for...
being used in Tanzania for the treatment of irregular menstruation, rheumatism and cancer (Chhabra & Viso, 1990) and, in Limpopo Province, South Africa, for treatment diarrhea (Mathabe, 2006). However, X. americana Linn. is the most common, being native to Australia and Asia where is commonly known as Yellow Plum or Sea Lemon. It is found mainly in tropical regions (Africa, India, New Zealand, Central America and south America), specially Africa and Brazil. The plant is characterized as a small tree spinose 3-4 feet tall, gray or reddish bark, with leaves small, simple, alternate, of bright green color and with a strong smell of almonds. The flowers are yellowish-white, curved and aromatic. Fruit are yellow-orange, aromatic, measuring 1.5 to 2.0 cm in diameter, surrounding a single seed and have a pleasant plum-like flavor (Matos, 2007). In Asia, the young leaves are consumed as a vegetable, however, the leaves also contain cyanide and need to be thoroughly cooked, and should not be eaten in large amounts.

X. americana, commonly called “ameixa do mato”, “ameixa de espinho” and “ameixa da Bahia”, is widely distributed in northeast Brazil. A tea obtained from its barks has been used in popular medicine as cicatrizing, adstringent and as an agent against excessive menstruation. As a powder, it treats stomach ulcers and the seeds are purgative (Braga, 1976; Pio-Correia, 1984). This specimen has been recently examined (Araújo et al., 2008,2009) and the stem ethanolic extract afforded steroids (stigmasterol and sitosterol), triterpenoids (betulinic acid, oleanolic acid, 28-O-(D-glucopyranosyl) oleanolic acid, 3-oxo-oleanolic acid, 3β-hydroxycholest-24(E)-ene-26-oic acid and sesquiterpenoids (furanoic and widdrane type). A large number of sesquiterpenes are constituents of essential oils of higher plants and seem to intervene in the pharmacological properties attributed to these volatile fractions (Bruneton, 1999). It has been clarified that the biological activities of the liverworths are due to terpenoids and lipophilic aromatic compounds (Atta-ur-Rahman, 1988). Steroids and triterpenes with therapeutic interest and manufacturing employment, are a group of secondary metabolites of outstanding importance (Bruneton, 1999). Considerable recent work strongly indicates the great potential of the triterpenoids as source of use medicinal (Mahato et al., 1992).

Investigations in the past 10 years showed that the constituents of X. americana have shown several biological activities such as, antimicrobial, antifungal, anticancer, antineoplastic, antityrpanosomal, antirheumatic, antioxidant, analgesic, moluscicide, pesticidal, also having hepatic and haematological effects.

In general, the compounds found in X. americana were saponins, glicosydes, flavonoids, tannins, phenolics, alkaloids, quinones and terpenoids types. In addition, the plant is potentially rich in fatty acids and glycerides and the seeds contain derivatives cyanide. The identified compounds did not demonstrate a representative pattern of each class. For example, the sesquiterpene were furanoic and widdrane while, triterpenes exhibited oleanane and cycloartane skeletal type. Concerning the fatty acids, in addition to common C16, C18 and C22, a distinctive feature is the presence of acetylenic, as well as, very long chain fatty acids.

We can see, from all the information summarized above, that work on plants of the genus Ximenia is justified, particularly Ximenia americana species, where systematic study is still not satisfactory, specially, relative to specific biological activity of their chemical constituents.
The present review compiles the published chemical and pharmacological information on the species *X. americana* and update important data reported in the last ten years in the scientific literature.

2. Biological activity

2.1 Antimicrobial and antifungal activities

To evaluate the scientific basis for the use of numerous plants species used to treat diseases of infectious origin, crude extracts of these plants were investigated. The antimicrobial activity of the extracts of the various parts of the investigated plants such as roots, leaves, seeds, stem barks and fruits, appears to be due to the presence of secondary metabolites such as polyphenols, triterpenes, sterols, saponins, tannins, alkaloids, glycosides and polysaccharides (Geyid *et al.*, 2005; James *et al.*, 2007; Maikai *et al.*, 2009; Ogunleye *et al.*, 2003).

*X. americana* is a plant used in traditional medicine for the treatment of malaria, leproutic ulcers and infectious diseases of mixed origin by natives in Ethiopia, Guinea, Sudan and in the Northern part of Nigeria (Geyid *et al.*, 2005; James *et al.*, 2007; Magassouba *et al.*, 2007; Maikai *et al.*, 2009; Ogunleye *et al.*, 2003; Omer & Elnima, 2003).

The crude extracts of *X. americana* show antimicrobial and antifungal activities. The crude aqueous, methanolic, ethanolic, butanolic and chloroform extracts from different parts (leaves, root, stem and stem bark) of the plant were subjected to phytochemical screening and from the test carried out, it was observed that the secondary metabolites contained were saponins, flavonoids, tannins, terpenoids, sterols, quinones, alkaloids, cyanogenetic glycosides, cardiac glycosides and carbohydrates in the form of sugars and soluble starch. The results of phytochemical screening of various parts solvent extracts of *X. americana* are presented in Table 1.

The MeOH extract from leaves of *X. americana* inhibited or retarded growth of *Neisseria gonorrhea* organism at dilution as low as 250 µg/ml. This same extract showed antifungal effect against *Candida albicans* and *Cryptococcus neoformans* in concentration of 4000 µg/ml. Chemical screening conducted on the extract showed the presence of several secondary metabolites as tannins, sterols, terpenoids, flavonoids and saponins (Geyid *et al.*, 2005). The antimicrobial activities of ethanol extract of the leaves were evaluated against six common bacterial isolates (*Pseudomonas aeruginosa*, *Proteus vulgaris*, *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus aureus* and *Candida albicans*) and was active against all of them. The highest degree of activity was for *P. aeruginosa* (inhibition zone: 20 mm), followed by *B. subtilis* and *C. albicans* (inhibition zone: 10 mm). Activity of the organic extract of the plant was comparable to that of commercially available penicillin disc (2 µg) which was more active against *P. aeruginosa* but less effective against *S. aureus*. The results of phytochemical analysis indicated the presence of saponins, flavonoids, tannins and cyanogenetic glycosides. Alkaloids and anthraquinones were not present (Ogunleye *et al.*, 2003). The root, stem bark and leaves aqueous and methanolic extracts of *X. americana* were tested against five bacteria and they inhibited the growth of *Staphylococcus aureus* and *Klebsiella pneumoniae* while *Shigella flexineri* was inhibited by only methanolic leaves, aqueous bark and aqueous leaves extracts. *Salmonella typhi* and *Escherichia coli* were not affected by these extracts. The
Some extracts showed the presence of carbohydrates in the form of sugars and soluble starch (James et al., 2007 & Ogunleye et al., 2003); few extracts showed also the presence of cyanogenetic glycosides (Ogunleye et al., 2003). Quinones are of the anthraquinone type; terpenes are sesquiterpenes and triterpenes type (Araújo et al., 2008, 2009).

Table 1. Phytochemical screening of stem bark, leaves, root and stem extracts of X. Americana. (Placed on the table 1)

Minimum Inhibitory Concentration (MIC) was only evident for the methanolic extracts at 1.25x10^4 µg mL^-1 (1:4) against *Staphylococcus aureus* while the Minimum Bactericidal Concentration (MBC) of the extracts was obtained at 2.50x10^4 µg mL^-1 (1:2) (James et al., 2007). From the results, inhibitory activity of extracts (methanolic root) was more pronounced on *Klebsiella pneumonia* whereas it shows no activity against *Escherichia coli*, *Salmonella typhi* and *Shigella flexineri*. The methanolic root extract showed highly significant (p<0.05) activity on *Klebsiella pneumonia* when compared with leaf extracts and methanolic bark extract. The phytochemical constituents present in the extracts were carbohydrates in the form of sugars and soluble starch (except for aqueous and leaves extracts), cardiac

| Plant part           | Solvent | Tannins | Steroids | Terpenes | Saponins | Flavonoids | Alkaloids | Cardiac | Glycosids | Quinones |
|---------------------|---------|---------|----------|----------|----------|------------|-----------|---------|-----------|----------|
| Leaves              | MeOH    | +       | +        | -        | +        | -          | -         | Geyid et al., 2005 |
| Leaves              | H₂O     | +       | -        | -        | +        | -          | +         | Ogunleye et al., 2003 |
| Leaves              | EtOH    | +       | -        | -        | +        | -          | +         | James et al., 2007 |
| Leaves              | H₂O     | +       | -        | -        | +        | -          | +         |         |
| Leaves              | MeOH    | +       | -        | -        | +        | -          | +         |         |
| Stem bark            | H₂O     | +       | -        | -        | +        | -          | +         | Maikai et al., 2009 |
| Stem bark            | MeOH    | +       | -        | -        | +        | -          | +         |         |
| Root                 | H₂O     | +       | -        | -        | +        | -          | +         | Omer & Elnima, 2003 |
| Root                 | MeOH    |         |          |          |          |            |           |         |
| Root                 | CHCl₃   |         |          |          |          |            |           |         |
| Stem                 | EtOH    | +       | +        |          |          |            |           | Araújo et al., 2008, 2009 |
| Stem                 | MeOH    | +       | +        |          |          |            |           |         |

+: present; -: absent; Ref.: references
glycosides, saponins, tannins and flavonoids while alkaloids were absent in all the extracts. It was concluded that the extracts of methanolic roots, stem bark and leaves have bacteridal activities over the concentration of 2.5x10^4 - 1.25x10^4 μg·mL⁻¹ and that the presence of carbohydrates, glycosides, flavonoids and tannins in the different extracts are responsible for their antibacterial activity. The antimicrobial properties of the bark, leave, root and stem extracts of *Ximenia americana* were screened against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* (Table 2) using the cup-plate agar diffusion method and the minimum inhibitory concentration by agar dilution method (Omer *et al.*, 2003).

| Part used | Solvent system | % Yield | Inhibition zone (mm) | MIC (mg/ml) |
|-----------|----------------|---------|----------------------|-------------|
| Bark      | CHCl₃          | 1.1     | 13 12 11 15          | N.D N.D N.D N.D |
|           | MeOH           | 21.1    | 23 30 19 22          | 0.31 0.62 19.79 19.79 |
|           | H₂O            | 8.9     | 18 18 16 14          | 0.40 1.62 3.24 1.62 |
| Leaves    | CHCl₃          | 10.7    | 13 14 - 12           | N.D N.D N.D N.D |
|           | MeOH           | 26.6    | 23 22 - 25           | 1.55 0.77 9997 12.45 |
|           | H₂O            | 5.0     | 17 19 16 22          | 0.59 1.19 >25.5 19.11 |
| Root      | CHCl₃          | 2.2     | 15 13 12 13          | N.D N.D N.D N.D |
|           | MeOH           | 3.7     | 15 21 19 15          | 3.27 6.54 >34.88 >34.48 |
|           | H₂O            | 5.7     | 13 13 - -             | 2.68 10.74 28.65 28.65 |
| Stem      | CHCl₃          | 2.7     | - 11 11 -             | N.D N.D N.D N.D |
|           | MeOH           | 11.8    | 20 25 - 24           | >72.75 3.41 >72.75 >72.75 |
|           | H₂O            | 2.7     | 17 17 13 13          | 5.12 5.12 >13.65 >13.65 |

B.s, *Bacillus subtilis*; S.a, *Staphylococcus aureus*; E.c, *Escherichia coli*; Ps.a, *Pseudomonas aeruginosa*; concentration of extracts 100 mg/ml, 0.1 ml/cup; inhibition zones are the mean of three replicates. MIC, minimum inhibitory concentration; N.D, not detected.

Table 2. Antibacterial activity of *Ximenia americana* extracts against standard organisms. (Placed on the table 2)

The methanolic extract was the most active one. The aqueous extract also exhibited high activity which justifies its traditional use. *Staphylococcus aureus* was the most susceptible bacterium among the tested organisms. The table 3 show the antibacterial activity of *Ximenia Americana* against the pharmaceuticals patterns.

Several other studies to determine the presence of antimicrobial activity in crude extracts of *Ximenia americana* were performed (Magassouba *et al.*, 2007; Maikai *et al.*, 2009). In all, the various extracts were found to have broad spectrum effect against standard organisms (*Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Proteus vulgaris*, *Candida albicans*, *Bacillus subtilis*, *Salmonella typhi* and *Shigella flexineri*) and supports the traditional usage of this plant as remedy in treatment of microbial infections.

In general, the antimicrobial activity of extracts of the various parts of the plants appears to be due to presence of secondary metabolites. In some experiments, was remarked that the
| Reference drugs | Concentration μ/ml | B.s | S.a | E.c | Ps.a |
|-----------------|-------------------|-----|-----|-----|------|
| Ampicillin      | 40                | 14  | 25  | -   | -    |
|                 | 20                | 13  | 22  | -   | -    |
|                 | 10                | -   | 19  | -   | -    |
|                 | 5                 | -   | 18  | -   | -    |
| Benzyl penicillin| 40              | -   | 37  | -   | -    |
|                 | 20                | -   | 33  | -   | -    |
|                 | 10                | -   | 28  | -   | -    |
|                 | 5                 | -   | 24  | -   | -    |
| Cloxacillin     | 40                | -   | 29  | -   | -    |
|                 | 20                | -   | 27  | -   | -    |
|                 | 10                | -   | 22  | -   | -    |
|                 | 5                 | -   | 18  | -   | -    |
| Gentamicin      | 40                | 24  | 18  | 25  | 22   |
|                 | 20                | 22  | 16  | 17  | 15   |
|                 | 10                | 17  | 14  | 16  | 12   |
|                 | 5                 | 15  | 13  | 11  | -    |

Interpretation of sensitivity test results: Gram(+) bacteria*; Gram(-) bacteria **; >18 mm (M.DIZ)= sensitive; >16 mm (M.DIZ)=sensitive; 14-18 mm (M.DIZ)= intermediate; 13-16 mm (M.DIZ)= intermediate; <14 mm (M.DIZ)= resistant; and < 13mm (M.DIZ)= resistant.

Table 3. The activity of *Ximenia Americana* against the clinical isolates. (Placed on the table 3)

Plants which accumulate polyphenols, tannins and unsaturated sterols/terpenes showed to inhibit or significantly retard growth of eight of the ten test organisms; the species, which constitute polyphenols and unsaturated sterols/terpenes; and polyphenols, tannins, unsaturated sterols/terpenes, saponins and glycosides inhibited six organisms each while, those with polyphenols, tannins, unsaturated sterols/terpenes, saponins; and alkaloids and unsaturated sterols/terpenes inhibited growth of five bacterial strains each (Geyid et al., 2005). Cyanogenetic glycosides are reported to possess antimicrobial activity (Finnermore et al., 1988). Tannins have been traditionally used for protection of inflamed surfaces of the mouth and treatment of catarrh, wounds, haemorrhoids and diarrhea and as antidote in heavy metal poisoning. They have the ability to inactive microbial adhesions, enzymes, cell envelope transport proteins and also complex with polysaccharide (Maikai et al., 2009; Scalbert, 1991; Ya et al., 1988). Flavonoids are naturally occurring phenols, which posses numerous biological activities including anti-inflammatory, antiallergic, antibacterial, antifungal and vasoprotective effects and, also have been reported to complex with extracellular and soluble proteins and to complex with bacterial cell walls (Dixon et al., 1983; Geyid et al., 2005; Hostettman et al., 1995; James et al., 2007; Maikai et al., 2009; Ogunleye et al., 2003). Terpenoids have also been reported to be active against bacteria, the mechanism of action involve membrane disruption by the lipophilic compounds (Geyid et al., 2005; James...
et al., 2007; Maikai et al., 2009; Ogunleye et al., 2003). Although it is difficult to speculate on the mechanism of action of the constituents of the extracts on the basis of studies conducted to date, the antimicrobial activity of these extracts is due, no doubt, the presence of these secondary metabolites. In the case of extracts of *Ximenia americana*, probably, due the presence of tannins, flavonoids, triterpenes/steroids, saponins or cyanogenetic glycosides.

In summary, the results justified the use of *X. americana* as having antibacterial properties and support its use as agent in new drugs for therapy of infectious diseases caused by pathogens.

2.2 Pesticidal activity

Oleaceous seed oils are a rich source of acetylenic lipids and unsaturated fatty acids (Badami & Patil, 1981 & Sptizer et al., 1997). Acetylenic metabolites show some biological activities including, insecticidal activity (Jacobson, 1971). *X. americana* was recorded to contain octadec-11-en-9-ynoic acid, named xymeninc acid as well as icosenoi-triacontenoic acids, all of which belong to the ω-9 series (Rezanka, & Sigler, 2007). Bioactivity-driven fractionation of the CHCl₃ extract of the root of *X. americana* using the Brine Shrimp Lethality Test (BST) and hatchability test with *Clavigralla tomentosicollis* eggs yielded two fractions (F006, soluble in petroleum ether and F005, soluble in 10% H₂O in MeOH) as the most actives (F005, BST LC₅₀ 78 (129-48) µg/mL and F006, BST LC₅₀ 76(121-49) µg/mL) (Fatope et al., 2000). A combination of F005 and F006 was submitted to hatchability test (inhibition of hatching = 68 % of control) and successive BST-directed fractionation on silica gel column and preparative TLC yielded oleanene palmitates (1), β-sitosterol (2) and C₁₈ acetylenic fatty acids (3 and 4) as yellow oils.

The substance 4 suppressed the hatchability of *C. tomentosicollis* eggs at 92 % of control when tested at 4 x 10⁻⁴ µg/mL (correcting for unhatched eggs in the control using Abbott’s formula):

\[
\text{% control} = \left[ \frac{(\text{% unhatched of treated group} - \text{% unhatched of untreated group})}{(100 - \text{% unhatched of untreated group})} \right] \times 100
\]

These acetylenic fatty acids show characteristic spectrometric data. The ¹³C NMR spectrum of 3 displayed absorptions diagnostic of acetylenic carbons at δC 80.4 (C) and 80.1 (C) and of carboxylic carbon at δC 189.1 (C), in agreement with its IR spectrum which exhibited bands at 2200 and at 1713 cm⁻¹, characteristic of acetylenic and acid groups, respectively. Compound 3 had molecular formulaC₁₈H₃₂O₂, as established by HREI-MS (m/z 280.2378 for [M⁺]) in combination with its ¹H and ¹³C NMR spectra. From analysis spectral data compound 3 was thus established as octadeca-5-ynoic acid (tariric acid). Compound 4 had a
mol wt 6 mass units less than that of 3 with molecular formula C\textsubscript{18}H\textsubscript{26}O\textsubscript{2} as revealed by HREI-MS (m/z 274.2021 for [M\textsuperscript{+}]) in combination with its \textsuperscript{1}H and \textsuperscript{13}C NMR spectra. The \textsuperscript{13}C NMR spectrum of 4 displayed absorptions diagnostic of acetylenic carbons at \(\delta\textsubscript{C} 83.4\) (C) and 74.1 (C) and of carboxylic carbon at 179.3 (C), in agreement with its IR spectrum which exhibited bands at 2232 and 1702 cm\(^{-1}\), characteristic of acetylenic and acid groups, respectively. The \textsuperscript{13}C RMN spectrum also exhibited six resonance at \(\delta\textsubscript{C} 148.2\) (CH), 140.9 (CH), 136.9 (CH), 129.8 (CH), 109.3 3(CH) and 108.6 (CH), revealing the presence of three double bonds. From a detailed spectral analysis considering, especially, the multiplicity of signals and coupling constants in the \textsuperscript{1}H NMR spectrum, as well as the presence of diagnostic peaks in the mass spectrum, compound 4 was thus established as 10Z,14E,16E-octadecano-10,14,16-triene-12-ynoic acid, a one-ene-yneene acetylenic fatty acid (Fatope et al., 2000).

\[
\begin{align*}
\text{CH}_3\text{CH} &= \text{C}(\text{CH}_3)\text{CO}_2\text{H} & 3 \\
\text{CH}_3\text{CH} &= \text{C}(\text{OH})\text{CH} = \text{C}(\text{CH}_3)\text{CH} = \text{C}(\text{OH})\text{CH} = \text{C}(\text{H}_2)\text{CO}_2\text{H} & 4
\end{align*}
\]

In addition, Ximenia seed oil have been found to contain fatty acids with more than 22 carbon atoms (very long fatty acids) which are found only rarely in nature. Using liquid chromatography in combination with mass spectrometry was found that Ximenia oil to contain fatty acids with chain length \(C\textsubscript{34}\) and \(C\textsubscript{36}\) (Rezanka & Sigler, 2007). Effectively, two very long chain unsaturated fatty acids \(C\textsubscript{40}\) and \(C\textsubscript{35}\) (5 and 6) were isolated (Saeed & Bashier, 2010) from X. americana seeds and fruits, respectively. The mass spectrum of the major component (5) showed a molecular ion at m/z 604 corresponding to the molecular formula \(C\textsubscript{40}H\textsubscript{76}O\textsubscript{5}\). The IR spectrum of 5 showed a broad absorption band at 3600-3200 cm\(^{-1}\) (OH) and the presence of strong absorption at 1742 cm\(^{-1}\) attributed to ester group. The base peak appeared at m/z 55 \((C_4H_7+\)) due to allylic bond cleavage and peaks at m/z 479 and 151 furnished from fragmentation in \(C\textsubscript{28}C\textsubscript{29}\) and \(C\textsubscript{29}C\textsubscript{27}\), respectively. In addition, the peaks at m/z 31, 59, 73 and 74 (McLafferty rearrangement) were compatible with unit \(CH_2OCO(CH_2)\textsubscript{3}\). The compound 5 was identified as methyl-14,14-dimethyl-18-hydroxyheptatracont-27,35-dienoate. The mass spectrum of 6 showed a molecular ion at 578, corresponding to the molecular formula \(C\textsubscript{35}H\textsubscript{62}O_6\). The IR spectrum showed bands at 3500, 1731 and 1645 cm\(^{-1}\) corresponding to OH, C=O and C=C groups, respectively. The base peak appeared at m/z 73 \((C_7H_2O_2+\)) which is characteristic for the methyl ester, reinforced by additional peaks at m/z 31, 59 and 74 (McLafferty rearrangement). An peak at m/z 479 was due to M-\(C_3H_2O_2\) and one at m/z 339 is due to the cleavage \(C_{13}C_{14}\) while, those at m/z 126 and 265 were due to \(C_2H_{10}O_2\) and M-\(C_7H_2O_2\), respectively. The compound 6 was identified as dimethyl-5-Methyl-28,29-dihydroxydotriacont-3,14,26-trienidioate.

\[
\begin{align*}
\text{[CH}_3\text{OCO(CH}_2)_{2}C(\text{CH}_3)_{2}(\text{CH}_2)_{2}\text{CHOH(CH}_2)_{2}\text{CH} = \text{CH(CH}_2)_{6}\text{CH} = \text{CHCH}_3] & 5 \\
\text{[CH}_3\text{OCOCH}_2\text{CH} = \text{CHCH}_3(\text{CH}_2)_{2}\text{CH} = \text{CH(}CH_2)_{10}\text{CH} = \text{CH(}CHOH)_{2}(\text{CH}_2)_{2}\text{COOCH}_3] & 6
\end{align*}
\]

2.3 Analgesic activity

The aqueous extract of stem bark of X. americana has analgesic properties that justify its use popular in countries such as Tanzania, Senegal, Zimbabwe and Nigeria. The extract of X.
*Ximenia americana* in doses containing 10 to 100 mg/kg P.C, inhibits contractions of the abdomen with analgesic effects comparable to those of phenylbutazone. In fact, at doses of 100 mg/kg P.C, phenylbutazone causes an inhibition of pain in 45.2±2%. The percentage of inhibition by extract of *X. americana* is 61.1±% in the same concentration. These properties are probably due to the presence of flavonoids and saponins, detected in the extract (Soro et al., 2009). The analgesic activity of the methanol extract of *X. americana* leaf was investigated in chemical models of nociception in mice. The extract at doses of 200, 400 and 600 mg/kg i.p. produced an inhibition of 54.13, 63.74, and 66.4% respectively, of the abdominal writhes induced by acetic acid in mice. In the formalin test, the administration of 200, 400 and 600 mg/kg i.p. had no effects in the first phase (0 to 5 min) but produced a dose dependent analgesic effect on the second phase (15 to 40 min) with inhibitions of the licking time of 29.3, 47.8 and 59.8%, respectively. These observations suggested that methanol extract of *X. americana* leaf possesses analgesic activity (Siddaiah et al., 2009).

### 2.4 Antipyretic activity

The bark of stem of *X. americana* has been used in West Africa for the treatment of pain and fever. To verify this second property, the treatment of rats in hyperthermia with *Ximenia americana* stem bark aqueous and with beer yeast was compared to those obtained with lysine acetylsalicylate (Aspegic). The study showed an antipyretic action of the extract. Moreover, the toxicological study of the stem extract indicated a LD₅₀ of 237.5 mg/kg P.C according to the classification of Diezi this plant is relatively toxic. The experiments show that the properties of *X. americana* could due to the presence of saponosides, as show by screening tests performed in this study. These results justified the use of *X. americana* in traditional cure of fever treatment (Soro et al., 2009).

### 2.5 Antitrypanosomal activity

The in vitro antitrypanosomal activity of methanolic and aqueous extracts of stem bark of *Ximenia americana* was evaluated on Trypanosoma congolense. Blood obtained from a high infected mice with *T. congolense* (10⁷) was incubated with methanolic and aqueous extracts at 20, 10 and 5 mg/ml and Diminal(R) (diminazene aceturate) at 200, 100 and 50 µg/ml in a 96 micro plate. The results revealed that methanol and aqueous extracts had activity at 20 and 40 mg/ml however, the methanolic extracts were more active than aqueous extracts at 10 and 5 mg/ml. Phytochemical screening of the methanolic and aqueous extracts of the bark showed that they both had flavonoids, anthraquinones, saponins, terpenes and tannins. The aqueous and methanolic extracts appears to show some potential activity against *T. congolense* (Maikai et al., 2008).

### 2.6 Anticancer activity

Plants have been show to provide a useful source of natural products that are effective in the treatment of human neoplastic diseases. Information recorded from ancient civilizations has demonstrated the use of plants in search of treatment for various types of cancer (Hartwell, 1967-1971). An analysis of plant materials that had been studied at the National Cancer Institute (NCI), USA for discovering new anticancer drugs showed that if ethnopharmacological information had been used, the yield of plants harboring antineoplastic activity would have been significantly increased (Spjut & Perdue, 1976).
list of natural products stored for study as more effective drugs for the treatment of human
cancers (NCI) were generated by searching for specific structural types (Steven & Russel,
1993). However, the presence of some large class cannot be ruled out. Examples of
anticancer agents developed from higher plants are the antileukemic bis-indole alkaloids
vinblastine and vincristine from the *Catharanthus roseus* (Apocynaceae); diterpene taxol, used
to treat breast cancer, lung cancer, and ovarian cancer and also used to treat AIDS-related
(Kaposi’s sarcoma) from *Taxus breviflora* (Taxaceae); pyrrolo[3,4,b]-quinoline alkaloid
camptothecin (antileukemic) from *Camptotheca acuminata* (Nyssaceae) and pyridocarbazole
alkaloid elipticine (antitumor) contained in *Ochrosia elliptica* (Apocynaceae). A large number
of other active natural products with toxicity to cells in culture (Walker carcinosarcoma 256,
mouse L-1210 leukemia, Ehrlich ascite tumor, sarcoma 180 and mouse P-388 leukemia cell
lines) have been detected (Geran *et al.*, 1972 & Lee *et al.*, 1988).

| Tumor cell lines | IC\textsubscript{10} (ug/ml medium) | IC\textsubscript{50} (ug/ml medium) | IC\textsubscript{90} (ug/ml medium) | IC\textsubscript{90}/IC\textsubscript{10} (medium) |
|------------------|-----------------------------------|----------------------------------|-------------------------------|---------------------------------|
| MCF7             | 0.6                               | 1.7                              | 10                            | 16.7                            |
| BV173            | 0.4                               | 1.8                              | 7.0                           | 17.5                            |
| CC531            | 0.8                               | 3.3                              | 12                            | 15.0                            |
| U87-MG           | 1.0                               | 9.0                              | 100                           | 100                             |
| K562             | 5.0                               | 11                               | 180                           | 36                              |
| SKW-3            | 3.1                               | 20                               | 700                           | 226                             |
| HEP2             | 5.0                               | 21                               | 100                           | 20                              |
| NC1-H460         | 4.0                               | 21                               | 150                           | 38                              |
| PC3              | 3.5                               | 26                               | >1000                         | >300                            |
| MDA-MB231        | 5.0                               | 33                               | 100                           | 20                              |
| HT29             | 8.0                               | 40                               | 350                           | 44                              |
| U333             | 7.0                               | 65                               | 300                           | 43                              |
| SAOS2            | 20                                | 66                               | 1000                          | 50                              |
| LAMA84           | 10                                | 90                               | 600                           | 60                              |
| HL60             | 30                                | 90                               | 1000                          | 33                              |
| CML-T1           | 2.5                               | 160                              | 1000                          | 400                             |
| AR230            | 17                                | 170                              | 700                           | 41                              |

| Non tumor cell lines | IC\textsubscript{90} (ug/ml) | IC\textsubscript{90}/IC\textsubscript{10} (medium) |
|----------------------|-----------------------------|---------------------------------|
| MCF10                | >100                        | >2.0                            |
| MDCK                 | 27                          | 5.0                             |
| NIH/3T3              | 33                          | >50                             |
| PNT-2                | 20                          | >50                             |

\( ^a \)Inhibitory concentration 10 (concentration inhibiting the cell growth by 10%), as accessed by MTT assay;
\( ^b \)Inhibitory concentration 50 (concentration inhibiting the cell growth by 50%), as accessed by MTT assay.
\( ^c \)Inhibitory concentration 90 (concentration inhibiting the cell growth by 90%), as accessed by MTT assay.
\( ^d \)Ratio of IC\textsubscript{90} and IC\textsubscript{10} values.

Table 4. Antiproliferative activity of an aqueous extract from *X. americana* in 16 human and
one rodent tumor cell lines and in 4 immortalized non-tumor cell lines.
The antineoplastic activity in vitro of various extracts from *Ximenia americana*, plant used in African traditional medicine for the treating cancer, was investigated (Voss *et al.*, 2006, 2006). The most active, aqueous extract was subjected to a detailed investigation in a panel of 17 tumor cell lines (Table 4) originating from human (16 lines) and rat (1 line), showing an average IC₅₀ of 49 mg raw powder/ml medium. The majority of cell lines (11 out of 17) were classified as sensitive (the sensitivity varied from 1.7 mg/ml in MCF7 breast cancer cells to 170 mg/ml in AR230 chronic-myeloid leukemia cells) and three of these (MCF7 breast cancer, BV173 CML and CC531 rat colon carcinoma) showed a particularly high sensitivity, with ratios lower than 0.1 of the average IC₅₀. The *in vivo* antitumor activity was determined in the CC531 colorectal rat model and significant anticancer activity was found following peroral administration, indicating a 95% reduced activity.

A comparison of the antineoplastic activity of the extract with three clinically used agents is given in Table 5. The cytotoxicity profiles of four cell lines are illustrated by the respective IC₅₀, IC₅₀ and IC₉₀ values, as well as by the corresponding IC₉₀ to IC₅₀ ratio, describing the slope of the concentration-effect curve. Most prominently, the ranking in sensitivity differed between the extract and the positive controls. In variance to the extract, which resulted in the lowest IC₅₀ and IC₉₀/IC₅₀ ratio in MCF7 cells, miltefosine and cisplatinum caused the lowest IC₅₀ and IC₉₀/IC₅₀ ratio in HEp2 cells. Similar to the extract, the lowest IC₅₀ following gemcitabine exposure was seen in NCF7 cells. However, this agent differed from all the others by its lack in effecting 90% growth inhibition, were the HEp2 cells; notably, the cells were most resistant to the agent. In contrast, SAOS2 cells were found to best most resistant to the extract as well as to miltefosine and cisplatinum.

| Cell line | Treatment       | IC₅₀ | IC₅₀ | IC₉₀ | IC₉₀/IC₅₀ |
|-----------|-----------------|------|------|------|-----------|
| MCF7      | Extract (µg/ml) | 0.6  | 1.8  | 10   | 16.7      |
|           | Miltefosine (µM)| 6.5  | 40   | 80   | 12.3      |
|           | Cisplatinum (µg/ml) | 0.22 | 2.2  | 10   | 45        |
|           | Gemcitabine (µM) | 0.001 | 0.012 | >100 | >10⁵      |
| U87-MG    | Extract (µg/ml) | 1.0  | 9.0  | 100  | 100       |
|           | Miltefosine (µM) | 4.7  | 27   | 70   | 14.9      |
|           | Cisplatinum (µg/ml) | 0.12 | 1.6  | 18   | 150       |
|           | Gemcitabine (µM) | 0.002 | 0.014 | >100 | >5x10⁴    |
| HEp2      | Extract (µg/ml) | 5.0  | 21   | 100  | 20        |
|           | Miltefosine (µM) | 1.2  | 2.8  | 8.0  | 6.7       |
|           | Cisplatinum (µg/ml) | 0.09 | 0.4  | 1.4  | 15.6      |
|           | Gemcitabine (µM) | 0.2  | 0.47 | 17   | 85        |
| SAOS2     | Extract (µg/ml) | 20   | 66   | 1000 | 50        |
|           | Miltefosine (µM) | 5.0  | 40   | 120  | 24        |
|           | Cisplatinum (µg/ml) | 0.11 | 3.1  | 10   | 91        |
|           | Gemcitabine (µM) | 0.007 | 0.034 | >100 | >10⁴      |

Table 5. Cytotoxicity profiles of the extract and three standard antineoplastic agents in a subpanel of the cell lines
In order to define the substance class of the active component(s) (Voss et al., 2006) experiments were carried out on physicochemical properties. In the process, lipids and lipophilic plant secondary metabolites could be excluded, since the biological activity was only extracted by strongly polar solvents. Large amounts of tannins were identified in the aqueous extract. However, extracts prepared in methanol or 70% acetone, both solvents known to efficiently extract tannins from plant materials, had only a low (methanol) or no (70% acetone) cytotoxic activity. Molecules smaller than 10 kDa were excluded by ultrafiltration. Out of the known class of plant cell macromolecules, DNA and RNA were not found in the aqueous extract and digestion experiments with DNase or RNase had not effect biological activity. However, proteins and polysaccharides were shown to be present in the aqueous extracts and could not be further separated by physicochemical methods. Digestion experiments with trypsin and proteinase K hinted at a protein being responsible for the cytotoxic activity.

A well-defined family of cytotoxic plant proteins is that of the type II ribosome-inactivating proteins (RIPs). These proteins with molecular weight of about 60 kDa, consist of two polypeptide chain, termed A- and B- chain, with an MW of about 30 kDa each, being held together by disulphide bridge. Cumulative evidences (cytotoxic effects, MW, two-chain structure of the proteins in the affinity-purified fraction and one mass-spectrometrically sequenced tryptic peptides) strongly suggests that the active components of the plant material are so far unknown proteins belonging to the type II RIP family.

By a combination of preextraction, extraction, ion exchange and affinity chromatography, a mixture of two cytotoxic proteins was isolated. The eluted peptides were analyzed by electro-spray ionization mass spectrometry (MS/MS). The MS/MS mass spectrum is a method in which a first analyzer isolates a precursor ion which then undergoes a fragmentation yielding a product ions and neutral fragments. A second spectrometer analyzes the product ions. MS/MS applications are plentiful in the study of fragmentation mechanisms, observation of ion-molecule reactions, applications to high-selectivity and high-sensitivity analysis and determination of elementary compositions. Thus, it is a rapid selective analysis method for the components of a complex mixture and macromolecules in biological fluids. The homology of the translated protein sequence from isolated peptides to known type II RIP precursor protein sequence demonstrates that the new protein termed “riproximin” is a so far unknown member of this class. In conclusion, from biological activity of each of the two proteins as well as from MS/MS sequence analysis, showing the presence of two B-chain and two A-chain in the mixture, the X. americana extract analyzed contains a mixture of two new proteins, riproximin, belongs to the family of type II ribosome-inactivating proteins.

Two sesquiterpenes (7 and 8) isolated from the EtOH extract of the stems of X. americana did not inhibit the growth of HL-60 (human leukemia), HTC-8 (human colon) and MDA-MB-435 (human breast cancer) cell lines.
The compounds 7 and 8 were recently isolated and their structures were elucidated on the basis of spectral analysis (IV, MS and NMR) and the complete assignment of the $^1$H and $^{13}$C NMR signals were achieved by 1D($^1$H, $^{13}$C and DEPT) and 2D ($^1$H - $^1$H COSY, $^1$H - $^{13}$C HMBC, $^1$H-$^{13}$C HMBC and $^1$H - $^1$H NOESY) NMR experiments. The sesquiterpene 7, isolated as a white powder, has molecular formula $C_{12}H_{20}O_4$ deduced from its EIMS (M$^+$ 264) in combination with its $^1$H and $^{13}$C NMR spectra. The $^1$H and $^{13}$C NMR spectra combined with distortionless enhancement by polarization transfer (DEPT) technique exhibited signals that allowed characterize the three isoprene units (C-1, C-2, C-3, C-4 and C-13; C-8, C-9, C-10, C-11 and C-12; C-5, C-6, C-7, C-14 and C-15) of 7. Thus, the $^{13}$C NMR spectra exhibited signals for six sp$^2$ carbons [olefinic bond: C-2 ($\delta_C$128.9), C-3 ($\delta_C$141.7) and furan ring: C-9 ($\delta_C$127.9), C-10 ($\delta_C$147.1), C-11 ($\delta_C$144.4), C-12 ($\delta_C$108.9)], two carbonyl [conjugated ketone, C-8 ($\delta_C$195.3) and conjugated carboxylic acid, C-1 ($\delta_C$173.1)], three methylene [C-4 ($\delta_C$41.2), C-6 ($\delta_C$36.5) and C-7 ($\delta_C$35.9), three methyl [C-13 ($\delta_C$12.4), C-14 ($\delta_C$25.9) C-15 ($\delta_C$25.9) and one quaternary carbon [C-5 ($\delta_C$34.3)]. One conjugated ketone ($\delta_C$195.3) was also evident from the absorption at 1682 cm$^{-1}$ in the IR spectrum. In the HMBC spectrum, obvious long-range connectivities between the methylene group 2H-7 ($\delta_H$2.71, dd, 7.9, 6.0 Hz) and C-8 ($\delta_C$195.57) and between the methylene group 2H-4 ($\delta_H$2.20, d, 7.7 Hz) and C-5 ($\delta_C$34.56) allowed the assembly of the molecule and show it to consist of a furanoid sesquiterpene. Others diagnostic $^1$H-$^1$H COSY, $^1$H-$^{13}$C HMQC and $^1$H-$^{13}$C HMBC correlations permitted to assign all the hydrogen and carbon atoms. The sesquiterpene 8, isolated as a white solid, has molecular formula $C_{12}H_{18}O_2$ deduced from its EIMS (M$^+$ 234) in combination with its $^1$H and $^{13}$C NMR spectra. The $^1$H and $^{13}$C NMR spectra combined with distortionless enhancement by polarization transfer (DEPT) technique exhibited signals that allowed characterize the three isoprene units (C-1, C-2, C-3, C-11 and C-12; C-4, C-5, C-6, C-13 and C-14; C-7, C-8, C-9, C-10 and C-15) of 8. The $^{13}$C NMR spectra exhibited signals for four sp$^2$ carbons [three substituted, C-8 ($\delta_C$132.34) and C-9 ($\delta_C$145.01) and disubstituted, C-1 ($\delta_C$154.71) and C-12 ($\delta_C$111.63) bonds; one conjugated carboxylic acid, C-15 ($\delta_C$173.71), besides signals to five methylene, two methyne, one quaternary and two methyl carbons. The possibility of himachalano type structure was eliminated based on the interpretation of spin-spin interactions revealed by $^1$H-$^1$H COSY spectrum, which clearly showed the presence of cross peaks corresponding to the couplings of two atoms of hydrogen 2H-6 [$\delta_H$1.68 (m) and 1.50 (m)] with H-5 hydrogen [$\delta_H$1.81 (m)] and with the two hydrogen atoms 2H-7 [$\delta_H$ 2.45 and 2.35) besides interaction of H-5 ($\delta_H$ 1.81) with H-11 ($\delta_H$ 2.50, q). This sequence does not appear in the skeleton type himachalano. The trans configuration fusion ring was supported by correlations observed in NOESY NMR spectrum, that exhibited the presence of nOes indicating that the hydrogens 3H-13 ($\delta_H$ 1.01, s), H-5 ($\delta_H$ 1.81) and H-3ax ($\delta_H$ 1.58, t, 10.8 Hz) are oriented on the same side (a) of the molecule, while the hydrogens 3H-14 has the same orientation (a) that the hydrogens H-11 ($\delta_H$ 2.50, q), H-6ax ($\delta_H$ 1.50) and H-3eq ($\delta_H$ 1.74, dd, 10.8 , 8.9). Others diagnostic $^1$H-$^1$H COSY, $^1$H $^{13}$C HMOC and $^1$H $^{13}$C $^{13}$C HMBC correlations permitted to assign all the hydrogen and carbon atoms.

2.7 Others activities

2.7.1 Antiviral effect

The stem bark MeOH extract of X. americana as well as several others plant species used by the Maasai pastoralis of East Africa showed antiviral effect against measles virus in vitro by
plaque reduction neutralization assay. Potentially active constituents from extracts of all the plants include polyphenols, alkaloids, tannins, sterols, terpenes, saponins and glycosides, between others (Parker et al., 2007).

2.7.2 Hepatic and heamatological effects

A study (James et al., 2008) was conducted from the leaves, stem bark and root aqueous extract of X. americana with albino rats. The results of this work shows that the extracts significantly (P<0.05) increasing the level of serum alanine transaminase (ALT) and aspartate transaminase (AST), results indicative of hepatocellular damage. The result also shows that the root has the ability to impair albumin synthesis as observed by the decrease of level of serum albumin. The weight of the animal showed a significant (P<0.05) reduction on administering the leaves extract as compared to the control and the others extracts. This reduction might be due to poor intake and utilization of food by the animals in the leaves extract group. The significantly (P<0.05) higher content of hydrogen cyanide, saponins, and oxalates in the root extracts indicates that the root extracts may be more toxic. Hydrogen cyanide is known to cause gastrointestinal inflammation and inhibition of cellular respiration. Saponins are known to have haemolytic properties and the ability to reduce body cholesterol by preventing its reabsorption. The high saponin content in the root may lead to gastroenteritis manifested by diarrhea. Oxalates have been known to cause irreversible oxalate nephrosis when ingested in large doses. Thus, there is need to isolate the specific component(s) responsible for the toxicity in the root extract in order to standardized the preparation for maximum therapeutic benefit.

2.7.3 Toxicity

The stem bark of X. americana was evaluated for its phytochemical constituents and acute toxicity effect on the Swiss albino mice (Maikai et al., 2008). The results from the extracts administered intraperitoneally/orally at doses of 10, 100 and 1000 mg/kg body weight revealed no death with doses up 5000 mg/kg body weight. Post mortem, hematological and histopathological examination did not show any significant (P<0.05) weight changes. Phytochemical screening of the aqueous extract stem bark revealed the presence of cardiac glycosides, flavonoids, saponins and tannins. The results suggested that the aqueous extract is not acutely toxic to the mice.

2.7.4 Food composition and cosmetic use

Glyceride blends containing ximenylic acid (9) (found in X. americana) are useful for the preparation of food compositions or food supplements, including margarine, chocolate, ice cream, mayonnaises, cheese, dry soups, drinks, cereal bars and sauces and snack bars. The blend provides a composition providing health benefits consisting of insulin resistance, or related disorders such as diabetes, delaying the onset of symptoms related to development of Alzheimer’s disease, improving memory function, lowering blood lipid levels, anticancer effects or skin antiageing effects (Koenen et al., 2004). Food X. americana flowers are a replacement for orange blossoms with similar fragrance and soothing cosmetic properties (Paolo, 1979).

\[
\text{CH}_3(\text{CH}_2)_5\text{CH} \rightleftharpoons \text{C} \equiv \text{C(\text{CH}_2)_7\text{CO}_2\text{H}}
\]
3. Others constituents isolated from *X. americana*

Besides the substances mentioned in the text of this chapter, several other originated from *Ximenia americana* were isolated.

**Isoprenoids**

![Isoprenoids](image)

**Fatty acids**

![Fatty acids](image)

**Triterpenes**

![Triterpenes](image)
4. Summary/conclusion/future directions

From an extensive literature review was observed that the *Ximenia americana* is widely used as a popular alternative remedy in certain regions of some countries of the Africa (Guinea, Ethiopia, Nigeria, Sudan) and in the Brazil. The plant, used by their crude extracts, especially, aqueous and methanolic, showed several biological activities such as antimicrobial, antifungal, anticancer, antitrypanosomal, antirheumatic, antioxidant, analgesic, moluscicide, pesticidal, antipyretic, antifugal, among others. There are several papers in the literature confirming these activities. The crude extracts consist of complex mixture of compounds called secondary metabolites produced by plants, which include, mainly, flavonoids, saponins, alkaloids, quinones, terpenoids, phenols, glycosides and sterols.

Many plants have a prolonged and uneventful use that may serve as indirect evidence to their efficacy. However, in the absence of objective proof of efficacy and without the knowledge of the constituents responsible for the physiological actions, the validity of the remedies is questionable and its use restricted. It generally was observed that the more the constituents in a given species, the more diverse the micro-organisms it acts upon. The difference of activity appears to be directly related to the qualitative and/or quantitative diversity of the compounds that are being accumulated by the plants investigated.
However, detailed studies on the toxicity of extracts revealed through phytochemical screening showed that many constituents chemicals can affect the animal positively or negatively as a result of prolong usage. Thus, was founded that tannins and anthraquinones are thought to have both prooxidant and antioxidant effects on the body. While the antioxidant protects, the prooxidant damage the tissues and organs. Also, was observed that the presence of tannins and other compounds interferes with absorption of nutrients such proteins and minerals resulting in weight loss. The extracts contained the presence of saponins has been reported to produce free radicals and hydrogen peroxide during its oxidation to semiquinone in the body, is thought to damage the cells of the body. The results of several studies conducted so far have produced a scientific basis that can justify the use of *Ximenia americana* in medicine. As we see the many works on *X. americana* show its effectiveness in treating various diseases. In all studies, were highlighted the participation and importance of secondary metabolites produced by them. However, there are still many details to be clarified. As mentioned above, in general, it was observed that the more the constituents in a given species, the more diverse the micro-organisms it acts upon. Moreover, the activity of plant extracts seems to be related to quality and quantity of metabolites present, possibly due to the possibility of synergism while, different types of metabolites appear to be related to specific biologic actions. In this context it is important to point out that the norisoprenoid isophorane (10), shown to be carcinogenic agent (Mevy *et al.*, 2006), was identified in the leaves of *X. americana*, which would conflict with its use in treating cancer. The last report about compounds isolated from *X. americana* up to date were the sesquiternes 7 and 8, triterpenoids 18-22 and steroids 24-26, all from ethanol extract of stems (Araújo *et al.*, 2008, 2009). Some of them have not yet been exhaustively investigated from the point of view of biological activity.

Future studies should be performed using chromatographic methods such as HPLC (high performance liquid chromatography) and LC-MS (Liquid chromatography coupled to mass spectroscopy) to obtain the chromatographic profile of the chemical composition of the extracts. Then carry out guided study (biological activity) in order to isolate and identify the pure constituents. Finally, as reported, many compounds may exhibit both carcinogenic and anticarcinogenic effects but it is not excluded that the occurrence of compounds other than volatile constituents may act in the anticarcinogenic process. Consequently, these results encourage further investigations to extracts and identify the active chemical compounds responsible for the specific biological activity in order to standardized the plant preparation for maximum therapeutic benefit.

5. References

Araújo, M. R. S.; Assunção, J. C. C., Dantas, I. N. F., Costa-Lotufo, L. V. & Monte, F. J. Q. (2008). Chemical Constituents of *Ximenia americana*. *Natural Products Communications*, Vol. 3, No. 6, pp. 857-860, ISSN 1934-578X

Araújo, M. R. S.; Monte, F. J. Q. & Braz-Filho, R. (2009). A New Sesquiterpene from *Ximenia americana* Linn. *Helvetica Chimica Acta*, Vol. 92, pp. 127-129, ISSN 0018-019X.

Atta-ur-Rahman. (1988). *Studies in Natural Products Chemistry, Structure Elucidation*, Vol.32, Elsevier, New York, U.S.A.
Ximenia americana: Chemistry, Pharmacology and Biological Properties, a Review

Atta-ur-Rahman (Elsevier) (2005). Studies in Natural Products, Bioactive Natural Products (Part L), Vol. 32, Atta-ur-Rahman, Karachi, Pakistan, ISBN 9780444521712.

Badami, R. C. & Patil, K. B. (1981). Structure and Occurrence of Unusual Fatty Acids in Minor Seed Oils. Progress in Lipid Research, Vol. 19, pp. 119-153, ISSN 01637827.

Braga, R. (3ª Ed.). (1976). Plantas do Nordeste, especialmente do Ceará, Escola Superior de Agricultura, Mossoró, Brasil.

Brasileiro, M. T.; Egito, M. A. & Lima, J. R.; Randau, K. P.; Pereira G. C.; Neto, P. J. R. (2008). Ximenia americana L: botânica, química e farmacologia no interesse da tecnologia farmacêutica. Revista Brasileira Farmacognosia, 89, 2, pp. 164-167, ISSN 0370-372X.

Bruneton, J. (3ª Ed) (1999). Pharmacognosie, phytochimie, plantes médicinales, Tec & Doc Ed., Angers, France.

Chhabra, S. C.; Viso, F. C., (1990). A Survey of the Medicinal Plants Eastern Tanzania for Alkaloids, Flavonoids, Saponins and Tannins. Fitoterapia, Vol. 61, No. 4, pp. 307-316, ISSN 2367326X.

Dixon, R. A.; Dey, P. M. & Lamb, C. J. (1983). Phytoalexins: enzymology and molecular biology. Advance Enzymology, Vol. 55, pp. 1-69.

Fatope, M. O.; Adoum, O. A. & Takeda, Y. (2000). C18 Acetylenic Fatty Acids of Ximenia americana with Potential Pesticidal Activity. Journal of Agricultural and Food Chemistry, Vol. 48, pp. 1872-1874, ISSN 00218561.

Finnermore, H. J. M. Cooper, M. B. Stanlet, J. H. Cobcroft & L. J. Harris, (1988). Journal of the Indian chemical Society, Vol. 57, pp. 162-169 ISSN 0019-4522.

Geran, R. T.; Greenberg, M. N.; MacDonald, A. M.; Schumacher, A. M. & Abbot, B. J. (1972). Protocols for screening chemical agents and natural products against animal tumors and other biological systems. Cancer Chemotherapy Reports, Vol. 3. p. 1, ISSN 00690112.

Geyid, A.; Abebe, D.; Debella, A.; Makonnen, Z.; Aberra, F.; Teku, F.; Kebede, T.; Urga, K.; Yersaw, K.; Biza, T.; Mariam, B. H. & Guta, M. (2005). Screening of medicinal plants of Ethiopia for their anti-microbial properties and chemical profiles. Journal of Ethnopharmacology, Vol. 97, pp. 421-427, ISSN 0378-8741.

Hartwell, J. L. (1967; 1968; 1969; 1970; 1971). Plants used against cancer. Loydia, Vol. 30 p. 379; Vol. 31, p. 71; Vol. 32, p. 71, 153, 247; Vol. 33, p. 98, 288; Vol. 34, p. 103, 204, 310, 386.

Hostettman, K.; Marston, A. J.; Wolfender, L & Miallard, M. (1995). Screening for flavonoids and related compounds in medicinal plants by LC-UV-MS and subsequent isolation of biactive compounds, Akademiiai, Kiaho, Budapest, Hungry.

Jackson, M. (1971). Naturally Occurring Insecticides, M. Crosby. D. G. Eds.: Dekker, New York, U.S.A.

James, D. B.; Abu, E. A.; Wurochekke, A. U. & Orgi, G. N. (2007). Phytochemical and Antimicrobial Investigation of the Aqueous and Methanolic Extracts of Ximenia americana. Journal of Medical Science, Vol. 7, No. 2, (15th February 2007), pp. 284-288, ISSN 20721625.

James, D. B.; Owolabi, A. O.; Ibiyeye, H.; Magaji, J. & Ikugiyi, Y. A. (2008). Assessment of the hepatic effects, hematological effect and some phytochemical constituents of

www.intechopen.com
Ximenia Americana (Leaves, stem and root) extracts. African Journal of Biotechnology, Vol. 7, No. 23, (December, 2008), pp. 4274-4278, ISSN 1684-5315.

Koennen, C.; Schmid, U.; Rogers, J.; Peilow, A.; Bosley, J.; Eggink, M. & Stam, W. (2004). Blend used in preparing, food composition, e. g. margarine, comprises ximenynic acid originating from natural source and fatty acids or glycerides. Derwent Innovations Index, patent No. EP1402787-A1, (June 2004), U.S.A., 4p.

Loganathan, D.; Trivedi, G. K. & Chary, K. V. R. (1990). A Two Dimensional NMR Strategy for the Complete 1H Chemical Shift Assignment of Extended Proton Spin Systems in Triterpenoids. Magnetic Resonance in Chemistry, 28, 11, (July 1990), pp. 925-930, ISSN 1097-458X.

Magassouba, F. B.; Diallo, A.; Kouyaté, M.; Mara, F.; Mara, O.; Bangoura, O.; Camara, A.; Traoré, S.; Diallo, A. K.; Zaoro, M.; Lamah, K.; Diallo, S.; Camara, G.; Kéïta, A.; Camara, M. K.; Barry, R.; Kéïta, S.; Oularé, K.; Barry, M. S.; Donzo, M.; Camara, K.; Toté, K.; Vanden Berghe, D.; Totté, J.; Pieters, L.; Vlietinck, A. J. & Baldé, A. M. (2007). Ethnobotanical survey and antibacterial activity of some plants used in Guinean traditional medicine. Journal of Ethnopharmacology, Vol. 114, pp. 44-53, ISSN 0378-8741.

Mahato, S. B.; Nandy, A. K. & Roy, G. (1992). Triterpenoids. Phytochemistry, Vol. 31, pp. 2199-2249, ISSN 0031-9422.

Maikai, V. A.; Kobo, P. I. & Adaudi, A. O. (2008). Acute toxicity studies of aqueous stem bark extract of Ximenia Americana. African Journal of Biotechnology, Vol. 7, No. 10, (May, 2008), pp. 1600-1603, ISSN 1684-5315.

Maikai, V. A.; Maikai, B. V. & Kobo, P. I. (2009). Antimicrobial Properties of Stem Bark Extracts of Ximenia americana. Journal of Agricultural Science., Vol.1, No. 2, (December 2009), pp. 30-34. ISSN 00218596.

Maikai, V. A.; Nok, J. A.; Adaudi, A. O. & Alawa, C. B. I. (2008). In vitro antitrypanosomal activity of aqueous and methanolic crude extracts of stem bark of Ximenia americana on Trypanosoma congolense. Journal of Medicinal Plants, Vol. 2, No. 3, pp. 55-58, ISSN 16840240.

Mathabe, M. C.; Nikova, R. V.; Lall, N. & Nyazema, N. Z. (2006). Antibacterial activities of medicinal plants used for the treatment of diarrhoea in Limpopo province, South Africa. Journal of Ethnopharmacology, 105, pp. 286-293, ISSN 0378-8741.

Matos, F. J. A. (2007). Plantas medicinais: guia de seleção e emprego de plantas usadas em fitoterapia no Nordeste do Brasil, Imprensa Universitária, Fortaleza, Brasil.

Mevy, J-P.; Bessiere, J-M.; Greff, S.; Zombre, G. & Viano, J. (2006). Composition of the volatile oil from leaves of Ximenia americana L. Biochemical Systematics and Ecology, Vol. 34, pp. 549-553, ISSN 0305-1978.

Ogunleye, D. S.; Ibitoye & Trop, S. F. (2003). Studies of antimicrobial activity and chemical constituents of Ximenia americana. Journal of Pharmaceutica Research, Vol. 2, No. 2, (December 2003), pp. 239-241, ISSN 00223549.

Omer, M. E. F. A. & Elnima, E. I. (2003). Antimicrobial activity of Ximenia americana. Fitoterapia, Vol. 74, pp. 122-126, ISSN 0367326X.

Paolo, R. (1979). Cosmetic use of the oil and flowers of Ximenia americana. Rivista Italiana Essenze, Vol. 61, No. 5, pp. 190-193, ISSN 0391-4658.
Parker, M. E.; Chabot, S.; Ward, B. J. & Johns, T. (2007). Traditional dietary additives of the Maasai are antiviral against the measles virus. *Journal of Ethnopharmacology*, Vol. 114, pp. 146-152, ISSN 0378-8741.

Pio-Correia, M. (1984). *Dicionário de Plantas Úteis do Brasil e das Éxoticas Cultivadas*, Imprensa Nacional, Rio de Janeiro, Brasil.

Rezanka, T & Sigler, K. (2007). Identification of very long chain unsaturated fatty acids from *Ximenia* oil by atmospheric pressure chemical ionization liquid chromatography-mass spectroscopy. *Phytochemistry*, Vol. 68, pp. 925-934, ISSN 00319422.

Saeed, A. E. M. & Bashier, R. S. M. (2010). Physico-chemical analysis of *Ximenia americana* L. oil and structure elucidation of some chemical constituents of its seed oil and fruit pulp. *Journal of Pharmacognosy and Phytotherapy*, Vol. 2, No. 4, pp. 49-55. ISSN 21412502.

Scalbert, A. (1991). Antimicrobial properties of tannins. *Phytochemistry*, Vol. 30, pp. 3875-3883, ISSN 00319422.

Siddaiah, M.; Jayavcera, K. N.; Mallikarjuna, R. P.; Ravindra, R. K.; Yasodha, K. Y. & Narender, R. G. (2009). Phytochemical screening and analgesic activity of methanolic extract of *Ximenia americana*. *Journal of Pharmacy and Chemistry*, Vol. 3, No. 1, pp. 23-25, ISSN 0973-9874.

Soro, T. Y.; Traore, F.; Datte, J. Y. & Nene-Bi, A. S. (2009). Antipyretic activity of aqueous extract of *Ximenia americana*. *Phytoterpie*, Vol. 7, No. 6, pp. 297-303, ISSN 1624-8597.

Soro, T. Y.; Traore, F. & Sakande, J. (2009). Activité analgésique de l’ extrait aqueux de *Ximenia americana* (Linné) (Olacaceae). *Comptes Rendus Biologies*, Vol. 332, pp. 371-377, ISSN 16310691.

Spjut, R. W. & Perdue Jr., R. E. (1976). Plant folklore: a tool for predicting sources of antitumor activity ?. *Cancer Treatment Reports*, Vol. 60, pp. 979-985.

Sptizer, V.; Tomberg, W. & Aichholz, R. (1997). Analysis of Seed Oil of *Heisteria silvanii* (Olacaceae) – A rich Source of Novel C18 Acetylenic Fatty Acid. *Lipids*, Vol. 32, pp. 1189-1200, ISSN 00244201.

Steven, M. C. & Russel, J. M. (1993). *Bioactive Natural Products*, CRC Press, ISBN 0-8493-4372-0, Boca Raton, U. S. A.

Tassou, C. C.; Drosinos, E. H. & Nychas, G. J. E. (1995). Effects of essential oils from mint (*Mentha piperita*) on *Salmonella enteritidis* and *Listeria monocytogenes* in model Food systems at 4° and 10°C. *Journal of Applied Bacteriology*, Vol. 78, pp. 593-600, ISSN 00218847.

Taylor, R. S.L.; Edet, F. Manandhar, N. P. & Towers, G. H. N. (1996). Antimicrobial activities of southern Nepalese medicinal plants. *Journal of Ethnopharmacology*, Vol. 50, pp. 97-102, ISSN 0378-8741.

Voss, C.; Eyol, E. & Berger, M. R. (2006). Identification of potent anticancer activity in *Ximenia americana* aqueous extracts used by African traditional medicine. *Toxicology and Applied Pharmacology*, Vol. 211, pp. 177-178, ISSN 0041-008X.

Voss, C.; Eyol, E.; Frank, M.; von der Lieth, Claus-W & Berger, M. R. (2006). Identification and characterization of riproximin, a new type II ribosome-inactivating protein
with antineoplastic activity from *Ximenia americana*. *Toxicology and Applied Pharmacology*, Vol. 20, pp. 334-345, ISSN 0041008X.

Ya, C.; Gaffney, S. H.; Lilley, T. H. & Haslam. E. (R. W. Heminway and J. J. Karchesy Ed). (1988). *Carbohydrate-polyphenol complexation*, Plenum Press, New York, U.S.A.
Phytochemicals are biologically active compounds present in plants used for food and medicine. A great deal of interest has been generated recently in the isolation, characterization and biological activity of these phytochemicals. This book is in response to the need for more current and global scope of phytochemicals. It contains chapters written by internationally recognized authors. The topics covered in the book range from their occurrence, chemical and physical characteristics, analytical procedures, biological activity, safety and industrial applications. The book has been planned to meet the needs of the researchers, health professionals, government regulatory agencies and industries. This book will serve as a standard reference book in this important and fast growing area of phytochemicals, human nutrition and health.

How to reference
In order to correctly reference this scholarly work, feel free to copy and paste the following:

Francisco José Queiroz Monte, Telma Leda Gomes de Lemos, Mônica Regina Silva de Araújo and Edilane de Sousa Gomes (2012). Ximenia americana: Chemistry, Pharmacology and Biological Properties, a Review, Phytochemicals - A Global Perspective of Their Role in Nutrition and Health, Dr Venketeshwer Rao (Ed.), ISBN: 978-953-51-0296-0, InTech, Available from: http://www.intechopen.com/books/phytochemicals-a-global-perspective-of-their-role-in-nutrition-and-health/ximenia-americana-chemistry-pharmacology-and-biological-properties-a-review