

Bioactivities and Health Benefits of *Ximenia americana* L.: A Wild Edible Fruit

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Abstract

Ximenia americana is one of the most valuable wild edible fruits in the world, but it is still neglected and underexplored. The fruit is reported as indispensable source of phytochemicals and health imparting components. However, review on the bioactivities of *X. americana* is still scarce. *X. americana* contain many bioactive compounds, such as polyphenols, anthocyanins and flavonoids. Many studies have shown that *X. americana* possess various bioactivities and health benefits, such as free radical scavenging, antioxidant, anti-inflammatory, antidiabetic, antimicrobial, antitrypanosomal, antiviral, anticancer and analgesic activities. It was demonstrated that the fruit's antioxidant activity was correlated with its anthocyanin, flavonoid, and polyphenol contents. They are also used as food source for the native people. Therefore, *X. americana* has the potential to be developed into functional foods or pharmaceuticals to enhance, prevent and treat a variety of chronic diseases. In this study, we review researches regarding the bioactivities and health benefits of *X. americana*, which is important for its exploitation and utilization. The therapeutic efficacy of *X. americana* is no longer in doubt. It is anticipated that this review will aid researchers, herbal medical practitioners and agriculturists, and it will also improve the plant's optimal utilization for its several benefits.

Keywords: *Ximenia americana* L., Polyphenols, Flavonoids, Vitamin C, Antioxidant activity

Introduction

Wild edible fruits have the potential to be valuable and intriguing sources of nutrients, such as dietary fiber and bioactive compounds with strong antioxidant activity. These nutrients could serve as the basis for functional foods, food supplements, and nutraceuticals (Heinrich et al., 2006). Unfortunately, these species' potential as a source of energy, carbohydrates, vitamins, minerals, and bioactive substances is still unknown, and they are still neglected and unexplored. These wild edible fruits can be used as food source for the native people (Hegazy et al., 2019). Due to decrease in both immune and non-immune defenses, deficiencies of essential micronutrients can increase the risk of illness or death from infectious diseases. In low and middle-income countries where wild fruits are a source of these compounds, such nutrient deficiencies are widespread (Fernández-Ruiz et al., 2017). Because wild fruit contain phytochemicals with diverse bioactivities, researchers suggest that their consumption may help in the prevention or treatment of numerous diseases such as diabetes, cardiovascular problems, digestive and urinary tract disorder (Erşan et al., 2020; Islyar et al. 2016).

Ximenia americana is one of the wild edible fruit which belongs to Olacaceae family. *X. americana* is a small tree or shrub, native to tropical area of Africa and seen distributed in many parts of the world. The fruit can be used for innovative drug formulation due to its medicinal value. Generally, the fruit is obtained in Africa, India, New Zealand, Central America and South America (Mohamed & Feyissa, 2020). *Ximenia* has common names as wild plum, sour or monkey plum, sea lemon or false sandal wood and is known in the Northern part of Nigeria as 'Tsada', and in Eastern part (Igbo land) as 'Anyá Nwona'; while the in Western part (Yoruba) it is called 'Igo' (Adamu et al., 2005). The various parts of the plant are used traditionally to treat a variety of ailments (Agyigra et al., 2017). The fruit is green colored at the early stage of ripening and turn to yellow or red colored when ripen (Maikai et al., 2009).

Research revealed that the flesh of the *X. americana* fruit has a significant amount of total polyphenol, vitamin C, and free radical scavenging activity. Not only the fruit flesh but also the seed presents high polyphenols and antioxidant activity making it potential raw material for medicinal use (Sarmiento et al., 2015; Almeida et al., 2016; Lamien-Meda et al., 2008; Muhammad et al., 2019). The leaves are reported to have antibacterial activity and also used in the treatment of fever, tuberculosis, tooth decay and wounds (Ogunleye & Ibitoye, 2003). Numerous studies have confirmed the effectiveness of using roots to cure wounds, syphilis, leprosy, and dysentery. There have been reports of anti-trypanosomal properties in the stem bark. Northern Nigerians employ *X. americana* leaves and roots as herbal remedies to treat a variety of illnesses (Maikai et al., 2008a; Maikai et al., 2008b). The aqueous and methanolic leaf extracts of *X. americana* showed significant antioxidant and anti-inflammatory activities in previous studies (Arun et al., 2015).



In a study conducted in Africa with various wild fruit trees, including *X. americana*, it was observed that the fruits of this specimen was among those with the potent antioxidant activity, correlated to the contents of phenolics and flavonoids compounds. This suggests *X. americana* to be a potential source of antioxidants that can be used medically or as food to avoid the oxidation of cells in the human body (Lamien-Meda et al., 2008).

It was confirmed by a study conducted in some semi-arid regions of the Brazilian northeast that *X. americana* are used in the area of pharmacology and as medicinal plant in rural communities (Oliveira et al., 2010). A phytochemical analysis of the plant extract made with the stem bark, revealed the presence of several bioactive compounds, as alkaloids, anthraquinones, glycosides, flavonoids, saponins, tannins, terpenoids, giving it an elevated antioxidant activity (Maikai et al., 2010). According to findings from another study, extracts from the stem containing these compounds can be used for the treatment of infectious diseases caused by pathogens with *S. aureus*, *P. aeruginosa*, *E. coli*, *B.subtilis*, *P. vulgaris* and *C. albicans* (Maikai et al., 2009).

From an extensive literature review it was observed that *X. americana* is widely used as a popular substitute remedy in certain regions of the Africa (Guinea, Ethiopia, Nigeria, Sudan) and in the Brazil. Several biological activities such as antimicrobial, pesticidal, analgesic, antipyretic, anticancer and antitrypanosomal among others were demonstrated by the plant extracts, particularly aqueous and methanolic (Magassouba et al., 2007; Maikai et al., 2008a, 2008b; Maikai et al., 2009; Rezanka & Sigler, 2007; Siddaiah et al., 2009; Soro et al., 2009; Voss et al., 2006). A further investigation revealed that *Ximenia americana* leaf extracts, both aqueous and methanolic, were potent anti-inflammatory and antioxidant agents (Arun et al., 2015).

Nonetheless, there is paucity of data on the review of bioactive compounds of the fruit. Considering this and its various phytotherapeutic properties, the present article aimed to review the bioactive compounds and health benefits of fruits of *X. americana*.

Botanical description of *Ximenia americana*

Ximenia americana L., commonly known as wild plum, blue sour plum and tallow nut belongs to family *Olacaceae*. It is a spiny shrub or small tree up to 6 m, commonly less than 4 m, that spreads or, less often, scrambles. Branches normally arching down often armed with straight spines. Leaves are simple, alternate or clustered on spur shoots with rounded and slightly notched; broadly tapering base or rounded and occasionally softly haired. Small greenish white, fragrant flowers, born on short shoots (Maundu et al., 1999) and greenish-cream, scented and 5-10 mm long; in small, branched inflorescences (Sacande & Vautier, 2006). Fruits are oval, shiny and up to 3 cm long. Light green, turning yellow, orange or red on ripening and contains one large endospermic seed within its green pulp containing a small embryo near a thin testa. They have up to 60% oil content. Seedling morphology is variable, when young the leaves are densely hairy, but become smooth and shiny with growth (Maundu et al., 1999; Sacande & Vautier, 2006).



Figure 1: *Ximenia americana*

Importance of *Ximenia americana* in Different Parts of the World

The fruits and leaves of *X. americana* have traditionally been used in a variety of humans and animals medications (Mwangi et al., 1994). The plant's leaves and twigs are used for fever, cold, as a solution for toothaches, as a laxative and eye lotion, and poison cure (De Menezes et al., 2019; Le et al., 2012; Feiberger et al., 1998). The plant's root parts also used to treat guinea worm attack, skin burns, leprosy, some sexually transmitted diseases,



headaches, hemorrhoids, sleeping thickness, and puffiness (Teo, 1997). The fruits are eaten in large quantities and act as a vermifuge to treat constipation caused by eating heavy foods (Kuroki & Conn, 1989; Niemi et al., 2005). Following various local processing methods such as drying and powdering, the bark is applied topically to cure skin ulcers. Headaches can be treated using the leaves. Additionally, evidence suggests that *Ximenia americana* has a significant role in controlling many more different humans as well as animal diseases (Le et al., 2012; Omer et al., 1998).

Ximenia americana bark contains approximately 17% oils; heartwood and flowers contain essential oils (Fatope & Adam 2005). The processed and extracted oil which is mainly edible, nondrying, can also be used to make soap, as lubricant, traditionally as body anointing, and as a cure for dry chapped feet (Sallamander, 2010).

It is reported that *Ximenia americana* oil have a higher amount of saturated and monounsaturated fatty acids (about 99%), which gave it stability to oxidation. Research conducted on the oil revealed that it is highly effective in treating dry skin, which is prone to premature senescence and increases sebaceous tissue activity. The primary function of unsaturated fatty acids derived from the plant's fruit is to moisturize, soften, and revitalize skin (Sarmiento et al., 2015).

Orally taken *Ximenia americana* as fresh or processed form also works well for healing skin sores, hemorrhoids, and helps with looseness of the bowels. It also functions as a decent pain-relieving agent that lowers fevers; at the same time and effective against viral diseases like the measles (Koné & Atindehou, 2004). Certain compounds found in this plant have been shown to help treat insulin-resistant diabetes, treat Alzheimer's disease, enhance cognition, and lower cholesterol.

Powerful compounds with anticancer, antifungal, antiallergic, antiparasitic, antiviral, and antibacterial activities have been found in the fruit and the stems and it is also a very good antioxidant (Maikai et al., 2009; Omer & Elnima, 2003; Anonymous, 2010). Additionally, evidence suggests that it works well to relieve arthritis. The seeds contain higher amount of healthy fatty acids, and the leaf extract has shown to have antibacterial capacity comparable to penicillin and is effective for killing gonorrhea and cancer cells (Anonymous, 2010).

Shagal et al., (2013) concluded that phytochemical screening of three different plant parts using ethanol and water as solvent revealed the presence of tannins, saponins, flavonoids, phenols, and volatile oils. Additionally, ethanol extracts of the plant parts were found to have antimicrobial activity on *S. aureus*. They also found that the water extract showed antimicrobial activity on *S. aureus* and *E. coli*.

The orange shaped fruit that tastes a little bit like almonds has been found by researchers worldwide to be extremely high in vitamin C. Vitamin C is a great antioxidant that helps to prevent cancer, strokes and cardiovascular disease. According to reports, *Ximenia* fruit has high protein content along with significant amount of fiber, carbohydrates, starches, minerals, and vitamin E. It also has nonessential proteins, and the tree's stem, bark, and leaves also are rich in naturally occurring steroids that may be used in the future for treating diseases such as strokes and cardiovascular disease (Hou et al., 2008; Oladipo et al., 2013; Lucilania et al., 2016).

This suggests that the plant has numerous advantages on the environment, food security, and medicinal value, input for industries, and if properly handled as well as invested on, it may be a source of income for developing countries.

Bioactivities of *Ximenia americana*

Antioxidant Activity

Normally, free radicals are produced as a byproduct of cellular metabolism. Free radicals are capable of killing bacteria, damaging biomolecules, trigger immunological reactions, activate oncogenes, causing atherogenesis, and accelerate the ageing process (Ansari, 1997). Reactive oxygen and nitrogen species (ROS and RNS) are the most important classes of radical species generated in living systems. Numerous chronic human diseases, including as atherosclerosis, diabetes mellitus, cancer, rheumatoid arthritis, cataracts, and Parkinson's disease, may be significantly impacted by the overproduction of ROS and RNS (Halliwell & Gutteridge, 1990). Various natural products such as fruits, vegetables, cereal grains, edible flowers, wine, herbal plants, and their infusions have been proved to have antioxidant activities (Li et al., 2014; Li et al., 2013; Deng et al., 2012; Fu et al., 2011; Song et al., 2010; Alezandro et al., 2013; Margraf et al., 2016; Macedo et al., 2013; Granato et al., 2015). Therefore, natural resources of antioxidants have been considered as quite important. Numerous studies have demonstrated the antioxidant properties of numerous wild fruits, including *Ximenia americana*.

Antioxidants and Free Radical Scavenging Activity

DPPH is a stable free radical that is used to determine a fruit/plant extract's ability to scavenge free radicals (Silva & Sirasa, 2018). Ethiopian *X. americana* yellow and red colored varieties' flesh and seeds were examined for bioactive components, antioxidant activity, fatty acid profiles, and physicochemical characteristics (Bazezew et al., 2021). At 200 µg/mL concentration, the red flesh of *X. americana* fruit demonstrated stronger radical scavenging (97%) compared to the yellow *X. americana* flesh (94%) (Bazezew et al., 2021). At the same concentration, the red *X. americana* seed exhibited greater scavenging activity (75%) compared to the yellow *X.*



americana seed (68%). This may be because the fruit has a comparatively greater naturally occurring bioactive compound like total phenol in the fruit which enables it to be used in food and pharmaceuticals to prevent oxidation of cells in human body. The red *X. americana* seed also demonstrated higher antioxidant capacity ($IC_{50}= 147 \mu\text{g/mL}$) in comparison to the yellow fruit seed ($IC_{50}= 154 \mu\text{g/mL}$) without significant variations. According to Sarmiento (2015), the flesh and seed of the yellow *X. americana* fruit grown in Mossoró-Assu, RN, Brazilian semiarid region had also significant antioxidant activities.

According to studies by researchers from different countries Lamien-Meda et al., (2008); Le et al., (2012) and Sarmiento (2015), the yellow *X. americana* fruit had high antioxidant activity. Hence, the fruit can be used for the value addition in food processing and pharmaceutical industries due to the high free radical scavenging activities (Schubert et al., 2007).

Antidiabetic Activity

Approximately 25% of people worldwide, in both industrialized and developing nations are affected by diabetes mellitus (Kayarohanam & Kavimani, 2015; Benalla et al., 2010; Rahimi, 2015). With an estimated 110 million people living with the disease globally, China led the field, followed by the United States (30 million) and India (70 million). Diabetes is predicted by the WHO to rank seventh among all causes of death in 2030. Cardiovascular problems associated with diabetes constitute a serious hazard to human health, accounting for one fatality every ten seconds (Das & Rai, 2008). Due to societal influences and changes in lifestyle, the number of cases of diabetes is rising dramatically on a global scale (Gupta & Misra, 2007). Diabetes mellitus is considered as the group of metabolic disorders with different causes, which are characterized by imbalancing in carbohydrates, proteins and fat metabolism that lead to the effect on insulin action or secretion (American Diabetes Association, 2007). There is still no reasonable effective therapy or drug to cure diabetes in modern medicine (Ali et al., 2006). Anti-diabetic medicines that are currently available for use include thiazolidinedione, sulfonylureas, and α -glycosidase inhibitors like acarbose, which are commonly used to treat hyperglycemia. However, these drugs fail to cure the disease in addition, causes several diabetic complications and side effects, including diarrhea, stomach discomfort, and soft feces in colon (Ahmed et al., 2004; Davis & Granner, 2001).

When compared to other solvent extracts *in vitro* antidiabetic studies show that aqueous extract exhibited significant activity. The study provides scientific evidence that leaves of *Ximenia americana* have anti-diabetic efficacy (Shettar et al., 2017).

In another study, significant reduction of blood glucose was observed from the second day of the investigation on antidiabetic activity of *Ximenia americana* in alloxanised rats. The comparable effect of the extract with glibenclamide may suggest similar mode of action since alloxan permanently destroys the pancreatic B cells and the extract lowered blood sugar level in alloxanised rats, demonstrating that the extract possesses extra pancreatic effect. From the phytochemical analysis it was found that the main chemical constituents of the extract and some of this active principle including flavonoids are known to be used for the treatments of diabetes. Based on the above evidence, it is plausible that the observed antidiabetic activity is due to the presence of flavonoids and tannins (Siddaiah et al., 2011).

Antimicrobial Activity

Many bacterial, fungal, and viral species are known to cause diseases in plants, animals, and humans. These infections can lead to crop loss, food spoilage, or even food poisoning, which can be harmful to an individual's health (Cilerdzic et al., 2014; Garcia & Blanco, 2000). Therefore it is important to develop natural effective antimicrobial agents. Numerous researches have shown that *Ximenia americana* exhibited potential antiviral, antifungal, and antibacterial properties.

Antibacterial and Antifungal Activities

Some studies examined the antimicrobial activity of a certain species of *X. americana*. 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 presence of secondary metabolites such as polyphenols, triterpenes, sterols, saponins, tannins, alkaloids, glycosides, and polysaccharides appears to be the cause of the antimicrobial activity of the extracts of the different parts of the investigated plants, such as roots, leaves, seeds, stem barks, and fruits (Geyid et al., 2005; James et al., 2007; Maikai et al., 2009; Ogunleye et al., 2003).

According to Shagal et al., (2013), ethanolic and aqueous extracts were analysed for the qualitative phytochemicals of three different parts of *Ximenia americana*. The results indicated the presence of tannins, saponins, flavonoids, phenols, and volatile oils, as well as the fact that ethanol extracts of the plant parts exhibited antimicrobial activity against *S. aureus*. Additionally, they discovered that the water extract had antibacterial efficacy against *E. Coli* and *S. aureus* (Shagal et al., 2013).

At dilutions as low as 250 $\mu\text{g/ml}$, the MeOH extract from *X. americana* leaves prevented or retarded the growth of *Neisseria gonorrhoea*. At a dosage of 4000 $\mu\text{g/ml}$, the same extract demonstrated antifungal activity against *Cryptococcus neoformans* and *Candida albicans*. Chemical screening conducted on the extract revealed the presence of several secondary metabolites as tannins, sterols, terpenoids, flavonoids and saponins (Geyid et al.,



2005). *P. aeruginosa*, *P. vulgaris*, *B. subtilis*, *E. coli*, *S.aureus*, and *C. albicans* were the six common bacterial isolates against which the ethanol extract of the leaves was tested for antimicrobial activity, and it demonstrated activity against all of them. *P. aeruginosa* had the highest level of activity (inhibition zone: 20 mm), which was followed by *B. subtilis* and *C. albicans* (10 mm). The plant's organic extract exhibited similar levels of activity as the commercially available penicillin disc (2 µg), which demonstrated greater efficacy against *P. aeruginosa* but less effective against *S. aureus*. According to the findings of the phytochemical screening, cyanogenic glycosides, tannins, flavonoids, and saponins were present (Ogunleye et al., 2003). *X. americana* was tested against five different bacteria, the aqueous and methanolic extracts of its roots, stem bark, and leaves inhibited the growth of *S. aureus* and *Klebsiella pneumonia*, but only the methanolic leaf, aqueous bark, and aqueous leaf extracts inhibited the growth of *Shigella flexineri*. These extracts had no effect on *E. coli* or *S. typhi*. The Minimum Inhibitory Concentration (MIC) was only evident for the methanolic extracts at $1.25 \times 10^4 \mu\text{g mL}^{-1}$ (1:4) against *S. aureus* while the Minimum Bactericidal Concentration (MBC) of the extracts was obtained at $2.50 \times 10^4 \mu\text{g mL}^{-1}$ (1:2) (James et al., 2007). According to the findings, the extracts' (methanolic root) inhibitory action was more noticeable on *Klebsiella pneumonia*, while it was inactive against *Shigella flexineri*, *Salmonella typhi*, and *E. coli*. Comparing the methanolic bark extract and leaf extracts against *Klebsiella pneumonia*, the methanolic root extract exhibited highly significant ($p < 0.05$) activity. With the exception of aqueous and leaf extracts, the phytochemical constituents present in the extracts included cardiac glycosides, saponins, tannins, and flavonoids in addition to carbohydrates in the form of sugars and soluble starch. The findings indicate that methanolic root, stem bark, and leaf extracts exhibit bactericidal properties at concentrations between 2.5×10^4 and $1.25 \times 10^4 \mu\text{g mL}^{-1}$. The antibacterial properties of these extracts are attributed to the presence of flavonoids, carbohydrates, glycosides, and tannins.

To ascertain whether *Ximenia americana* crude extracts possessed antimicrobial activity, numerous more investigations were carried out (Magassouba et al., 2007; Maikai et al., 2009). Overall, it was discovered that the different extracts had a broad spectrum effect against standard organisms (*Salmonella typhi*, *Bacillus subtilis*, *Proteus vulgaris*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus aureus*, *Candida albicans*, and *Shigella flexineri*). This finding supports the plant's traditional use as a remedy for microbial infections.

In general, the presence of secondary metabolites appears to be the cause of antimicrobial activity of extracts of the various parts of the plants. Cyanogenic glycosides are reported to possess antimicrobial activity. Tannins have long been used as an antidote for heavy metal poisoning, as well as for the protection of inflamed surfaces of the mouth and treatment of catarrh, cuts, hemorrhoids, and diarrhea. They have the ability to inactivate 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 with a wide range of biological activities, such as anti-inflammatory, anti-allergic, antibacterial, antifungal, and vasoprotective properties. They have also been shown to form complexes with bacterial cell walls and extracellular and soluble proteins (Dixon et al., 1983; Geyid et al., 2005; Hostettman et al., 1995; James et al., 2007; Maikai et al., 2009; Ogunleye et al., 2003). There have also been report of Terpenoids 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). The existence of these secondary metabolites is undoubtedly responsible for the extracts' antimicrobial activity, even though it is challenging to infer the exact mechanism of action of the extracts' contents based on research done to date. In the case of extracts of *Ximenia americana*, probably, due the presence of tannins, flavonoids, triterpenes/steroids, saponins or cyanogenic glycosides.

In conclusion, the findings supported the use of *X. americana* as an agent in novel medications for the treatment of infectious diseases caused by pathogens and validated the plant's claimed antimicrobial properties.

Analgesic Activity

Because of its analgesic properties, the aqueous extract of *X. americana* stem bark is widely used in Tanzania, Senegal, Zimbabwe, and Nigeria. When taken in dosages ranging from 10 to 100 mg/kg P.C., the extract of *X. americana* suppresses abdominal contractions while having analgesic properties similar to those of phenylbutazone. In fact, 45.2% of patients get pain inhibition by phenylbutazone at doses of 100 mg/kg P.C. At the same concentration, the *X. americana* extract exhibits a percentage of inhibition of 61.1%. These characteristics are most likely caused by the extract's flavonoids and saponins (Soro et al., 2009).

Using chemical models of nociception in mice, the analgesic efficacy of *X. americana* leaf methanol extract was examined. The extract inhibited the acetic acid-induced abdominal writhes in mice by 54.13, 63.74, and 66.4% at dosages of 200, 400, and 600 mg/kg i.p. In the formalin test, the administration of 200, 400, and 600 mg/kg i.p. exhibited 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, but had no impact on the first phase (0 to 5 min). These findings suggested that *X. americana* methanol leaf extract has analgesic activity (Siddaiah et al., 2009).

Anti-trypanosomal Activity



Trypanosoma congolense was used to test the methanolic and aqueous extracts of *X. americana*'s stem bark for their *in vitro* anti-trypanosomal activity. Blood obtained from a high infected mice with *T. congolense* (10(7) 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 findings showed that at 20 and 40 mg/ml, both methanol and aqueous extracts had activity; however, at 10 and 5 mg/ml, methanolic extracts were more active than aqueous extracts. Phytochemical screening of the methanolic and aqueous extracts of the bark showed that they both revealed the presence of flavonoids, anthraquinones, saponins, terpenes and tannins. The aqueous and methanolic extracts appear to show some potential activity against *T. congolense* (Maikai et al., 2008).

Anticancer Activity

Worldwide, cancer is recognized as a leading cause of death. Fruit consumption has been linked to a lower risk of cancer (Chu et al., 2002; Liu, 2003). A variety of natural products, such as fruits, vegetables, and herbal plants, have been widely proved to possess antiproliferative activities (Li et al., 2013; Zhou et al., 2016; Li et al., 2013). It has been demonstrated that a number of wild fruits, including wild blueberries and red raspberries from Jamaica, have anticancer properties against cancer cells of the breast, colon, prostate, and cervical regions. It has been demonstrated that plants are a good source of natural compounds that can be used to cure human neoplastic diseases. Information recorded from ancient civilizations has shown the use of plants in search of treatment for various types of cancer (Hartwell, 1967-1971). Examples of anticancer agents developed from higher plants are the antileukemic bis-indole alkaloids vinblastine and vincristine from the *Catharantus 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). Various extracts from *Ximenia americana*, a plant used in African traditional medicine for treating cancer were tested for their antineoplastic activity *in vitro* (Voss et al., 2006). A detailed investigation of the most active aqueous extract was conducted on a panel of 17 tumor cell lines, 16 of which originate from human and 1 from rat, 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. Using CC531 colorectal rat model, the *in vivo* antitumor activity was assessed. Following peroral administration, significant anticancer activity was observed, showing 95% reduction in activity.

Antiviral Activity

By using the plaque reduction neutralization assay, the stem bark of MeOH extract of *X. americana* and a few other plant species employed by the Maasai pastoralis of East Africa demonstrated an antiviral activity against the measles virus *in vitro*. Extracts of all the plants contain potentially active constituents including polyphenols, glycosides, alkaloids, terpenes, tannins, sterols and saponins (Parker et al., 2007).

Food Use

Blends of glyceride containing ximenynic acid (9) from *X. americana* are useful for the preparation of food compositions or food supplements, such as margarine, mayonnaises, cheese, chocolate, drinks, icecream, dry soups, snack bars, cereal bars and sauces. The blends offers a composition with health benefits ranging from lowering blood cholesterol levels, improving memory function, preventing the onset of Alzheimer's disease symptoms, insulin resistance or related disorders like diabetes, anticancer effects, or skin anti-aging effects (Koenen et al., 2004).

Conclusion

There is no longer any doubt about *X. americana*'s medical potential. A wide range of diverse biological activities and industrial applications, including free radical scavenging, antioxidant, anti-inflammatory, antidiabetic, antimicrobial, antitrypanosomal, antiviral, anticancer, and analgesic activities, were demonstrated by the phytochemical diversity found in *X. americana*. Many of these activities support the assertions made by herbal medical practitioners, although more human subjects' clinical trials are still required. Many researchers have also linked some of the plant's medicinal activities to the high level of antioxidant components such as polyphenols, flavonoids, anthocyanins, Vitamins C and E and antioxidant property of the plant. On the other hand, the presence of other phytochemicals such as tannins, saponins, may also play valuable roles in the plant's activities. It is anticipated that more of the medicinal properties of the plant will be discovered, as researchers continue to focus their investigation on this plant. But little research has been done on the plant's chemistry. This is a major drawback. Hence, researchers should focus their investigation on the isolation and identification of the plant's bioactive compounds. It is essential to know the identity of the components that are responsible for each of the



identified medicinal properties of the plant. This could lead to the discovery of novel drugs from *X. americana*. It will also enhance the effective exploitation of the medicinal benefits of this significant yet underutilized plant.

References

- Ali, H., Houghton, P.J., & Soumyanath, A. (2006). Alpha-amylase inhibitory activity of some Malaysian plants used to treat diabetes; with particular reference to *Phyllanthus amarus*. *Journal of Ethnopharmacology*, 107, 449–455.
- Ahmed, I., Adeghate, E., Cummings, E., Sharma, A.K., & Singh, J.(2004). Beneficial effects and mechanism of action of Momordica charantia juice in the treatment of streptozotocin induced diabetes mellitus in rat. *Molecular and Cellular Biochemistry*, 261, 63–70.
- Ansari, K.N. (1997).The free radicals—The hidden culprits: An update. *Indian Journal of Medical Sciences*, 51, 319–336.
- Alezandro, M. R.,Granato, D., & Genovese, M.I. (2013). Jaboticaba (*Myrciaria jaboticaba* (Vell.) Berg), a Brazilian grape-like fruit, improves plasma lipid profile in streptozotocin-mediated oxidative stress in diabetic rats. *Food Research International*, 54, 650–659.
- Arun, K.S., Kotresha, K., Kaliwal, B.B., & Vedamurthy, A.B. (2015). Evaluation of in vitro antioxidant and anti-inflammatory activities of *Ximenia americana* extracts. *Asian Pacific Journal of Tropical Disease*. 5(11), 918–923.
- Anonymous, “(world agroforestry centre). *Ximenia americana*. Tree species reference and selection guide, agroforestry data base,” 2010,<http://www.worldagroforestry.org>.
- Adamu, H.M., Abayeh, O.J.,Agho, M.O., Abdullahi, A.L., Uba, A., Dukku, H.U., & Wufem, B.M. (2005). An ethnobotanical survey of Bauchi herbal plant and therapeutic antimicrobial activity, *Journal of Ethnopharmacology*, 99 1–4.
- Agyigra, I. A., Jane, I. E., & Mohammed, G. M. (2017). Acute and subchronic toxicity evaluation of methanol stem-bark extract of *Ximenia americana* Linn (Olacaceae) in Wistar rats. *Bulletin of Faculty of Pharmacy, Cairo University*, 55, 263–267.
- Almeida, M.L.B., de Souza Freitas, W.E., de Moraes, P.L.D., Sarmiento, J.D.A., & Alves, R.E. (2016). Bioactive compounds and antioxidant potential fruit of *Ximenia americana* L. *Food Chemistry*, 192, 1078–1082.
- American Diabetes Association, 2007. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 30, 42–46.
- Benalla, W., Bellahcen, S., & Bnouham, M. (2010). Antidiabetic medicinal plants as a source of alpha glucosidase inhibitors. *Current Diabetes Reviews*, 6, 247–254.
- Bazewo, A. M., Shimelis, A. E., & Mulugeta, T. S. (2021). Bioactive composition, free radical scavenging and fatty acid profile of *Ximenia americana* grown in Ethiopia. *Heliyon*, 7, e07187.
- Chu, Y. F., Sun, J., Wu, X. Z., & Liu, R.H. (2002). Antioxidant and antiproliferative activities of common vegetables. *Journal of Agricultural and Food Chemistry*, 50, 6910–6916.
- Cilerdzic, J., Vukojevc, J., Stajic, M., Stanojkovic, T., & Glamoclija, J. (2014). Biological activity of Ganoderma lucidum basidiocarps cultivated on alternative and commercial substrate. *Journal of Ethnopharmacology*, 155, 312–319.
- Das, A.K., Rai, (2008). A world without diabetes and its complications: a preventive program. In: Jayaram, B.M. (Ed.), Type 2 Diabetes and its Complications. A Preventive Program. Microlab limited, Bangalore, pp. 1–2.
- Davis, S.N., & Granner, D.K., (2001). Insulin. Oral hypoglycemic agents and the pharmacology of endocrine pancreas. In: Brunton, L.L., Lazo, J.S., Parker, K.L. (Eds.), Goodman and Gilman's: The Pharmacological Basis of Therapeutics, 11th ed. McGraw-Hill Medical Publication Division, New York, pp. 1706–1707.
- Deng, G. F., Xu, X. R., Guo, Y.J., Xia, E.Q., Li, S., Wu, S., Chen, F., Ling, W.H., & Li, H.B. (2012).Determination of antioxidant property and their lipophilic and hydrophilic phenolic contents in cereal grains. *Journal of Functional Foods*, 4, 906–914.
- Dixon, R. A., Dey, P. M. & Lamb, C. J. (1983). Phytoalexins: enzymology and molecular biology. *Advance Enzymology*, 55, 1-69.
- De Menezes, I. R. A., R. H. S. Da Costa, A. A. Boligon., M.Rolón, C. Coronel, C. Vega, H. D. M. Coutinho, M. S. da Costa, S. R. Tintino, R. L. S. Pereira, T. R. de Albuquerque, J. R. G. da S., Ameida, L. J., Quintans-Júnior (2019). “*Ximenia americana* L. enhances the antibiotic activity and inhibit the development of kinetoplastid parasites,” *Comparative Immunology, Microbiology and Infectious Diseases*, vol. 64, pp. 40–46.
- Ersán, S., Julia, B., Victor, J., Reinhold, C., Bianca, M., Ralf, S., & Christof, S. (2020). Phytochemical and mineral composition of fruits and seeds of wild growing *Bactrisguineensis* (L.) HE Moore palms from Costa Rica. *Journal of Food Composition and Analysis*, 94, 103611.



- Fernández-Ruiz, V., Morales, P., Ruiz-Rodríguez, B.M., TorijaIsasa, E. (2017). Nutrients and Bioactive Compounds in Wild Fruits Through Different Continents. *Wild Plants, Mushrooms and Nuts: Functional Food Properties and Applications*, Wiley Blackwell, New York, USA (2017), pp. 263–314.
- Fu, L. Xu, B. T., Gan, R. Y., Zhang, Y., Xu, X. R., Xia, E.Q., & Li, H.B. (2011). Total phenolic contents and antioxidant capacities of herbal and tea infusions. *International Journal of Molecular Sciences*, 12(4), 2112–2124.
- Feiberger, C. E., D. J. Vanderjagt, A. Pastuszyn et al., “Nutrient content of the edible leaves of seven wild plants from Niger, Plant foods human nutr,” *Dardrecht*, 53, 57–69, 1998.
- Fatope M. O. and Adam O. A., (2005) “C18 acetylene fatty acids of *Ximenia americana* with potential pesticidal activity,” *Journal Agriculture Food Chemistry*, 48(5), 1872–1874.
- Gupta, R., & Misra, A., (2007). Type 2 diabetes in India: regional disparities. *British Journal of Diabetes and Vascular Disease*, 7, 12–16.
- Granato, D., Karnopp, A.R., & van Ruth, S.M. (2015). Characterization and comparison of phenolic composition, antioxidant capacity and instrumental taste profile of juices from different botanical origins. *Journal of the Science of Food Agriculture*, 95, 1997–2006.
- Geyid, A., Abebe, D., Debella, A., Makonnen, Z., Aberra, F., Teka, 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*, 97, 421-427, ISSN 0378-8741.
- Garcia, M.E., & Blanco, J.L. (2000). Mycosis in domestic animals. *Revista Iberoamericana de Micologia Journal*, 17, 2–7.
- 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 bioactive compounds*, Akademiai, Kiahó, Budapest, Hungary.
- Heinrich, M., Nebel, S., Leonti, M., Rivera, D., & Obón, C. (2006). ‘Local Food- Nutraceuticals’: bridging the gap between local knowledge and global needs. *Forum of Nutrition*, 59, 1–17. Doi: 10.1159/000095205
- Hegazy, A.K., Mohamed, A.A., Ali, S.I., Alghamdi, N.M., Abdel-Rahman, A.M., & Al-Sobeai, S. (2019). Chemical ingredients and antioxidant activities of underutilized wild fruits. *Heliyon* 5 (6), e01874.
- Halliwell, B., & Gutteridge, J.M.C. (1999). *Free Radicals in Biology and Medicine*, 3rd ed.; Oxford University Press: New York, NY, USA, pp. 331–332.
- Hartwell, J. L. (1967; 1968; 1969; 1970; 1971). Plants used against cancer. *Lloydia*, 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.
- Hou X.-L., Takahashi, K., Tanaka, K., Tougou, K., Qui, F., Komatsu, K., Takahashi, K & Azuma, J. (2008). “Curcuma drugs and curcumin regulate the expression and function of P-gp in Caco-2 cells in completely opposite ways,” *International Journal of Pharmaceutics*, 358(1-2), 224–229.
- Islary, A., Sarmah, J., & Basumatary, S., (2016). Proximate composition, mineral content, phytochemical analysis and in vitro antioxidant activities of a wild edible fruit (*Grewia sapida* Roxb. ex DC.) found in Assam of North-East India. *Am. J. Physiol. Biochemical Pharmacology*, 5 (1), 1–11.
- 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
- Kayarohanam, S., & Kavimani, S., (2015). Current trends of plants having antidiabetic activity: a review. *Journal of Bioanalysis & Biomedicine* 7, 055–065.
- Koenen, 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.
- Kuroki G. W. & Conn E. E., (1989). “Mandelonitrile lyase from *Ximenia americana* L.: stereospecificity and lack of Bavin prosthetic group,” *Proceedings of the National Academy of Sciences*, 86(18), 6978–6981.
- Koné W. M., Atindehou, K. K., Terreaux, C., Hostettmann, K., Traoré, D. & Dosso, M. (2004). “Traditional medicine in North Côte-d’Ivoire: screening of 50 medicinal plants for antibacterial activity,” *Journal of Ethnopharmacology*, vol. 93, no. 1, pp. 43–49.
- Lucilania, M. B. A., F. D. S. L. Wallace, and L. D. M. Patrícia, J. S. A. Dárcio and R. Elesbão, (2016). “Bioactive compounds and antioxidant potential fruit of *Ximenia Americana* L.,” *Food Chemistry*, 192, 1078–1082.
- Lamien-Meda, A., Lamien, C.E., Compaore, M.M., Meda, R.N., Kiendrebeogo M., Zeba, B., Millogo, J.F., & Nacoulma, O.G. (2008). Polyphenol content and antioxidant activity of fourteen wild edible fruits from Burkina Faso. *Molecules*, 13 (3), 581–594.
- Li, A.N., Li, S., Li, H.B., Xu, D.P., Xu, X.R., & Chen, F. (2014). Total phenolic contents and antioxidant capacities of 51 edible and wild flowers. *Journal of Functional Foods*, 6, 319–330.
- Li, S., Li, S.K., Gan, R.Y., Song, F.L., Kuang, L., Li, H.B. (2013). Antioxidant capacities and total phenolic contents of infusions from 223 medicinal plants. *Industrial Crops and Products*, 51, 289–298.



- Liu, R.H. (2003). Health benefits of fruits and vegetables are from additive and synergistic combinations of phytochemicals. *The American Journal of Clinical Nutrition*, 78, 517S–520S.
- Li, F., Li, S., Li, H.B., Deng, G.F., Ling, W.H., Wu, S., Xu, X.R., Chen, F. (2013). Antiproliferative activity of peels, pulps and seeds of 61 fruits. *Journal of Functional Foods*, 5, 1298–1309.
- Li, F., Li, S., Li, H.B., Deng, G.F., Ling, W.H., & Xu, X.R. (2013). Antiproliferative activities of tea and herbal infusions. *Food & Function*, 4, 530–538.
- Le, N. H. T., Malterud, K. E., Diallo, D., Paulsen, B. S., Nergard, C. S., & Wangensteen, H. (2012) “Bioactive polyphenols in *Ximenia Americana* and the traditional use among Malian healers,” *Journal of Ethnopharmacology*, 139 (3), 858–862.
- Margraf, T., Santos, E.N.T., de Andrade, E.F., van Ruth, S.M., & Granato, D. (2016). Effects of geographical origin, variety and farming system on the chemical markers and *in vitro* antioxidant capacity of Brazilian purple grape juices. *Food Research International*, 82, 145–155.
- Maikai, V.A., Kobo, P.I., & Auda, A.O. (2008a). Acute toxicity studies of aqueous stem bark extract of *Ximenia americana*. *African Journal of Biotechnology*, 7(10), 1600–1603.
- Maikai, V. A., Nok, J. A., Auda, A. O., & Alawa, C. B. I. (2008b). *In vitro* antitrypanosomal activity of aqueous and methanolic crude extracts of stem bark of *Ximenia americana* on *Trypanosoma congolense*. *Journal of Medicinal Plants*, 2(3), 55-58.
- Maikai, V.A., Maikai, B.V., Kobo, P.I., (2009). Antimicrobial properties of stem bark extracts of *Ximenia americana*. *The Journal of Agricultural Science* 1(2), 30–34.
- Maikai, V. A., Kobo, P. I., & Maikai, B. V. O. (2010). Antioxidant properties of *Ximenia americana*. *African Journal of Biotechnology*, 9(45), 7744–7746.
- Mohamed, K., & Feyissa, T. (2020). *In vitro* propagation of *Ximenia americana* L. from shoot tip explants: a multipurpose medicinal plant. *Sinet*, 43 (1), 1–10.
- Muhammad, A., Haruna, S.Y., Birnin-Yauri, A.U., Muhammad, A.H., Elinge, C.M., (2019). Nutritional and anti-nutritional composition of *Ximenia americana* fruit. *American Journal of Applied Chemistry*, 7 (4), 123–129.
- Maundu, P.M., Nugugi, G.W., & Kabuye, C.H.S. (1999). Traditional Food Plants of Kenya. Kenya Resources Centre for Indigenous Knowledge. National Museums of Kenya, Nairobi.
- Macedo, L.F.L., Rogero, M.M., Guimaraes, J.P., Granato, D., Lobato, L.P., & Castro, I.A. (2013). Effect of red wines with different *in vitro* antioxidant activity on oxidative stress of high-fat diet rats. *Food Chemistry*, 137, 122–129.
- 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., Kéita, A., Camara, M. K., Barry, R., Kéita, S., Oularé, K., Barry, M. S., Donzo, M., Camara, K., Toté, K. V., 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*, 114, 44-53.
- Mwangi, J. W., Malii, P., Gathu, L., Tanaka, T., & Nonaka G., (1994). “Polyphenols of *Ximenia americana*,” *Fitoterapia*, 65(2), p. 185.
- Niemi, L., Wennström, A., & Ericson, L., (2005). “Insect feeding preferences and plant phenolic glucosides in the system *Gonioctena linnaeana*—*salix triandra*,” *Entomologia Experimentalis et Applicata*, 115(1), 61–66.
- Oliveira, F. C. S., Barros, R. F. M., & Moita Neto, J. M. (2010). Plantas medicinais utilizadas em comunidades rurais de Oeiras, semiárido piauiense. *Revista Brasileira de Plantas Medicinais*, 12(3), 282–301.
- Oladipo, G. O., I. Eromosele, C., and Folarin, O. M., (2013). “Formation and characterization of paint based on alkyd resin derivative of *Ximenia americana* (wild olive) seed oil,” *Environment and Natural Resources Research*, 3(3), 52–62.
- Ogunleye, D. S., Ibitoye & Trop, S. F. (2003). Studies of antimicrobial activity and chemical constituents of *Ximenia americana*. *Journal of Pharmaceutical Research*, 2(2), 239-241.
- Omer, M. E. A., & Ali M. A. Z. (1998). “Sudanese plants used in folkloric medicine screening for antimicrobial activity” *Fitoterapia*, 69, 542–545.
- Omer, M. E. F. A., & Elnima, E. I. (2003). Antimicrobial activity of *Ximenia americana*. *Fitoterapia*, 74, 122-126.
- 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*, 114, 146-152.
- 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*, 68, 925–934.
- Rahimi, M., (2015). A review: anti diabetic medicinal plants used for diabetes mellitus. *Bulletin of Environment, Pharmacology and Life Sciences*, 4, 163–180.





- Shagal, M. H., Kubmarawa, D. & Barminas, J.T. (2013). Evaluation of antimicrobial property of *Ximenia americana*. *Journal of Biotechnology and Pharmaceutical Research*, 4(6), 99-102. Available online at <http://www.e3journals.org/JBPR>
- Sallamander C., (2010). “*Ximenia* oil. esoteric oils CC, Sallamander concepts (Pty) Ltd 1998–2010,” <http://www.essentialoils.co.za.htm>.
- Sarmiento, J. D. A., Dantas de Morais, P. L., Israël de Souza, F., and Alcântara de Miranda, M. R. (2015). “Physical-chemical characteristics and antioxidant potential of seed and pulp of *Ximenia americana* L. from the semiarid region of Brazil,” *African Journal Biotechnology*, 14(20), 1743–1752.
- 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*, 3, 23–25.
- Soro, T.Y., Traore, F., Datte, J.Y., & Nene-Bi, A.S. (2009). Antipyretic activity of aqueous extract of *Ximenia americana*. *Phytoterapie* 7, 297–303.
- Sacande, M. & Vautier H. (2006). *Ximenia americana*. Seed Leaf Let No 112, April 2006 *Millennium Seed Bank Project*, Kew. Forest & landscape, Denmark. www.Kew.org/Msbp (Accessed 27 April, 2010).
- Shettar, A.K., Sateesh, M.K., Kaliwal, B.B., Vedamurthy, A.B. (2017). *In vitro* antidiabetic activities and GC-MS phytochemical analysis of *Ximenia americana* extracts. *South African Journal of Botany*, 111, 202–211.
- Siddaiah, M., Jayaveera K.N., Souris, K.Y., Krishna J.P & Kumar, P.V. (2011). Phytochemical Screening and Anti Diabetic Activity of Methanolic Extract of Leaves of *Ximenia Americana* in Rats. *International Journal of Innovative Pharmaceutical Research*, 2(1), 78-83.
- Song, F.L., Gan, R.Y., Zhang, Y., Xiao, Q., Kuang, L., H.B. Li. (2010). Total phenolic contents and antioxidant capacities of selected Chinese medicinal plants. *International Journal of Molecular Sciences*, 11, 2362–2372.
- Silva, K., & Sirasa, M. (2018). Antioxidant properties of selected fruit cultivars grown in Sri Lanka. *Food Chemistry*, 238, 203–208.
- Sarmiento, J.D.A., (2015). Bioactive compounds and antioxidant activity of *Ximenia americana* coming from different collection sites. *Archivos Latinoamericanos de Nutrición*, 65 (4).
- Schubert, A., Pereira, D.F., Zanin, F.F., Alves, S.H., Beck, R.C., & Athayde, M.L. (2007). Comparison of antioxidant activities and total polyphenolic and methylxanthine contents between the unripe fruit and leaves of *Ilex paraguariensis* A. St. Hil. *Die Pharmazie. International Journal Pharmaceutical Sciences*, 62 (11), 876–880.
- Scalbert, A. (1991). Antimicrobial properties of tannins. *Phytochemistry*, 30, 3875-3883.
- Teo S. P., (1997). “Root hemi parasitism in Malayan oleaceae,” *Gardens’ Bulletin Singapore*, 49(4), 1–7.
- 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*, 211, 177–178.
- Ya, C., Gaffney, S. H., Lilley, T. H. & Haslam, E. (1988). (R. W. Heminway and J. J. Karchesy Ed). *Carbohydrate-polyphenol complexation*, Plenum Press, New York, U.S.A.
- Zhou, Y., Li, Y., Zhou, T., Zheng, J., Li, S., Li, H.B. (2016). Dietary natural products for prevention and treatment of liver cancer. *Nutrients*, 8, 156.

