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Review Article

Ethnomedicinal, Phytochemistry and Pharmacological Actions of Leaf Extracts of *Spondias mombin*: A Narrative Review

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ABSTRACT

Spondias mombin Linn is one of the species belonging to the (Family: Anacardiaceae), its ethnomedicinal uses may be justified through many studies that reported potential pharmacological properties due to its phytochemical compounds. This review aimed at examining the ethnomedicinal uses, phytochemical compounds and pharmacological properties of *S. mombi*n leaf extract on the African continent, to justify its use in the management and/ or treatment of viral infections and cancers. Electronic databases such as Google Scholar, SciHub, PubMed and Science Direct with search dates between 1999 and 2019 were used. Findings from this review confirm the ethnomedicinal uses, of decoctions and infusions of S. *mombin* leaf extracts for management diseases such as malaria, sore throat, and inflammation disorders; studies confirmed the presence of phytochemical compounds such as Geraniin, 2-O-Caffeoyl-(+)-allohydroxycitric acid, Quercetin-3-O-β-D-glucopyranoside and pelandjuaic acid, responsible for the antiviral and chemotherapeutic properties. However, there is a need for bio-assay-guided extractions, isolation, identification and characterization of phytochemical compound(s) in the leaf extracts of *S. mombi*n that may be responsible for antiviral and anti-cancer activity. Investigations of the pharmacological action, in silico and in vitro studies of known and /or newly isolated compounds are warranted in the management and /or treatment of viral infections such as Severe Acute Respiratory Syndrome Coronavirus 2, and cancers to justify the use of leaf extracts of *S. mombin* on the African continent for the management of viral infections and or cancer.

Keywords: *Spondias mombin, phytochemistry, ethnomedicine, pharmacological activity*

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INTRODUCTION

Communicable diseases (infectious/transmissible) are caused by viruses, bacteria, fungi, and parasites. The World Health Organization(Organization, 2016) reported that communicable diseases, such as Human Immunodeficiency Virus (Global) and associated Acquired Immunodeficiency Syndrome(AIDS), and *Tuberculosis* (TB) were some of the diseases with the highest mortality rate in the world, with approximately 9.6 million people and 2 million people diagnosed worldwide with TB and HIV/AIDS in 2014, respectively(Organization, 2016). Infectious diseases spread rapidly by human- to – human (HIV, Hepatitis and TB), Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), animal-to-human (Ebola) or non-human such as mosquitoes, and from the environment (Würz *et al.*, 2013) and can cause an epidemic to a large population of humans and animals(Würz *et al.*, 2013). The largest cause of death worldwide is infectious diseases, with over 29 million deaths recorded in 2002(Yach *et al.*, 2004). Sub-Saharan African regions continue to experience many diseases such as NCDs coupled with epidemics of infectious diseases such as HIV and Ebola, Coronaviruses(Alam *et al.*, 2014).

Conventional medicines, used in the management of infections, although have reduced mortality of diseases such as HIV/AIDS to a chronic manageable disease, there are limitations to this success and potential long-term toxicity (Volberding and Deeks, 2010). Some effects in terms of antiretroviral therapies (ART's) in the management of HIV infections are that patients are at risk of opportunistic diseases including but not limited to heart, bone, liver, kidney, and neurocognitive diseases (Volberding and Deeks, 2010). Another limitation is the cost of the financial burden on the patient (Ernst, 1997). Some patients default on their treatment regimens due to adverse side effects but not limited to the same, such as mental disorders (Bhatti *et al.*, 2016).

Concerning side-effects of western medicine, patients may turn to the use of traditional medicine. As traditional medicines made from natural products such as plants have been reported to have fairly little to no side effects(Cordell,

2017). Asuquo *et. al.,* (2013) reported that leaf extract of *S. mombin* had no significant side effect on the liver of Winstar rats in a liver functioning test(Asuquo *et al.,* 2013b). Using the heart weight/body ratio test, the hydroethanolic leaf extract of *S. mombin* showed no adverse effect (Akinmoladun *et al.,* 2010).

The conventional development and treatment of diseases by the use of the one drug; one target disease is giving way to the adoption of multi-therapies, that use multiple active phytochemicals in the development of drugs(Weber and Noels, 2011). This gradual shift has partly been due to the multiple drug resistance (MDR), in the effectiveness of one drug in the treatment of chronic diseases and side effects of mono-synthetic drugs. Diseases such as HIV, hepatitis, Ebola, diabetes, tuberculosis and cancer have recently been managed or treated with combination therapy(Weber and Noels, 2011, Zhou *et al.,* 2016). Knowledge from traditional medicine practitioners (TMPs) on indigenous plants in the treatment of diseases is important and the ability of scientists to bring this ethnomedicinal knowledge to the laboratory. This is to establish the phytochemicals responsible for these therapeutic properties of the medicinal plants.

The acquisition of indigenous knowledge from local communities although critical, but sometimes causes conflict due to academic interests and challenges of local communities (Cochran *et al.,* 2008). This conflict is caused by either inappropriate methods and or/or practices(Cochran *et al.,* 2008). Planning of public health programs by some southern African countries has been based primarily on knowledge, attitude and practice survey of indigenous communities, but there are challenges such as the socio-cultural factors that affect the treatment of certain diseases (Launiala, 2009).

Natural products, especially plant-derived extracts have anti-cancer phytochemical compounds that represent about 50% of the chemotherapeutic drugs on the market against cancer to date(Ntie-Kang *et al.,* 2014). In both developed and emerging countries, one of the stress on the public health system is cancer disease (Chanda and Nagani, 2013). Alkaloids exhibit analgesic and antispasmodic activities while tannins can eliminate protein deficiency syndrome known as "kwashiorkor(Abidemi, 2013). Furthermore, tannins are responsible for the healing of wounds in humans(Usman and Osuji, 2007). Flavonoids have a good anti-oxidant potential that helps with the reduction of oxidative stress(Goldman *et al.,* 1996). Saponins serve as natural antibiotics(Oluwaniyi, 2017). Phenols and pro-anthocyanidin have anti-oxidant activities(Folasade *et al.,* 2016). Del Rio *et al.* (2010) report that phenolic compounds may be the most researched phytochemicals because of their ability to affect human health positively.

Description of the Spondias mombin Linn (S.mombin): *Spondias mombin* Linn (*S.mombin*), is commonly known as yellow plum or hug-plums. Some other common names are Atoa (Ghana), Bala (Costa Rica), Jobito (Panama), Jobo blanco (Colombia), Jobo corronchoso (Venezuela), Hoeboe (Surinam), Acaiba, Caja, Pau da tapera (Brazil), Ubo (Peru), Hobo (Mexico), Iyeye (Yoruba), Uvuru (Igbo) (Coelho-Ferreira, 2009, Osuntokun, 2019, Shaw and Forman, 1967).

Kingdom	:	Plantae
Order	:	Asterales
Family	:	Anacardiaceae
Genius	:	***Spondias***
Species	:	***mombin***

Spondias as a genus in the Anacardiaceae family are found in tropical, subtropical and some coastal areas in the world. There are 18 species in the genus *Spondias,* with *Spondias mombin* Linn(*S.mombin*) being one of the species(Sameh *et al.,* 2018). *S. mombin* can grow up to a height of 22m. The long compound alternate leaves have odd number leaflets that are long compound; they also have a turpentine-like smell when crushed and fruits are long oval yellow plum with leathery skin and oval seed, rich in vitamins B1 and C (Ayoka *et al.,* 2006). *S. mombin* has been reported to have a lot of promising ethnomedicinal use(Lawal *et al.,* 2010). The most preferred part of medicinal plants for treatments In Traditional African Medicines (TAM) is the young leaves are the preferred part used in ethnomedicines; however, other parts such as the roots stem and even flowers have been used(Akah *et al.,* 2004, Asante *et al.,* 2016).

All parts of *S. mombin* have been used in traditional medicine around the world from Africa to South America (Ayoka *et al.,* 2008). In Brazil *S. mombin,* stem bark tea, or bath has been reported to be used by the locals in ovarian cysts, uterine, vaginal itching, vaginal cleansing, diarrhea, women's infections, healing sores, post-partum uterine cleansing(Coelho-Ferreira, 2009). In Ghana, *S. mombin*, aqueous leaf extracts have been reported to be used in the treatment of hepatitis-related jaundice(Hamenoo, 2010) and the stem bark used in the treatment of malaria(Pesewu *et al.,* 2008). In some South American countries such as México and other African countries, Nigeria and Ghana, the astringent bark and crushed leaves of *S. mombin* are used externally for wound healing and inflammations(Ayoka *et al.,* 2008). The decoctions of the bark are also used to expel calcifications from the bladder, treatment of gonorrhea, diahrea and dysentery(Ayoka *et al.,* 2008). The fruits are made into juice as a diuretic. Tea and decoctions of the leaves and flowers are used for throat inflammations, stomach-aches, dysentery, diarhea and urethritis, with root and gum used as purgative and expulsion of tapeworm respectively(Ayoka *et al.,* 2008). Aqueous leaf decoctions of *S. mombin* are reported in Nigeria to be used as a haematinic by the local community(Adeyemi and Gbolade, 2006). Leave extracts of SM have been used by traditional healers in Nigeria to treat mental disorders in some patients(Ayoka *et al.,* 2005).

Spondias species demonstrated pharmacological properties due to the presence of some class of phytochemical compounds, such as phenolics, that have antidiabetic and anti-oxidant properties, flavonoids, sterols, saponins, tannins and triterpenes (Ayoka *et al*., 2006, Sameh *et al*., 2018). In vivo study using zebrafish (*Danio rerio*) in Brazil showed that using ethanolic leaf extracts of *S.mombin* has anxiolytic and antidepressant properties(dos Santos Sampaio *et al.,* 2018). The aqueous leaf extracts and gum of *S.mombin* have also been reported to be used as an abortifacient, and expectorant in Brazil and Belize, respectively(Rodrigues *et al*., 2000, Offiah and Anyanwu, 1989, Rodrigues and Samuels, 1999). In Ghana, it was reported that aqueous leaf extract of *S. mombin* is safe to use at doses of 50-1500mg/kg in rats and mice(Hamenoo, 2010).In Cote d'Ivoire in vivo studies from stem and bark methanolic and aqueous extracts on Wistar rats have anti-oxidant activity and hemolytic effect, respectively(Boni *et al*., 2015, Moussa *et al*., 2018). In Nigeria, *S. mombin* leaf extracts have been reported to possess anti-cancer properties(Abdullahi *et al.,* 2018). In the same country, an in vitro study of the methanolic stem and bark extract had antimycobacterial activities(Olugbuyiro *et al*., 2013). The aqueous, methanolic and ethanolic leaf extracts of *S. mombin* have shown anxiolytic properties by facilitating gamma–amino butyric acid (GABA) transmissions (Ayoka *et al.,* 2005) in albino Wistar rats and Swiss mice(Asuquo *et al.,* 2013a). Hexane leaf extracts of *S. mombin* were reported to less toxic but exhibit profound pharmacological activity in vitro towards prostate cancer (PC3)(Guedes *et al.,* 2020).

Metabolism of drugs is essential in the determination of the pharmacological properties of many important medicines. This includes metabolic stability, drug-drug interactions and drug toxicity(Li, 2001). Polyherbal medicines have been reported to possess pharmacological superiority compared to isolated single phytochemicals due to the pharmacological synergy of the constituents(Wang *et al.,* 2012, Spinella, 2002). *"Synergy is defined as the interaction of two or more agents to produce a combined effect greater than the sum of their individual effects*"(van Vuuren and Viljoen, 2011).

Compounds isolated from ethanolic fruit extracts of *S. mombin* yielded caryophyllene, myrcene, hexanal, 3-hexenol and (e)-2-hexenal (Ceva-Antunes *et al.,* 2003). From ethanolic stem extract, four phytochemicals, namely mombirin, mombincone, mombinoate and mombinol were isolated with antimycobacterial properties against *Mycobacterium tuberculosis* (H37Rv and EJA-2011) (Olugbuyiro, 2013). In the hexane stem extract of *S. mombin*, a Beta-lactamase inhibitor was isolated (Olugbuyiro, 2013). Estra-17-propoxy, 3,4–dimethoxy–3yl benzoate have been isolated from the ethanolic leaf extract of *S*. mombin (Echeme *et al.,* 2014).(Pieters and Vlietinck, 2005) reported the isolation of lead compounds of tannins and caffeoyl esters that had antiviral properties, with alkenyl phenols having molluscicidal and insecticidal properties.

Triterpenes such as Lupeol have been reported to possess anti-pancreatic cancer activity(Gallo and Sarachine, 2009). It also provides a lead scaffold for synthetic chemical attempts to optimize pharmacological potency(Gallo and Sarachine, 2009). Lupeol is potentially an anti-inflammatory, anti-microbial, anti-protozoal, anti-proliferative, anti-invasive, and anti-angiogenic agent. In vitro and in vivo suggests that it has therapeutic efficiency and a selective target of diseased human cells but not affecting normal and healthy cells (Siddique and Saleem, 2011). Lupeol has been isolated from the hydroethanolic leaf extract of *S. mombi**n*** (de Lima *et al.,* 2016) (Liu *et al.,* 2015).

Decades of advancements in research to investigate and identify new compounds, that have pharmacological activities have been made(Schinazi *et al.,* 2009). In the 21st century, recent studies have used molecular structures to predict the pharmacological effects of certain phytochemicals(Li, 2001). Bringing ethnomedical knowledge to the laboratory requires immense effort, which is time-consuming and expensive but will assist in the isolation and characterization of novel pharmacologically active compounds. This review aimed at examining the ethnomedicinal uses of *S. mombi*n on the African continent, its potential phytochemical compounds and pharmacological properties which might justify the use of leaves of S. *mombi*n either alone or in polyherbal mixtures for the management and treatment of Ebola virus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), hepatitis B, and cancers.

MATERIALS AND METHODS

This review was compiled from electronic databases such as Google Scholar, SciHub, PubMed and Science Direct. Efforts were made to limit the search between 1999 and 2019. These electronic databases were searched with words such as *S. mombin*, taxonomy, ethnomedicinal uses, phytochemistry, pharmacological properties, and toxicity.

RESULTS

Ethnomedicinal use of leaf extract-*Spondias mombin* (*S. mombin*): On the African continent, *S. mombi*n has been used in the management and /or treatment of several ailments. For example, (Lawal *et al.,* 2010)indicated that aqueous oral administration of decoction of leaf extracts was used in the treatment of stomach disorders, malaria, and diabetes in Nigeria. In Edo state Nigeria, the leaves are used to treat athlete's foot, childbirth aid, cough, sore throat, antiseptic soap, malaria and stomach ache(Adedokun *et al.,* 2010). In some parts of Akwa-Ibom State, Nigeria, the Ifa Nkari people, the aqueous decoction of *S. mombi*n leaves taken at 150ml; three times daily have been used in the treatment of male infertility such as azoospermia, oligozoospermia, tetratozoospermia and athenozoospermia (Erhabor *et al*., 2013a). In the district of Kankan, Guinea, aqueous decoction of *S. mombi*n leaves is used to treat sexually infectious diseases(Samba *et al.,* 2015). The infusions of leaf extracts of *S. mombi*n were used for the treatment (Erhabor *et al*., 2013b) of tuberculosis (Ogbole and Ajaiyeoba, 2010).

The decoction of aqueous *S. mombi*n leaf extracts is used in the management and treatment of diarrhea, dysentery, and improvement in mental disorders and good memory in some West African countries such as Benin, Nigeria, and Togo (Adams *et al.,* 2007). Ethnomedicinal uses of *S. mombi*n are summarized in Table 1.

Table 1:
Studies on ethnomedicinal uses of leaf extracts of *Spondias mombin*

Nr	Country	Study design	Sample size	Plant part used	Treatment modalities	Diseases treated	Reference(s)
1	Nigeria	Survey	20 people	leaf	Oral aqueous administration (decoction)	Male infertility	(Erhabor *et al.*, 2013a)
2	Nigeria	Questionnaire	90 people	Leaves	Not stated	Malaria, coughs, sore throat and cough. Inflammation, fever.	(Adedokun *et al.*, 2010)
3	Nigeria	Oral interview and questionnaire	105 people	leaves	Oral aqueous administration (decoction)	Gonorrhea	(Ajibesin *et al.*, 2011)
4	Guinea	survey	258 people	leaves	Oral aqueous administration (decoction)	Malaria	(Traore *et al.*, 2013)
5	Nigeria	experiment	N/A	leaves	Leave extract	Inflammation disorders	(Nworu *et al.*, 2011)
6	Nigeria	N/A	N/A	leaves	Oral aqueous administration (decoction)	treatment of dizziness, associated with childbirth	(Nworu *et al.*, 2011)
7	Nigeria	N/A	N/A	leaves	Oral aqueous administration (decoction)	Treatment of laryngitis, sour throat, tooth decay; labor induction, augmentation, and as post-partum astringent in childbirth	(Nworu *et al.*, 2007)
8	Nigeria	survey	50 people	leaves	Oral aqueous administration (decoction)	Tuberculosis	(Ogbole and Ajaiyeoba, 2010)
9	Nigeria	N/A	N/A	leaves	Oral administration (infusion)	Diabetes, intestinal disorders, typhoid fever and as an abortifacient.	(Fred-Jaiyesimi *et al.*, 2009)
10	Nigeria	Ethnobotanical survey	N/A	leaves	Oral aqueous administration (decoction)	gain and retain a good memory	(Adams *et al.*, 2007)
11	Nigeria	N/A	N/A	leaves	Oral aqueous administration (decoction	Typhoid fever	(Aromolaran and Badejo, 2014)
12	Nigeria	Ethnobotanical survey	50	leaves	Oral aqueous administration (infusion)	Tuberculosis	(Ogbole and Ajaiyeoba, 2010)
13	Nigeria	N/A	N/A	leaves	Oral aqueous administration (decoction)	stomach aches, diarrhea, dyspepsia, gastralgia, colic, and constipation	(Awogbindin *et al.*, 2014)
14	Togo	Ethnobotanical survey	121	leaves	Oral aqueous administration (decoction)	Asthma	(Gbekley *et al.*, 2017)

N/A; Not applicable; Nr: number

Phytochemistry of *Spondias mombin* leaf extracts

Extraction methods and solvents: Maceration: leaf powder of S. *mombi*n was macerated in 80% methanol for 72 hours at room temperature and sequentially fractionated in order of increasing polarity into dichloromethane, ethyl acetate, n-butanol and water (Akinmoladun *et al*., 2015, Fred-Jaiyesimi *et al*., 2009, Fred-Jaiyesimi *et al*., 2017). (dos Santos Sampaio *et al*., 2018, Accioly *et al*., 2012) , macerated leaf powder of S. *mombi*n using 75% hydroethanolic solutions at room temperature for 168 and 48 hours, respectively.

Soxhlet extraction:(Ayoka *et al.,* 2006) extracted *S. mombin* leaf powder by Soxhlet extraction using hydroethanolic(1:1 ratio) solvent system, Asuquo *et al*. (2012) reported the use of 95% ethanol in Soxhlet extraction of *S. mombi*n leaf powder(Asuquo *et al.,* 2012).

Class of phytochemicals: Crude methanolic leaf extracts of *S. mombin* showed the presence of alkaloids, anthraquinones, coumarins, cardiac glycosides, flavonoids, phenols, saponins, steroids tannins (Ibikunle *et al.,* 2017), and terpenoids (Adegoke *et al.,* 2016). In ethanolic and aqueous leaf extracts of S. *mombi*n, tannins, flavonoids, saponins, alkaloids, phenols(Shittu *et al.,* 2014), anthraquinones, and cardiac glycosides (Maduka *et al.,* 2014). In another study, aqueous leaf extracts of *S. mombin* indicated that tannins, flavonoids, glycosides, alkaloids, steroids, and terpenoids were present (JOEL *et al.,* 2018). Igwe *et. al.,* (2010) reported that leaf extracts of SM contained saponins, alkaloids, flavonoids, tannins, oxalates, phytates, and cyanogenic glycosides. Phenolic derivatives obtained from ethanolic and methanolic *S. mombin* leaf extracts have antiherpes against the Herpes simplex 1 virus and anti-oxidant properties(Corthout *et al.,* 1992).

Nutrients in leaf extracts of *S. mombin*: Apart from phytochemical compounds, reported nutrients in leaf extracts of S. *mombi*n consisted of carbohydrates, crude protein, fat, and fibre (Igwe *et al.,* 2010). Calcium, potassium, sodium, magnesium, phosphorus, selenium, iron, zinc and manganese(Igwe *et al.,* 2010). Vitamins A, C and Vitamin E(Igwe *et al*., 2010, Maduka *et al*., 2014). It was reported by (Njoku and Akumefula, 2007) that ascorbic acid, niacin, riboflavin, and thiamine were obtained from ethanolic leaf extract of *S. mombin.*

Isolated and characterized phytochemical compounds with tested pharmacological properties: A hydromethanolic leaf extract of *S. mombin* contained tannins, including isolated compound galloylquinic acids with leishmanicidal properties against promastigotes and amastigotes of *Leishmania chagasi*(Accioly *et al.,* 2012). Ethanolic leaf extracts of *S. mombin* contained geraniin and galloylgeraniin that had antiviral activity against Coxsackie B_2 and Herpes simplex 1 virus(Corthout *et al.,* 1991). Phenolic lactones; ellagic acid have also been isolated from methanolic(Ajaegbu *et al.,* 2016) and hexane(dos Santos Sampaio *et al.,* 2018) leaf extracts of *S. mombi*n with adulticidal activity against *Aedes aegypti*(Ajaegbu *et al.,* 2016). Quercetin-3-O-β-D-glucopyranoside, a flavonol glycoside that has prophylactic and chemotherapeutic properties against oral cancer, cervical cancer, breast cancer and lung cancer, was isolated from methanolic and hydroethanolic leaf extracts(Akinmoladun *et al*., 2015, dos Santos Sampaio *et al*., 2018).

Isolated phytosterols from leaf extracts of *S. mombin*, such as mombintane I ($C_{29}H_{52}O_2$) and Mombintane II($C_{29}H_{50}O$), possess glucose-lowering activities; in vitro on α-amylase inhibitory assay (dos Santos Sampaio *et al.,* 2018, Olugbuyiro *et al.,* 2013). Phenolic acids isolated from ethanolic leave extract yielded pelandjuaic acid [6-(8'Z,11'Z,14'Z-heptadecatrienyl)-salicylic acid, 6-(8'Z,11'Z-heptadecadienyl)-salicylic acid, and 6-(10'Z-heptadecenyl)-salicylic acid], 6-(12'Z-non-adecenyl)-salicylic acid and 6-(15'Z-heneicosenyl)-salicylic acid has antibacterial properties against *Bacillus cereus*, *Streptococcus pyogenes*, and *Mycobacterium fortuitum* and molluscicidal activity against *Biomphalaria glabrata.* (Nishizawa *et al.,* 1989, Corthout *et al.,* 1994). Anti-oxidant and anti-inflammatory properties have been reported in chlorogenic acid and ellagic acid that were isolated from hydroethanolic leaf extract of *S. mombin*(Gomes *et al.,* 2020).

Saponins such as 1-O-Galloyl-6-O-luteoyl-α-D-glucose are natural glycosides of steroid or triterpene that can activate the mammalian immune system and(dos Santos Sampaio *et al.,* 2018) have adulticidal(Ajaegbu *et al.,* 2016) activity against *Aedes aegypti*(Sun *et al.,* 2009, Kaur *et al.,* 2017). Esters and hydrocarbons, 3 β -olean-12-en-3-yl (9Z)-hexadec-9-enoate ($C_{46}H_{78}O_2$) and undec-1-ene ($C_{11}H_{22}$) respectively have also been isolated from leaf extracts of *S. mombin*(Akinmoladun *et al.,* 2015, dos Santos Sampaio *et al.,* 2018) 2-O-Caffeoyl-(+)-allohydroxycitric acid (2-o-caffeoylhydroxycitric acid $C_{15}H_{14}O_{11}$) has antiviral properties against Coxsackie and Herpes simplex viruses(Corthout *et al.,* 1992).

Alkaloids isolated from ethanolic leaf extracts of *S. mombin* were reported to have anticonceptive property, by inhibiting ovarian function in women. (Asuquo *et al.,* 2012). Lupeol was isolated from hydroethanolic leaf extract of *S. mombi**n*** with reported anti-cancer activities both in vitro and in vivo (de Lima *et al*., 2016, Liu *et al*., 2015). Volatile oils isolated from hydroalcoholic leaf extracts of *S. mombin* are α and β-Pinene, caryophyllene, humulene, iIndene and cadinene(de Lima *et al.,* 2016).

DISCUSSION

The stem bark, flower and root decoction have been reported to be used by traditional healers in Nigeria for the management of gonorrhea (Lawal *et al*., 2010), diarrhea, dysentery, haemorrhoids and gonorrhea, Stomach ache, urethritis, biliousness cystitis, eye and throat inflammation(Ayoka *et al*., 2008), this justifies the findings of the ethnomedicinal use of the plant(Nworu *et al*., 2011). The use of the fruits reported by (Lawal *et al*., 2010) in the treatment of gonorrhea, stomach disorder, malaria, diabetes, abdominal pain, dizziness and fibroid is in line with indications reported by(Adedokun *et al*., 2010) and confirms the ethnomedicinal findings in Table 1.

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Table 2:
Studies on pharmacological actions of leaf extracts of *Spondias mombin*

	Country	Study design	Object/specimen	Plant part used	Treatment modalities	Pharmacological action	Outcomes/ Recommendation(s)	Reference(s)
1	Nigeria	In vivo	Rats	Leaf	Methanolic extract	Hepatoprotective activity	Exhibit potent antioxidant.	(Awogbindin *et al.*, 2014)
2	Nigeria	In vivo and In vitro	Wistar rats	Leaf	Methanolic extract	Anti-inflammatory activity	A positive result against carrageenan-induced paw edema in rats	(Nworu *et al.*, 2011)
3	Nigeria	In vivo	Albino Wistar rats	Leaf	Aqueous extract	Hypoglycemic effect	It also improves the lipid profile of diabetic rats.	(Nkanu *et al.*, 2016)
4	Nigeria	Experimental	Male Wistar rats	Leaf	Aqueous leaf extract	Hepatic and renal toxicological effect	Prolonged use may cause hepatic and renal toxicity.	(Asuquo *et al.*, 2012)
5	Nigeria	In vivo	Rats	Leaf	Hydroethanolic extract	Antioxidant capacity	Significant improvements in induced memory deficit against scopolamine	(Ishola *et al.*, 2018)
6	Nigeria	In vivo	Swiss Albino Rats	Leaf	Methanolic extract	Antimicrobial activity	Hematological properties on rats.	(Oladunmoye, 2007)
7	Nigeria	Experimental	Wistar albino rats	Leaf	Aqueous extract	Gastroprotective and antioxidative potentials	Effect on gastric ulceration.	(Sabiu *et al.*, 2015)
8	Nigeria	Experimental (chloramphenicol model)	Rats	Leaf	Aqueous extract	Anti-anemic activity	Possess anti-anemic activities	(Ohadoma, 2016)
9	Togo	Experimental	Albino Wistar Rats	Leaf	hydro-ethanolic extract	Estrogenic and haemostatic activities	Reduction in labor time, induce vaginal opening, increase uterus and ovarian weight and reduce coagulation time.	(Pakoussi *et al.*, 2013)
10	Nigeria	In vitro	Cell lines	leaf	Ethanolic extract	Anti-microbial activity	The inhibition against *Staphylococcus aureus*	(Maduka *et al.*, 2014)

It also demonstrates the use of aqueous leaf extracts of S. mombin in Brazil on the treatment of gastric ulcers (Oluwatoyin and Deborah, 2019). The ethnomedicinal use of leaf of S. mombin for the treatment of malaria is confirmed by (Pesewu *et al*., 2008) in Ghana. In Brazil *S. mombin* leaf extracts have been used in the treatment of cold sores; this demonstrates its use on the African continent (Siqueira *et al*., 2020).

In vivo study of methanol and ethyl acetate fractions, S. mombin leaves extracts on sodium arsenite-induced male albino rats indicated hepatoprotective, nephroprotective and genoprotective activities (Ola-Davies *et al*., 2019). The gastro-protective properties of aqueous leaf extracts of S. mombin against pylorus ligation, alcohol and ibuprofen-induced ulcer model were reported in Nigeria and it is in line with the findings of this review(Oluwatoyin and Deborah, 2019). The anti-microbial activity of S. mombin reported in the findings are confirmed by (Aromolaran and Badejo, 2014) with methanolic ethanolic, and acetone leaf extracts showed activity against Enterobacter aerogens, Staphylococcus aureus, Salmonella typhi and Klebsiella pneumonia, respectively, while the aqueous leaf extract had antibacterial properties against Serratia marcescens (Aromolaran and Badejo, 2014). In line with the pharmacological action in table 2, hypoglycemic effect, hepatotoxic effect and glucose-lowering effect in Alloxan-induced diabetic rats in vivo from ethanolic seed extract of S. mombin in Nigeria were reported (Iweala and Oludare, 2011). Methanolic leaf extract of S. mombin used in Nigeria to control the population of Aedes aegypti, Anopheles gambiae and Culex quinquefasciatus that cause malaria, dengue and filariasis confirm the adulticidal properties in the findings of this review(Eze *et al*., 2014). The adulticidal, antibabesial and antimalarial properties of the saponin, 1-O-Galloyl-6-O-luteoyl-α-D-glucose was reported in methanolic leaf extracts of S. mombin and Phyllanthus niruri(dos Santos Sampaio *et al*., 2018, Kaur *et al*., 2017).

Mombintane I and Mombintane II have been isolated from methanolic stem bark extracts of S. mombin that have antimycobacterial properties in vitro against Mycobacterium tuberculosis(Olugbuyiro *et al*., 2013). This confirms that some phytochemicals can be present in both leaf and stem extracts and can have different pharmacological activities. The hepatoprotective properties against CCl4 induced liver damage reported in Ghana are in line with pharmacological findings in other countries(Hamenoo, 2010).

Flavanoids have anti-oxidant, anti-cancer, anti-microbial, anti-aging, anti-lukemic, radical scavenging and vasodilatory properties(Sharma, 2006). Quercetin derivatives have been reported to be linked to anti-carcinogenic and anti-inflammatory properties due to their free radical scavenging activities(Harwood *et al*., 2007). A compound quercetin-3-O-β-D glucopyranoside (Q3G) was reported to be found in leaf extracts of S. mombin was also isolated in Albizia anthelmintica and Sclerocarya birrea (Anacardiaceae)(Masoko *et al*., 2008). Q3G was reported to have anti-oxidant scavenging activity towards diphenyl-picrylhydrazine (DPPH)(Kokila *et al*., 2013). The same compound Q3G was isolated from the hydroethanolic leaf extract of Echinophora cinerea and was found to act as a cytoprotective dietary compound(Shokoohinia *et al*., 2015). These pharmacological properties of Q3G are in agreement with its action obtained from the pharmacological investigations of S. mombin.

Phenolics such as ellagic acid may be responsible for pharmacological benefits against oxidation-linked chronic diseases (Vattem and Shetty, 2005). Phenolic compounds, which are anti-oxidants, can affect positively the negative effects of oxidative stress (Vattem and Shetty, 2005). This is in line with the anti-cancer properties of aqueous stem extract of S. mombin studied in vivo with induced cancer in rats (Ataman *et al*., 2002).

Geraniin was reported to possess anti-cancer properties in Xenograft tumor in vivo studies (Wang *et al*., 2017). The same compound was isolated from Phyllanthus amarus and Geranium sibiricum L, with lung cancer cells, anti-inflammatory, and anti-hyperglycemic activities (Wang *et al*., 2016, Ko, 2015, Boakye *et al*., 2016, Mao *et al*., 2016). Another study in China shows that Geraniin was isolated from ethyl acetate fraction of ethanolic extract of Geranium carolinianum L. that indicated anti-hepatitis B virus properties (Li *et al*., 2008). In Brazil, Geraniin, isolated from leaf extract of S. mombin, has been reported to possess antiherpes properties both in silico and in vitro against glycoproteins and herpes simplex virus type 1, respectively (Siqueira *et al*., 2020).

Some isolated compounds from S. mombin leaf extracts show that tannic acids to which galloylquinic acids are a part, such as 3,5-di-O-galloyl-4-O-digalloylquinic acid, 3,4-di-O-galloyl-5-O-digalloylquinic acid, 3-O-digalloyl-4,5-di-O-galloylquinic acid, and 1,3,4,5-tetra-O-galloylquinic acid, have been reported to inhibit human immunodeficiency virus (Global) reverse transcriptase (RT)(Mahmood *et al*., 1997). Tannic acids isolated from aqueous leaf extracts Cuscuta reflexa have anti-HIV properties that are in agreement with the same compounds isolated S. mombin leaf extracts with the same pharmacological action(Mahmood *et al*., 1997).

Conclusion

Findings from this review confirm the ethnomedicinal uses of S. mombin leaf extracts for disease management; studies confirmed the presence of phytochemical compounds responsible for its pharmacological activities such as antiviral, leishmanicidal, adulticidal and chemotherapeutic properties. However, there is a need for bio-assay guided extractions, isolation, identification and characterization of phytochemical compound(s) in the leaf extracts of S. mombin and responsible for the antiviral and anti-cancer activity, namely the management and /or treatment of Ebola virus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), hepatitis B, prostate and womb cancers. To this end, investigation of the pharmacological action, in silico and in vitro studies of known and /or newly isolated compounds as stand-alone or synergy with other medicinal plants are warranted in the management and /or treatment of Ebola virus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), prostate and womb cancers to justify the ethnomedicinal use of leaf extracts of S. mombin and other aerial medicinal plant extracts as part of polyherbal mixtures in local communities on the African continent for the management of viral infections and cancer.

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