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**Review** Article

# Phytopharmacological Activities of Spondias mombin Linn: A Review

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#### ABSRTACT

This review describes the phytopharmacological activities of *Spondias mombin*. *Spondias mombin* (*S. mombin*) is a fructiferous tree native to tropical areas like America, Brazil, Nigeria and West India. It belongs to the cashew family of Anacardiaceae. *Spondias mombin* has been used as an herbal medicine from ancient times. *Spondias mombin* plant parts (leaves, bark, seeds, and fruits) are used for therapeutic purposes. Traditionally, the plant is being used in inducing labour, preventing miscarriages, reducing inflammation, reducing blood glucose level, amongst others. Various plant parts are also used for non-medicinal purposes like the production of cider-like drinks, wine, soap and ornamental purposes. The main bioactive compounds reported in *S. mombin* include tannins, phenols, saponins, anthraquinones, berberine, naphthoquinones, sesquiterpenes, indole and quinoline alkaloids, proanthocyanins, and flavonoids. *Spondias mombin* possesses beneficial pharmacological properties that are well-utilized in medicinal herbal therapy of several disease conditions.

Keywords: Anacardiaceae, ethnopharmacology, herbal medicine, phytochemicals, Spondias mombin

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### Introduction

Acceptance of herbal medicine usage in traditional medicine amongst developing countries continue to rise.<sup>1-3</sup> Among such medicinal plant is *Spondias mombin*, belonging to the family 'Anacardiaceae' (*Spondias* genus), commonly found in the lowland moist forest of the Amazon and tropics of Africa.<sup>4, 5</sup> It is popularly identified as yellow mombin or hog plum.<sup>6-8</sup>

*Spondias mombin* (*S. mombin*) is widely depended upon in certain health conditions, and essentially every portion of the tree have been found useful ranging from its thickly corky bark to its leaves, fruits and even its flower (Figure. 1-2). The plant's leaves have been shown to exhibit abortifacient, lipid-lowering, and hypoglycaemic actions.<sup>7, 9-11</sup> It is a medicinal plant that has wide acceptability and proven to exert certain beneficial health activities which include antiepileptic, antidementia, antipsychotic, anticancer, cytotoxic, anthelmintic, <u>antiviral, and anxiolytic</u> pharmacological activities.<sup>12-15</sup>

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Bioactive compounds such as tannins, phenols, saponins, anthraquinones, berberine, naphthoquinones, sesquiterpenes, indole and quinoline alkaloids, proanthocyanins and flavonoids have been found to be present following qualitative and quantitative phytochemical analysis.<sup>14, 16</sup> These phytochemicals are responsible for its important pharmacological actions.<sup>16</sup>

Although, there are documented instances of the harmful effects of medicinal herbs when utilized in traditional medicine following acute or repeated (sub-acute, sub-chronic and chronic) exposures, findings have shown that *S. mombin* is relate safe.<sup>17, 18</sup>

# **Materials and Methods**

This review adapted 71 articles which covered the periods of 2006 to 2023 retrieved following extensive literature search using search engines or databases including: Google, ResearchGate, PubMed and Elsevier. The keywords that directed our literature search were: Phytopharmacological activities, phytochemistry, ethnopharmacology and *Spondias mombin*.

#### Plant description

Spondias mombin L. (Anarcardiaeae) is a deciduous erect tree with a height of about 30 m and a trunk of 60-75 cm width, with branches 2-10 m above ground level to form a spreading crown up to 15 m in diameter and forming an open or densely closed canopy. Its trunk has some deep incisions located in the bark of the tree and sometimes, it produces a brown resinous substance.<sup>19</sup> The leaves and flowers of the plant are situated at the end of the branches. The tree exhibits a grayish bark with a somewhat buttressed, thick, and coarse trunk. The leaves have an alternate arrangement, with a single pinnate structure and an unusual terminal leaflet. Stipules are not present. The rachis is 30-70 cm in length. The leaflets are arranged in 5-10 pairs and are elliptic in

shape, measuring 5-11 x 2-5 cm. The apex of the leaflets is long and pointed, with an asymmetric, truncated or wedge-shaped base. The margins of the leaflets are smooth, and they are either hairless or sparsely covered in fine hairs. Commonly in young plants, the leaf stalk tends to be reddish towards the outer leaflets.<sup>19</sup> The fruit is an ovoid or ellipsoid drupe, 3-4 x 2-2.5 cm in diameter; dull light orange to yellow or brown; in clusters of 1-20; epicarp thin, enveloped by a succulent orange or yellow middle layer that is 3-6 mm thick. The endocarp is relatively large and has a soft, fibrous texture with grooves. It surrounds 4-5 tiny seeds.<sup>19</sup>

*Spondias mombin* is a fruit-bearing tree that is found in Nigeria, Brazil, and various other tropical forests worldwide. The tree is cultivated around Africa, India, Nepal, Bangladesh, Sri Lanka, Bahamas, and Indonesia. The plant is distributed in tropical America, Brazil, Nigeria, the West Indies, and several tropical rainforests worldwide. This plant is commonly found around the South West of Nigeria (Yoruba) and is commonly used in folk medicine. The plant is known by several names in various regions. In Costa Rica, it is called 'Bala', while in Panama it is known as 'Jobito'. In Colombia, it is referred to as 'Jobo blanco', and in Venezuela, it is called 'Jobo corronchoso'. In Surinam, it is known as 'Hoeboe', and in Brazil, it goes by the names 'Acaiba', 'Caja', and 'Pau da tapera'. In Peru, it is called 'Ubo', while in Mexico it is known as 'Hobo'. In Nigeria, the Hausa people refer to it as 'Tsardarmasar', while the Yorubas call it 'Iyeye' or 'Akika etikan', and in the Igbo language, it is known as 'Ichikara'.<sup>20, 21</sup>

#### Phytochemical constituents of S. mombin

*Spondias mombin* is rich in several secondary metabolites which includes phenols, sterols, triterpenes, saponins, essential oils, amino acids, and polysaccharides (Figure 3-5).<sup>16</sup> Geraniin and galloyl geraniin, which are phenolic compounds, were derived from the ethanol extract of the leaves and stems of *S. mombin*. Additionally, lupeol was obtained specifically from S. mombin leaves.<sup>22</sup> The methanolic extract of *S. mombin* bark yielded sterols, specifically stigmasta-9-en-3,6,7-triol and 3-hydroxy-22-epoxystigmastane.<sup>23</sup> Both *S. mombin* and *S. purpurea* leaves were subjected to hydrodistillation, resulting in the extraction and identification of several volatile oil constituents, including  $\alpha$ -pinene,  $\beta$ -pinene, caryophyllene, humulene, indene, and cadinene.<sup>22</sup>



Figure 1: Spondias mombin leaves with fruits



Figure 2: Thick bark of Spondias mombin

Abiodun and colleagues identified the following major compounds in the seed of *S. mombin*: dodecanoic acid (22.48%), tetradecanoic acid (17.95%), n-hexadecanoic acid (15.35%), and phenol amides capsaicin (12.11%) and dihydrocapsaicin (5.23%).<sup>24</sup> Lauric acid (dodecanoic acid) had antibacterial activity against *Propionibacterium* acnes in laboratory tests and demonstrated positive results in reducing inflammation caused by *Propionibacterium* acnes in a mouse ear model.<sup>25</sup> Tetradecanoic acid (myristic acid) serves as a dietary supplement and flavoring agent in the food industry. Furthermore, it is utilized in the cosmetic sector for producing facial creams, lotions, toiletries, and emulsifiers. Additionally, it finds application in the pharmaceutical industry.<sup>26,27</sup> Hexadecanoic acid (palmitic acid), capsaicin, and dihydrocapsaicin exhibit antioxidant, anti-inflammatory, and analgesic properties.<sup>28-30</sup>

The hydroethanolic extract obtained from *S. mombin* leaves contains significant quantities of the phenolic chemicals chlorogenic acid, ellagic acid, and isoquercetin.<sup>31</sup> A current study revealed the existence of (E)-ethyl cinnamate (14.06%) and methyl salicylate (13.05%) in the essential oils derived from the fruit and leaf of *S. mombin*, respectively.<sup>32</sup> The fruit essential oil contained significant quantities of benzyl benzoate (12.27%), n-hexadecanoic acid (8.14%), benzoic acid ethyl ester (5.89%), tetracosane (5.30%), and terpineol (4.61%), whilst the essential oil derived from leaves contained heptacosane (12.69%), caryophyllene (6.77%), octacosane (8.54%), and n-hexadecanoic acid (4.91%) in high amounts.<sup>32</sup>

Quantification of various phenolic chemicals, including flavonols, phenylpropanoids, benzoic acid derivatives, coumarins, stilbenes, dihydrochalcones, flavones, and flavonones, was performed using ultrahigh performance liquid-chromatography-MS/MS (UPLC-MS/MS) on the fruit peel of S. mombin.<sup>33</sup> A total of fourteen flavonol substances were measured and determined. Quercetin was the predominant component, with myricetin and Kaempferol-3-Glc following in abundance. The quantification of phenylpropanoids included cinnamic acid, and several derivatives of this chemical, such as certain hydroxycinnamic acids and sinapyl alcohol. The chemical that was most abundant was chlorogenic acid, with p-coumaric and cinnamic acid being present in lesser amounts. The predominant component was ellagic acid, which is a derivative of benzoic acid. Gallic acid was identified in a lesser proportion. Esculin is particularly notable among the quantifiable coumarins. Cis-piceid is notable among the quantified stilbenes in this experiment for its significantly high values. Sinensetin and Luteolin-7-O-Glc were the most prominent flavones.33

# Pharmacological properties of S. mombin Linn

*S. mombin* is of great ethnopharmacological relevance as virtually every component of the plant has shown useful therapeutic effects. Amongst its medicinal activities include:

#### Anti-anaemic activity

Reduction in red cell mass or in the quantity and quality of hemoglobin is characteristic of anaemia, which is majorly caused by reduction in haemoglobin production, increased destruction of hemoglobin (or blood loss) and blood pooling within the spleen.<sup>34</sup> In a study conducted to assess the hematinic properties of *S. mombin* leaf extract against phenylhydrazine (PHZ)-induced anaemia in rats, *S. mombin* (150 mg/kg; 300 mg/kg) improved the hematological parameters in comparison to the PHZ-alone treated rats.<sup>35</sup>

Adeyemi and Gbolade had previously reported the hematinic effect of *S. mombin* (dose range of 100-400 mg/kg) on chloramphenicol-induced anaemic rats, as there was a dose-dependent marked rise in haemoglobin and packed cell volume.<sup>36</sup> Likewise, doses of 250 mg/kg and 500 mg/kg of ethanol leaves extract of *S. mombin* has been described to cause significant an augmentation in their erythrocyte count, haemoglobin content, and PCV (packed cell volume) of experimental animals.<sup>37</sup> The anti-anaemic properties of *S. mombin* could very much connected to its phytochemical constituents.<sup>38</sup>

#### Anti-cancer activity

Plants and plant-based products usage are of positive therapeutic importance when used in therapy for cancer and tumour-related diseases. A study conducted by Metibemu and others revealed the presence of carotenoids (astaxanthin,  $\beta$ -carotene-15,15'-epoxide, and 7,7',8,8'-tetrahydro- $\beta$ ,  $\beta$ -carotene) extracted from the leaves of *S. mombin* are proapoptotic, displaying antineoplastic impact in DMBA (7,12-dimethylbenz[a]anthracene)-induced breast cancer in experimental rats through XIAP (X-linked inhibitor of apoptosis protein) antagonism.<sup>39</sup> Other studies have also stated the anti-tumour actions of *S. mombin.*<sup>12, 40-42</sup>

#### Anti-inflammatory activity

During early wound healing stages, inflammatory processes are vital in enhancing proper fibroblast and collagen remodelling and arrangement.<sup>43</sup> Extracts obtained from *S. mombin* L. (Anacardiacea) is very much claimed to be useful in the traditional medicine of Africa and Latin America to treat many inflammatory conditions. A study by Nworu and colleagues revealed that pre-treatment of rats with *S. mombin* leaf extract induced a substantial and dose-dependent reduction in swelling of the paw caused by carrageenan observed over a period of 4 hours, with a substantial lowering of lipopolysaccharide (LPS)inducible TNF- $\alpha$  levels in the *S. mombin* extract may reduce inflammatory reactions, maybe by inhibiting the production of proinflammatory mediators and cytokines such tumor necrosis factor- $\alpha$ (TNF- $\alpha$ ) and inducible nitric oxide (iNO).<sup>12</sup>

In another study, the anti-inflammatory property of the leaf extract of *S. mombin* was assessed via the carrageenan-induced peritonitis in mice (*in vivo* model).<sup>31</sup> The extract exhibited anti-inflammatory properties at varying doses, however, the ethyl acetate fraction at 200 mg/kg demonstrated particularly noteworthy benefits. The chemical components of *S. mombin*, namely ellagic acid and chlorogenic acid, at

quantities of 2.5, 5, and 10 mg/kg, effectively suppressed the movement of white blood cells to the inflammatory site.<sup>31</sup>

A recent study established that the essential oil derived from *S. mombin* leaves contains therapeutic components that accelerates wound healing through mechanisms including counter-inflammation, modulation of anti-inflammatory cytokines, modulating other biomarkers that help in formation of granulation tissues, neo formation of blood vessels and construction of extracellular matrix, converging activity of keratinocytes at the re-epithelization phase and tissue remodeling.<sup>44</sup>

#### Anti-ulcer activity

Pathologically, peptic ulcers are damages done to the mucosal wall, affecting components of the epithelial and connective tissue, including subepithelial myofibroblasts, smooth muscle cells, vessels, and nerves, which can reach from the muscle layer to deeper regions.<sup>45</sup> Findings have revealed that *S. mombin* possess antiulcer potential.<sup>46-48</sup> *S. mombin* L has shown favorable gastroprotective activities both with its leaves extracts and tablets formulations.<sup>49</sup> The gastroprotective effect is well related to both cytoprotective mechanisms, including the participation of endogenous prostaglandins and ATP-sensitive potassium (KATP) channels, and antisecretory properties with systemic actions.<sup>49</sup>

A study by Oluwatosin and Deborah indicated that leaf extract of *S. mombin* L. has antiulcer property as compared with standard drugs, showing protective effect on gastric mucosa in models of ibuprofen and alcohol-induced ulcer and an inhibitory effect on gastric acid secretion in the pylorus-ligated models.<sup>50</sup> The study suggested several potential pathways for *S. mombin* L. cytoprotective activity to include the non-protein sulfhydryl (NP-SH) and nitric oxide synthase (NOS) pathways.



Figure 3: Chemical structure of phenolic compounds isolated from Spondias species<sup>16</sup>



Figure 4: Chemical structure of sterols and terpenoids isolated from Spondias species<sup>16</sup>

#### Antioxidant activity

The antioxidant ability associated with an anti-inflammatory potential are desirable features of a bioactive compound. Antioxidants mitigate the impact of free radicals on biomolecules by consuming them. Increasein free radicals generation exceeding the host's antioxidant is deleterious.<sup>24, 51-53</sup>

Several researches have been done on the antioxidant efficacy of *S. mombin.*<sup>24, 54, 55</sup> A study evaluated the protective actions of the leaf and stem methanol extracts of *S. mombin* in rat model of carbon tetrachloride (CCl<sub>4</sub>)-induced hepatotoxicity. Pretreatment with 1000 mg/kg of the extracts markedly increased glutathione, catalase and superoxide dismutase levels.<sup>54</sup> *S. mombin* seed methanol extract was examined and shown to contain safe antioxidant chemicals, such as hexadecanoic acid, capsaicin, and dihydrocapsaicin. These compounds have potential applications in the pharmaceutical and cosmetics sectors for the creation of antioxidant agents.<sup>24</sup>

#### Hypoglycaemic activity

Induction of diabetes in experimental animals is commonly by chemical method with streptozotocin and alloxan.<sup>56-64</sup> It usually involve the destruction of the beta-cells of the Islets of Langerhans in the pancreas with a consequent reduction in synthesis and release of insulin.<sup>56, 63</sup> Numerous studies have reported the hypoglycemic activities of *S. mombin.*<sup>7, 65-67</sup>

Findings from study by Gobinath *et al.*<sup>67</sup> revealed that methanol extract of *S. mombin* leaves reduced glucose level in the blood and reversed the declined plasma insulin level of the diabetic induced rats following 28

days therapy. The potential mechanism of the extract in exerting hypoglycemic effects may involve the enhancement of insulin secretion from  $\beta$ -cells in the pancreatic islets, increased transportation of glucose from the bloodstream to peripheral tissues, inhibition of endogenous glucose production, or activation of gluconeogenesis in the liver and muscles.<sup>67</sup>

#### Learning and memory activity

Learning is involved with the acquisition of knowledge while memory is involved with the ability to retain the knowledge acquired. Stress and aging are among several factors that could influence learning impairment. Aging can lead to neurodegenerative diseases including memory loss, dementia and Alzheimer's disease.<sup>68</sup>

In a study by Asuquo *et al.*<sup>69</sup> on the effects of *S. mombin* on possible learning and memory while studying the histology of the cerebral cortex in adult male Wistar rats, reported that *S. mombin* administered at varying doses (400mg and 800mg/kg) improved learning behavior and enhanced memory which could be attributable to the observed alterations in the cerebrum's structure. The potential mechanism of *S. mombin* on learning and memory may involve a beneficial impact on the production of neurotransmitters (acetylcholine, noradrenaline, dopamine, and serotonin).

Ishola *et al.* reported that *S. mombin* leaf extract and the seed extract of *Cola acuminata* effectively improved the cognitive deficits caused by scopolamine, likely due to their antioxidant characteristics.<sup>70</sup> Another study provided further evidence for the beneficial impact of ethanol fruit extract from *S. mombin* on memory impairment caused by

scopolamine. This outcome is achieved via improving cholinergic function and reducing oxidative stress in the brains of mice.<sup>71</sup>

#### Conclusion

There is a growing interest in the use of ethnomedicinal plants as alternative therapeutic options in the management of various illnesses, hence their usefulness cannot be overemphasized as numerous researches have consistently reported their beneficial role against a wide array of pathologies. This review examined the pharmacological effects of *Spondias mombin* as a herbal medicine for various pathological conditions and its potential as a therapeutic agent in traditional medicine. Therefore, it is recommended to conduct clinical trials on the active constituents of *Spondias mombin* in order to develop safer and more effective drug formulations for the therapy of these diseases.

#### **Conflict of Interest**

The authors declare no conflict of interest.

# **Authors' Declaration**

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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Figure 5: Chemical structure of amino acids and carbohydrates isolated from Spondias species<sup>16</sup>

# References

- Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. Front Pharmacol. 2014;4:177. https://doi.org/10.3389/fphar.2013.00177.
- James PB, Wardle J, Steel A, Adams J. Traditional, complementary and alternative medicine use in Sub-Saharan Africa: a systematic review. BMJ Glob Health. 2018;3(5):e000895. https://doi.org/10.1136/bmjgh-2018-000895.
- Moke EG, Umukoro EK, Asiwe JN, Omogbiya AI, Erhirhie EO, Ben-Azu B, Anieh FU. Herbal Medicine: Education and Occupation Influences Its Practice among Residents of Port Harcourt, South-South Nigeria. Int J Pharm Phytopharmacol Res. 2021;11(2):38-44.
- Ayoka AO, Akomolafe RO, Akinsomisoye OS, Ukponmwan OE. Medicinal and Economic Value of *S. mombin*. Afr J Biomed Res. 2008;11(2):129–136.
- Mattietto RA, Matta VM. 15 Cajá (S. mombin L.). Editor(s): Yahia EM. Postharvest Biology and Technology of Tropical and Subtropical Fruits. Cambridge: Woodhead Publishing Ltd; 2011. p. 330-353
- Adedokun MO, Oladoye AO, Oluwalana SA, Mendie II. Socio-economic importance and utilization of *S. mombin* in Nigeria. Asian Pacific J Tropical Med. 2010;3(3):232-234.
- Moke EG, Ilodigwe EE, Okonta JM, Emudainohwo JOT, Ajaghaku DL, Erhirhie OE, Chinwuba P, Ahante E. Antidiabetic Activity and Toxicity Evaluation of Aqueous

Extracts of *S. mombin* and *Costus afer* on Wistar Rats. Br J Pharm Res. 2015;6(5):333-342.

- Esua OJ, Makinde OO, Arueya GL, Chin NL. Antioxidant potential, phytochemical and nutrient compositions of Nigerian hog plum (*S. mombin*) seed kernel as a new food source. Int Food Res J. 2016;23(Suppl):S179-S185.
- Nkanu EE, Jeje SO, Ikpi DE, Ujong GO. In vivo hypolipidemic and hypoglycemic effects of aqueous extract of Spondias mombin leaves and detoxification of reactive oxygen species in alloxan-induced diabetic rats. Int J Biol Chem Sci. 2016;10(4):1573-1579.
- 10. Uchendu CN, Isek T. Antifertility activity of aqueous ethanolic leaf extract of *S. mombin* (Anacardiaceae) in rats. Afr Health Sci. 2008;8(3):163-7.
- Ijioma SN, Osim EE, Nwankwo AA, Kanu KC, Orieke D. Southeast Nigerian polyherbal (AJUMBISE): A potential uterotonic and tocolytic agents. Scientific African. 2020;8:e00393. https://doi.org/10.1016/j.sciaf.2020.e00393
- Nworu CS, Akah PA, Okoye FB, Toukam DK, Udeh J, Esimone CO. The leaf extract of *S. mombin* L. displays an anti-inflammatory effect and suppresses inducible formation of tumor necrosis factor-α and nitric oxide (NO). J Immunotoxicol. 2011;8(1):10-6. https://doi.org/10.3109/1547691X.2010.531406.
- 13. Dos Santos Sampaio TI, de Melo NC, de Freitas Paiva BT, da Silva Aleluia GA, da Silva Neto FLP, da Silva HR, Keita H, Cruz RAS, Sánchez-Ortiz BL, Pineda-Peña EA, Balderas JL, Navarrete A, Carvalho JCT. Leaves of *S. mombin* L. a traditional anxiolytic and antidepressant: Pharmacological

evaluation on zebrafish (Danio rerio). J Ethnopharmacol. 2018;224:563-578. https://doi.org/10.1016/j.jep.2018.05.037.

- Ogunro OB, Oyeyinka BO, Gyebi GA, Batiha GE. Nutritional benefits, ethnomedicinal uses, phytochemistry, pharmacological properties and toxicity of *S. mombin* Linn: a comprehensive review. J Pharm Pharmacol. 2023;75(2):162-226. https://doi.org/10.1093/jpp/rgac086.
- Santos ÉMD, Ataide JA, Coco JC, Fava ALM, Silvério LAL, Sueiro AC, Silva JRA, Lopes AM, Paiva-Santos AC, Mazzola PG. Spondias sp: Shedding Light on Its Vast Pharmaceutical Potential. Molecules. 2023;28(4):1862. https://doi.org/10.3390/molecules28041862.
- Sameh S, Al-Sayed E, Labib RM, Singab AN. Genus Spondias: A Phytochemical and Pharmacological Review. Evid Based Complement Alternat Med. 2018;2018:5382904. https://doi.org/10.1155/2018/5382904.
- Porwal M, Gautam SK, Khan NA, Maheshwari KK. Evaluation of Toxicity and Antihyperlipidemic Activity of *S. mombin* 1. Leaves Methanolic Extract in Laboratory Rats. Cardiovasc Hematol Disord Drug Targets. 2020;20(4):289-296.

https://doi.org/10.2174/1871529X20999201027232556.

- Erhirhie EO, Moke GE. Repeated Systemic Toxicity Tests: A Call for Proper Understanding of Tests Durations Nomenclature. Asia Pac J Med Toxicol. 2022;11(2):72-76.
- Orwa C, Mutua A, Kindt R, Jamnadass R, Simons A. Agroforestree Database: a tree reference and selection guide version 4.0. World Agroforestry Centre, Kenya. 2009. Available via <u>https://www.worldagroforestry.org/output/agroforestree-</u> database. Accessed on 22 Mar 2023.
- Coelho-Ferreira M. Medicinal knowledge and plant utilization in an Amazonian coastal community of Marudá, Pará State (Brazil). J Ethnopharmacol. 2009;126:159-175.
- 21. Uchendu CN, Isek T. Antifertility activity of aqueous ethanolic leaf extract of Spondias mombin (Anacardiaceae) in rats. Afr Health Sci. 2008;8(3):163-7.
- 22. De Lima EQ, de Oliveira E, de Brito HR. Extraction and characterization of the essential oils from *S. mombin* L. (CajÃ<sub>j</sub>), Spondias purpurea L. (Ciriguela) and Spondia ssp (Cajarana do sertão). Afr J Agric Res. 2016;11(2):105-116. https://doi.org/10.5897/AJAR2014.10363.
- Olugbuyiro JAO, Moody JO, Hamann MT. Phytosterols from *S. mombin* linn with antimycobacterial activities. Afr J Biomed Res. 2013;16(1):19–24.
- Abiodun OO, Nnoruka ME, Tijani RO. Phytochemical Constituents, Antioxidant Activity, and Toxicity Assessment of the Seed of *S. mombin* L. (Anacardiaceae). Turk J Pharm Sci. 2020;17(3):343-348. https://doi.org/10.4274/tjps.galenos.2020.38801.
- Nakatsuji T, Kao MC, Fang JY, Zouboulis CC, Zhang L, Gallo RL, Huang CM. Antimicrobial Property of Lauric acid against Propionibacterium acnes: Its Therapeutic Potential for Inflammatory Acne Vulgaris. J Invest Dermatol. 2009;129:2480–2488.
- Or-Rashid MM, Odongo NE, Subedi B, Karki P, McBride BW. Fatty acid composition of yak (Bos grunniens) cheese including conjugated linoleic acid and trans-18:1 fatty acids. J Agric Food Chem. 2008;56:1654–1660.
- Meng Q, Yu M, Gu B, Li J, Liu Y, Zhan C, Xie C, Zhou J, Lu W. Myristic acid-conjugated polyethylenimine for braintargeting delivery: In vivo and ex vivo imaging evaluation. J Drug Target. 2010;18:438–446.
- Graikou K, Kapeta S, Aligiannis N, Sotiroudis G, Chondrogianni N, Gonos E, Chinou L. Chemical analysis of Greek pollen-antioxidant, antimicrobial and proteasome activation properties. Chem Cent J. 2011;5:33.
- 29. Aparna V, Dileep KV, Mandal PK, Karthe P, Sadasivan C, Haridas M. Antiinflammatory property of n-hexadecanoic

acid: Structural evidence and kinetic assessment. Chem Biol Drug Des. 2012;80:434–439.

- Fattori V, Hohmann MS, Rossaneis AC, Pinho-Ribeiro FA, Verri WA. Capsaicin: Current Understanding of Its Mechanisms and Therapy of Pain and Other Pre-Clinical and Clinical Uses. Molecules. 2016;21:844.
- Cabral B, Siqueira EM, Bitencourt MO, Lima MC, Lima AK, Ortmann CF, Chaves VC, Fernandes-Pedrosa MF, Rocha HA, Scortecci KC, Reginatto FH, Giordani RB, Zucolotto SM. Phytochemical study and anti-inflammatory and antioxidant potential of *S. mombin* leaves. Revista Brasileira de Farmacognosia. 2016;26(3):304-311. https://doi.org/10.1016/j.bjp.2016.02.002.
- 32. Ampadu GA, Mensah JO, Darko G, Borquaye LS. Essential Oils from the Fruits and Leaves of *S. mombin* Linn.: Chemical Composition, Biological Activity, and Molecular Docking Study. Evid Based Complement Alternat Med. 2022;2022:7211015. https://doi.org/10.1155/2022/7211015.
- 33. Brito GO, Reis BC, Ferreira EA, Vilela Junqueira NT, Sá-Barreto LCL, Mattivi F, Vrhovsek U, Gris EF. Phenolic Compound Profile by UPLC-MS/MS and Encapsulation with Chitosan of *S. mombin* L. Fruit Peel Extract from Cerrado Hotspot-Brazil. Molecules. 2022;27(8):2382. https://doi.org/10.3390/molecules27082382.
- Chaparro CM, Suchdev PS. Anemia epidemiology, pathophysiology, and etiology in low- and middle-income countries. Ann N Y Acad Sci. 2019;1450(1):15-31. https://doi.org/10.1111/nyas.14092.
- Innih SO, Omage SO, Omage K. Hematinic effects of S. mombin and its protective role against the spleenotoxic effect of phenylhydrazine. Clin Phytosci. 2020;6:30. https://doi.org/10.1186/s40816-020-00180-1.
- Adeyemi AA, Gbolade AA. Anti-anaemic activity of *S. mombin* and *Khaya grandifoliola* aqueous extracts on rats. J Pharm Bioresources. 2006;3(2):94-97. https://doi.org/10.4314/jpb.v3i2.32101.
- Asuquo RO, Ekanem BT, Udoh BP, Mesembe EO, Ebong EP. Haematinic Potential of *S. mombin* Leaf Extract in Wistar Rats. Adv Biores. 2013;4(2):53-56.
- Fagbohoun L, Nonvidé G, Orou A, Houngbèmè A, Sakirigui A, Gunin F, Gbénou J. Anti-Anaemic Activity and Potential Toxicity of Extracts of Four Tinctorial Plants Used in the Treatment of Anemia in Benin: Gossypium barbadense, Sorghum bicolor, Hibiscus sabdariffa and Justicia secunda. Am J Plant Sci. 2022;13:1460-1477. https://doi.org/10.4236/ajps.2022.1312100.
- Metibemu DS, Akinloye OA, Akamo AJ, Okoye JO, Ojo DA, Morifi E, Omotuyi IO. Carotenoid isolates of *S. mombin* demonstrate anticancer effects in DMBA-induced breast cancer in Wistar rats through X-linked inhibitor of apoptosis protein (XIAP) antagonism and anti-inflammation. J Food Biochem. 2020;44(12):e13523. https://doi.org/10.1111/jfbc.13523.
- Gbolade AA, Edom DN, Ogunleye JT, Muhammad ST. Antiproliferative and cytotoxic properties of *S. mombin* L. (*Anacardiaceae*) stem bark. J Pharm Allied Sci. 2019;16(5):3146-3154.
- Metibemu DS, Akinloye OA, Omotuyi IO, Okoye JO, Popoola MA, Akamo AJ. Carotenoid-Enriched Fractions From *S. mombin* Demonstrate HER2 ATP Kinase Domain Inhibition: Computational and *In Vivo* Animal Model of Breast Carcinoma Studies. Front Oncol. 2021;11:687190. https://doi.org/10.3389/fonc.2021.687190.
- 42. Akanji OC, Idu M, Omotuyi IO. Effect of *S. mombin* leaves' extracts on chemically induced tumor. J Med Herbs. 2022;13(2)2:7-17.
- 43. Nishikai-Yan Shen T, Kanazawa S, Kado M, Okada K, Luo L, Hayashi A, Mizuno H, Tanaka R. Interleukin-6 stimulates Akt and p38 MAPK phosphorylation and fibroblast migration in non-diabetic but not diabetic mice. PLoS One.

2017;12(5):e0178232.

https://doi.org/10.1371/journal.pone.0178232.

- Agbaje EO, Charles OO. Anti-inflammatory and Cytokines Modulatory Activities of *S. mombin* Linn. (Anacardiaceous) in Wound Healing: Roles of IL6. J Phytopharmacol. 2022;11(4):260-267. https://doi.org/10.31254/phyto.2022.11406.
- Lanas A, Chan F. Peptic ulcer disease. Lancet. 2017;390:613–624. https://doi.org/10.1016/S0140-6736(16)32404-7.
- 46. Sabiu S, Garuba T, Sunmonu T, Ajani E, Sulyman A, Nurain I, Balogun A. Indomethacin-induced gastric ulceration in rats: Protective roles of *S. mombin and Ficus exasperata*. Toxicol Rep. 2015;2:261-267. https://doi.org/10.1016/j.toxrep.2015.01.002.
- 47. Moke EG, Ilodigwe EE, Erhirhie OE. Evaluation of the ulcerogenic potential of the aqueous extract of *S. mombin* and Costus afer. IJAPBC. 2015;4(2):282-6.
- 48. Brito SA, Barbosa IS, de Almeida CLF, de Medeiros JW, Silva Neto JC, Rolim LA, da Silva TG, Ximenes RM, de Menezes IRA, Caldas GFR, Wanderley AG. Evaluation of gastroprotective and ulcer healing activities of yellow mombin juice from *S. mombin* L. PLoS One. 2018;13(11):e0201561.

https://doi.org/10.1371/journal.pone.0201561.

49. Araruna ME, Silva P, Almeida M, Rêgo R, Dantas R, Albuquerque H, Cabral I, Apolinário N, Medeiros F, Medeiros A, Santos V. Tablet of *S. mombin* L. Developed from Nebulized Extract Prevents Gastric Ulcers in Mice via Cytoprotective and Antisecretory Effects. Molecules. 2021;26(6):1581.

https://doi.org/10.3390/molecules26061581.

- Oluwatoyin AE, Deborah OW. Study of aqueous leaf extracts of *S. mombin* Linn. (Anacardiaceae) in gastric ulcer models and the possible mechanisms of action. J Phytopharmacol. 2019;8(5):238-247.
- 51. Gupta RK, Patel AK, Shah N, Chaudhary AK, Jha UK, Yadav UC, Gupta PK, Pakuwal U. Oxidative stress and antioxidants in disease and cancer: a review. Asian Pac J Cancer Prev. 2014;15(11):4405-4409. https://doi.org/10.7314/apjcp.2014.15.11.4405.
- 52. Moke EG, Mordi JC. Effect of Methanol Leaf Extract of Cuphea Hyssopifolia Kunth on Liver Enzymes Activity and Antioxidant Indices of Paracetamol-Induced Hepatotoxicity in Wistar Rats. Afr J Biomed Res. 2020;23(1):123-126.
- 53. Ali SS, Ahsan H, Zia MK, Siddiqui T, Khan FH. Understanding oxidants and antioxidants: Classical team with new players. J Food Biochem. 2020;44(3):e13145. https://doi.org/10.1111/jfbc.13145.
- 54. Nwidu LL, Elmorsy E, Oboma YI, Carter WG. Hepatoprotective and antioxidant activities of *S. mombin* leaf and stem extracts against carbon tetrachlorideinduced hepatotoxicity. J Taibah Univ Med Sci. 2018;13(3):262-271.

https://doi.org/10.1016/j.jtumed.2018.03.006.

- 55. Lucena TLC, Batista KS, Pinheiro RO, Cavalcante HC, Gomes JAdS, Silva LAd, Lins PP, Ferreira FS, Lima RF, Lima MdS, Aquino JdS. Nutritional Characterization, Antioxidant, and Lipid-Lowering Effects of Yellow Mombin (*S. mombin*) Supplemented to Rats Fed a High-Fat Diet. Foods. 2022;11(19):3064. https://doi.org/10.3390/foods11193064.
- Lenzen S. The mechanisms of alloxan- and streptozotocininduced Diabetes. Diabetologia. 2008;51:216–226.
- 57. Etuk EU. Animals models for studying diabetes mellitus. Agric Biol J North Am. 2010;1:130-134.
- Okafo SE, Moke EG, Obi CS. Formulation and evaluation of anti-diabetic tablets containing aqueous extract of Moringa oleifera seeds. J Pharm Allied Sci. 2019;16(5):3167-3176.

- Ji G, Sun R, Hu H, Xu F, Yu X, Veeraraghavan VP, Mohan SK, Chi X. Vannilic acid ameliorates hyperglycemiainduced oxidative stress and inflammation in streptozotocininduced diabetic rats. J King Saud Univ Sci. 2020;32(7):2905-2911.
- 60. Warri AO, Moke EG, Balogun AO, Nzeh KC, Umukoro EK, Erhirhie EO. Acute Toxicity and Hypoglycemic Effect of a Polyherbal Formulation on Blood Glucose in Oral Glucose Tolerance Test (OGTT) and Alloxan-Induced Diabetic Rats. Biol Med Natural Prod Chem. 2021;10(2):111-115.
- Akwu BP, Ajibade AJ, Abijo AJ, Ajibade TP, Kehinde DB, Siyanbade JA, Adelakun SA, Adeeyo OA. Co-administration of *S. mombin* and Metformin mitigates Streptozotocininduced hepatorenal injury. Phytomed Plus. 2022;2(4):100360.

https://doi.org/10.1016/j.phyplu.2022.100360.

- Asiwe JN, Moke EG, Asiwe N, Yovwin GD, Nwogueze BC, Daubry TME. *Dryopteris dilatata* leaf extract ameliorates streptozotocin-induced diabetic nephropathy in male Wistar rat. Nutrire. 2022;48:1. <u>https://doi.org/10.1186/s41110-022-00186-4.</u>
- 63. Moke EG, Omogbai EKI, Osagie-Eweka SDE, Uchendu AP, Omogbiya AI, Ben-Azu B, Eduviere AT, Edje KE, Umukoro EK, Anachuna KK, Asiwe JN, Ahante E, Oghoghovwe IJ. Co-administration of metformin and/or glibenclamide with losartan reverse N<sup>G</sup>-nitro-l-arginine-methyl esterstreptozotocin-induced hypertensive diabetes and haemodynamic sequelae in rats. Microvasc Res. 2023;147:104497.

https://doi.org/10.1016/j.mvr.2023.104497.

64. Okonofua DE, Asiwe JN, Moke EG, Igie NF, Sanusi KO, Yesufu JO, Fasanmade AA. Polycythemia, Thrombocythemia, and Hyperfibrinogenemia are Associated With Streptozotocin-induced Diabetes and Salt-induced Hypertension in Male Wistar Rats. Pharm Biomed Res. 2023;9(1):37-44.

http://dx.doi.org/10.32598/PBR.9.1.1077.1.

- 65. Fred-Jaiyesimi AA, Wilkins MR, Abo KA. Hypoglycaemic and amylase inhibitory activities of leaves of *S. mombin* Linn. Afr J Med Med Sci. 2009;38(4):343-9.
- 66. Moke EG, Umukoro EK, Okafo SE, Asiwe JN, Eduviere AT, Omorodion IL, Erhirhie EO, Uchendu AP, Isibor NP, Eboye R. The Role of Medicinal Plants in Diabetes Mellitus and Oxidative Stress. Int J Nutr Sci. 2023;8(2):2-11.
- Gobinath R, Parasuraman S, Sreeramanan S, Enugutti B, Chinni SV. Antidiabetic and Antihyperlipidemic Effects of Methanolic Extract of Leaves of *Spondias mombin* in Streptozotocin-Induced Diabetic Rats. Front Physiol. 2022;13:870399.

https://doi.org/10.3389/fphys.2022.870399.

- Wyss-Coray T. Ageing, neurodegeneration and brain rejuvenation. Nature. 2016;539(7628):180-186. https://doi.org/10.1038/nature20411.
- Asuquo OR, Udonwa UN, Eluwa MA, Ekanem TB. Effects of *S. mombin* Leaf Extract on the Cytoarchitecture of the Cerebal Cortex and on Learning and Memory in Wistar Rats. Int J Sci Res. 2013;2(9):5-8.
- Ishola IO, Ikuomola BO, Adeyemi OO. Protective role of *S. mombin* leaf and *Cola acuminata* seed extracts against scopolamine-induced cognitive dysfunction. Alexandria J Med. 2018;54(1):27-39. https://doi.org/10.1016/j.ajme.2016.08.001.
- Ajayi AM, Ben-Azu B, Godson JC, Umukoro S. Effect of S. mombin Fruit Extract on Scopolamine-induced Memory Impairment and Oxidative Stress in Mice Brain. J Herbs Spices Med Plants. 2021;27(1):24-36. https://doi.org/10.1080/10496475.2020.1777613.