



Syzygium jambos L. Alston: An Insight Into its Phytochemistry, Traditional Uses, and Pharmacological Properties

Melvin Adhiambo Ochieng^{1,2†}, Widad Ben Bakrim^{2,3†}, Gabin Thierry M. Bitchagno^{2*}, Mona F. Mahmoud⁴ and Mansour Sobeh^{2*}

¹School of Agriculture, Fertilization, and Environmental Sciences (ESAFE), Mohammed VI Polytechnic University, Ben-Guerir, Morocco, ²AgroBioSciences, Mohammed VI Polytechnic University, Ben-Guerir, Morocco, ³African Sustainable Agriculture Research Institute (ASARI), Mohammed VI Polytechnic University (UM6P), Ben-Guerir, Morocco, ⁴Department of Pharmacology and Toxicology, Faculty of Pharmacy, Zagazig University, Zagazig, Egypt

OPEN ACCESS

Edited by:

Jules-Roger Kuate,
University of Dschang, Cameroon

Reviewed by:

Subhalakshmi Ghosh,
Independent Researcher, Kolkata,
India
Njayou Frederic Nico,
University of Yaounde I, Cameroon

*Correspondence:

Gabin Thierry M. Bitchagno
gabin.bitchagno@um6p.ma
Mansour Sobeh
mansour.sobeh@um6p.ma

[†]These authors have contributed
equally to this work

Specialty section:

This article was submitted to
Ethnopharmacology,
a section of the journal
Frontiers in Pharmacology

Received: 30 September 2021

Accepted: 03 January 2022

Published: 24 January 2022

Citation:

Ochieng MA, Ben Bakrim W,
Bitchagno GTM, Mahmoud MF and
Sobeh M (2022) Syzygium jambos L.
Alston: An Insight Into its
Phytochemistry, Traditional Uses, and
Pharmacological Properties.
Front. Pharmacol. 13:786712.
doi: 10.3389/fphar.2022.786712

Medicinal plants have been used since ancient times for human healthcare as drugs, spices, and food additives. The progress in technology and medicine observed, the last decades, has improved the quality of life and healthcare but with worrisome drawbacks. Side effects caused by synthetic drugs for instance originate sometimes irreversible health disorders. Natural substances, in contrast, are biologically and environmentally friendly. *Syzygium jambos* L. (Alston) also known as rose apple conveys a long history as essential traditional medicine with a broad spectrum of application in various cultures. The plant discloses a diverse group of secondary metabolites and extracts that displayed major susceptibilities towards various health concerns especially stress-related and inflammatory diseases. Despite a rich literature about the plant, the chemistry and biology of *S. jambos* have not been comprehensively reviewed yet. Accordingly, we present herein a literature survey of rose apple which aims to draw the chemical identity of the plant and establish a consistent discussion on the respective biological application of plant extracts and their corresponding traditional uses. The present work could provide a scientific basis for future studies and necessary information for further investigations of new drug discovery.

Keywords: *Syzygium jambos*, medicinal plants, pharmacological activities, antioxidant, antiinflammatory

INTRODUCTION

The renown of alternative medicines nowadays is appealing although progress in technology and medicine encountered the last decades has improved the quality of life and healthcare around the world. Corresponding drawbacks are quite worrisome. Side effects caused by synthetic drugs for instance hurt human health system, sometimes with irreversible impacts (van Wyk and Wink 2015). Natural substances, in contrast, are biologically and environmentally friendly as they are recognized

Abbreviations: A375, Human melanoma cancer cell line; A431, Epidermoid carcinoma cancer cell line; AChE, Acetylcholinesterase; ALA, *Artemia* lethality assay; BuCE, Butyrylcholinesterase; COX-2, Cyclooxygenase-2 inhibition assay; DNA, Deoxyribonucleic acid; HEK-293, human embryonic kidney cells; HeLa, Cervical epithelial carcinoma; L6, Rat skeletal muscle cell line; MCF-7, Human breast cancer cell line; MDA, Malondialdehyde; MDR, Multidrug resistance; MIC, Minimum inhibitory concentration; MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide; ROS, Reactive oxygen species; SRB, Sulforhodamine-B; WSP, Water soluble polysaccharides; XTT, 2,3-Bis-(2-methoxy-4-nitro-5-sulphophenyl)-2H-tetrazolium-5-carboxyanilide salt; ZOI, Zone of infection.

by other organisms which facilitate their metabolisms. These substances are provided from plants, microorganisms, or animals with a pronounced interest since they constitute the main sources of foods and thus, our first resort in case of pain (van Wyk and Wink 2015).

Plants contain chemicals not essential for their metabolism rather for the fight against attacks and stress due to the plant habitats. These phytochemicals have shown distinct biological properties against numbers of illnesses (Iwu, 1993; van Wyk and Wink 2015). Both plants and compounds are of great interest in drug development to face new medical challenges.

Accordingly, numerous of research works have been conducted on plants from the genus *Syzygium* to elucidate its chemistry and pharmacology. Species of this genus, including *S. jambos*, offer edible fruits found under various formulation including juices, jellies, and jams (Sun et al., 2020). The decoction of these fruits serves to alleviate gastrointestinal disorders, wounds, syphilis, leprosy, as well as toothache (Chua et al., 2019). Reports have highlighted the occurrence of polyphenols, flavonoids, tannins, and sterols from various organs of *S. jambos* species. Meanwhile, plant extracts and compounds also claimed a broad spectrum of activities from antibacterial to anti-inflammatory activities through analgesic, antiviral, anti-dermatophyte, anticancer, and hepatoprotective properties (Sobeh et al., 2018). Two recent reviews very briefly highlighted the chemical composition, traditional uses and biological activities of the plant (Harsha et al., 2021; Subbulakshmi et al., 2021).

The present research survey tends to summarize the traditional uses, chemical constituents, and pharmacological properties of extracts and compounds from *S. jambos* in one document as much information as possible about this plant, which has many biological properties. This work could provide a scientific basis for future study and necessary information for further investigations of new drug discovery.

TAXONOMY AND BOTANICAL DESCRIPTION

The genus *Syzygium* contains approximately 1,200–1800 species, the majority of which are flowering plants (Khalaf et al., 2021). Its taxonomy has been disputed for long with that of the genus *Eugenia* (Mabberley, 2017). As a result, species of the later have been ranged in the genus *Syzygium*. Amongst them, *S. malaccense*, *S. suborbiculare*, *S. paniculatum*, *S. aqueum*, *samarangense*, and *S. jambos* (Sobeh et al., 2016; Cock and Cheesman, 2018). *S. jambos* L. Alston, synonym of *Eugenia jambos*, is native to Reunion Island, Central America (Guatemala), and South-East of Asia, especially in Nepal, Indonesia, Philippines, and Malaysia. It has been naturalized in India and claims various vernacular names in different cultures including malabar plum, plum rose, rose apple, and water apple (Maskey and Shah, 1982; Morton, 1987; Avila-Peña et al., 2007).

S. jambos belonging to the family Myrtaceae, is a medium sized tree reaching 7.5–12 m in height, **Figure 1** (Morton, 1987). Due to its physical characteristics and the aroma of the fruits, the

plant is often known as rose apple. It has a dense crown of slender with wide spreading branches. Leaves are opposite, lanceolate, and glabrous with 2.5–6.25 cm wide and 10–22 cm length. They are glossy and dark-green when mature while vibrant red when young. Flowers are in small terminal clusters, white or greenish white with a diameter of 5–10 cm. Usually, there are 4–5 flowers together in terminal clusters (Nawwar et al., 2016). The berries have a fleshy pericarp with 10–15 mm thick on the tree. They are sub-globose and whitish-to pinkish-yellow color. Every fruiting season, a mature rose apple tree produces about 35.57 g of fruit, with 7.16 cm length and 5.15 cm width. The epicarp of the fruit is thin, smooth, and reddish, while the mesocarp and endocarp are whitish and succulent, **Figure 1** (Daly et al., 2016; Mangini et al., 2020).

PHYTOCHEMICAL COMPOSITION

Phenolic compounds are mainly present in the leaves of *S. jambos*. They are represented by flavonoids, ellagitannins, phloroglucinols, and phenolic acids, **Table 1**; **Figure 2** (Rocchetti et al., 2019; Slowing et al., 1994; Slowing et al., 1996; Sobeh et al., 2018). Flavonoids are the most abundant group of compounds while quercetin sounds to be the most abundant monomer in every organ of the plant, except the stem bark. It is found in both aglycone and saponin forms. Only flavone and chalcone-types of flavonoids occur in *S. jambos* (Reynertson et al., 2008). Some anthocyanidins have also been detected in the plant mainly, petunidin 3-O-glucoside, pelargonidin 3-O-(6"-malonyl-glucoside) and delphinidin 3-O-galactoside (Rocchetti et al., 2019). Catechin has been identified from the leaves of the plant suggesting a tentative occurrence of non-hydrolysable tannins in the plant. As part of tannins, only ellagitannins (hydrolysable tannins) have been found in some plant extracts to date. Likewise, ellagic acid monomer derivatives have also been reported in the leaves and stem bark of the plant. Moreover, phenolic acids, listed as intermediates in the metabolism of flavonoids and ellagic acids like gallic acid and cinnamic acid, have also been alarmed in the leaves and fruit of *S. jambos*. Gallic acid is the most abundant and distributed phenolic acid in the plant. The other phenolic acids were either glycosylated benzoic acid or derivatives of phenylpropanoids. Phloroglucinols also occur in *S. jambos* leaves. Though only one report highlighted their presence in *S. jambos*, phloroglucinols are well distributed in Myrtaceae family. The seven compounds of this class were isolated from a Chinese species and no trace of one of this group of compounds was mentioned in the Egyptian or Brazilian varieties, **Table 1**; **Figure 2** (Li et al., 2015).

Pentacyclic triterpenoids are also abundant in the plant especially in the leaves and stem bark. They belong to oleanane, ursane, lupane and friedelane subclasses. The major ones were betulinic acid and friedelin. Saponins of triterpenes have not yet been isolated except the readily available β -sitosterol glucoside, **Table 1** (Kuiate et al., 2007; Li et al., 2015). Roots and flowers of the plant have not been investigated yet.

The essential oil of the plant leaves contain mostly volatile sesquiterpenes including δ -cadinene, cumaldehyde, β -

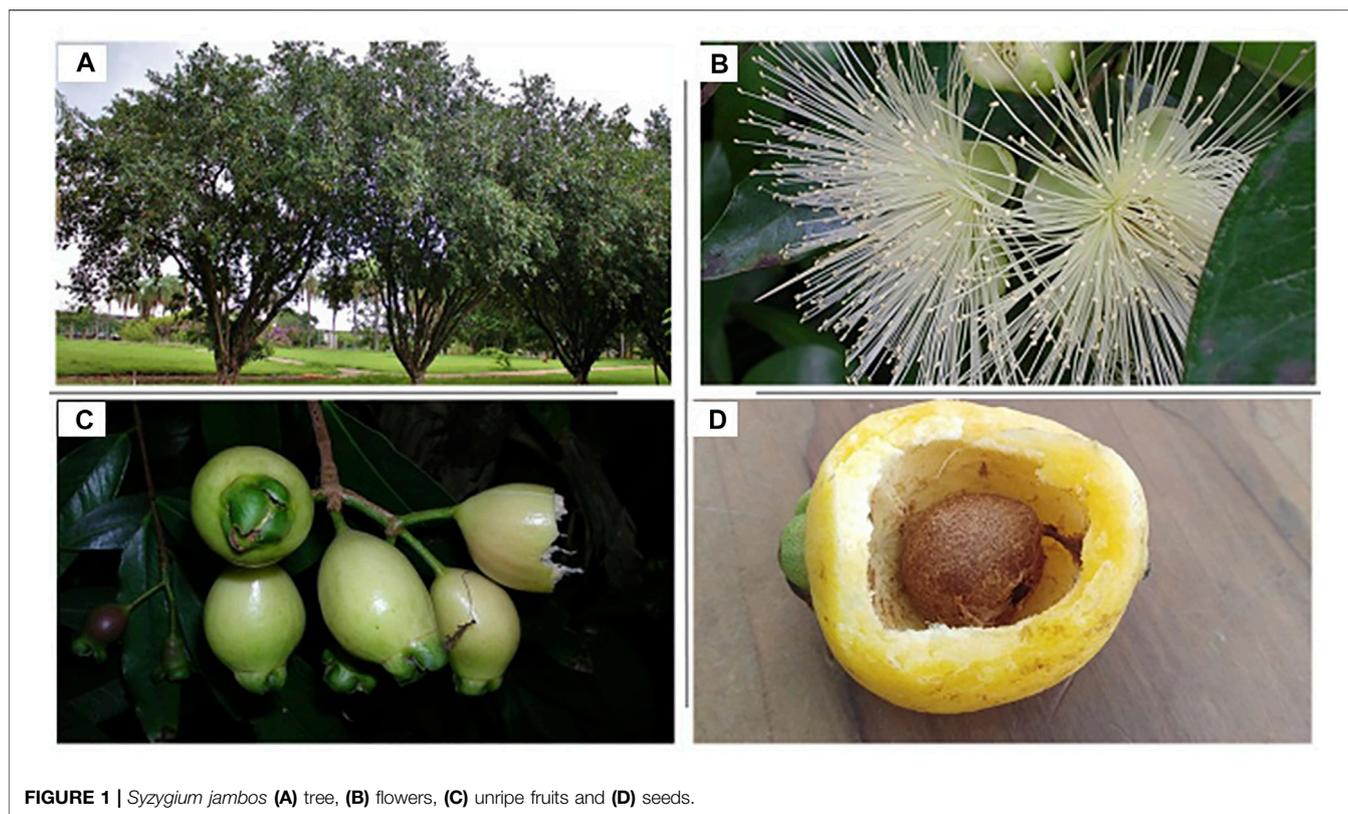


FIGURE 1 | *Syzygium jambos* (A) tree, (B) flowers, (C) unripe fruits and (D) seeds.

himachalene, isocaryophyllene, and β -cedrene, **Table 1** (Khalaf et al., 2021). Linalool is one of the essential oil markers in the identification of the plant fruit. Indeed, linalool, cinnamyl alcohol, and geraniol are the main volatile terpenes in the extracts. Differences were observed in the volatile aromatic composition of fruits from the Brazilian, Malaysian, and Egyptian species. Linalool was found as the main compound in the Brazilian fruits while 3-phenylpropyl alcohol (Z)-3-hexen-1-ol and (Z)-cinnamaldehydes were identified as major compounds in the Malaysian and Egyptian ecospecies (Vernin et al., 1991; Wong and Lai, 1996; Guedes et al., 2004; Ghareeb et al., 2017).

TRADITIONAL USES

Rose apple carries a long history as essential traditional medicine with a broad spectrum of application in various cultures. In India, the fruit tonic helps to improve brain and liver health while fruit infusions convey diuretic property (Morton, 1987). Moreover, the juices from macerated leaves in water were used as a febrifuge (Maskey and Shah, 1982). Dysentery is also alleviated by the seeds together with diarrhea, and catarrh. Furthermore, the flowers are assumed to relieve fever (Baliga et al., 2017). The infusion of the powdered leaves is beneficial to diabetes (Maskey and Shah, 1982). In South American cultures, the seeds have an anesthetic property whereas leaf decoction is applied to sore eyes, and used as diuretic, expectorant and to treat rheumatism

(Maskey and Shah, 1982). The decoction of the bark is administered to treat asthma, bronchitis, and hoarseness (Maskey and Shah, 1982). The plant is also used to treat hemorrhages, syphilis, leprosy, wounds, ulcers, and lung diseases due to its potency to relieve fever and pains. In China, each plant organ is used to treat digestive tract and tooth pains (Mahmoud et al., 2021; Reis et al., 2021).

BIOLOGICAL ACTIVITIES

The biological applications of *S. jambos* are rich and diverse. Isolates were screened in accordance with the traditional uses of the plant encountered worldwide. Mainly, plant extracts and compounds have presented antifungal, antibacterial, hepatoprotective, analgesic, antioxidant, anti-inflammatory, antidiabetic, anticancer, anti-pyretic activities, **Figure 3**. The main pharmacological characteristics of *S. jambos* are listed in **Tables 2–4**.

Toxicity Studies

To date, only few literatures have reported the toxicity of the plant. The leaf extract of *S. jambos* is safe at a dose up to 5 g/kg b.wt. assessed by the acute toxicity test (Dhanabalan and Devakumar, 2014). The toxicity of the methanol extract of *S. jambos* and its fraction were evaluated by shrimp lethality bioassay. Methanolic extract and carbon tetrachloride fraction displayed significant lethality with $LC_{50} = 6.97$ and 13.61 $\mu\text{g/ml}$,

TABLE 1 | Phytoconstituents from *S. jambos*.

Class of compounds	Compound names	Plant organs	Characterization methods	References	
Flavonoids	Quercetin	Fruit, whole plant, leaves	HPLC, ESI-MS, EIMS, IR, 1D and 2D NMR	Slowing et al., (1994), Reynertson et al., (2008), Bonfanti et al., (2013), Hossain et al., (2016) Reynertson et al. (2008) Ghareeb et al. (2017)	
	Quercitrin	Fruit			
	Rutin	Whole plant			
	5,4'-dihydroxy, 7-methoxy, 6-methyl-flavone				
	Isoetin-7-O- β -d-glucopyranoside				
	Myricetin 3-O-beta-d-xylopyranosyl (1->2) alpha-l-rhamnopyranosides	Leaves			
	Kaempferol				
	Quercetin 3-O-xylosyl-(1->2) rhamnoside	Whole plant			
	Quercetin 3-O-xylosyl- (1->2) xyloside				
	Quercetin 3-O-glucuronide				
	Myricetin 3-O-glucoside				
	Myricetin 7-methylether 3-O-xylosyl (1->2)rhamnoside				
	Myricetin 3',5'-dimethyl ether 3-O-xylosyl (1->2)rhamnoside				
	Myrigalone B	Leaves			Jayasinghe et al. (2007)
	Phloretin 4 -O-methyl				
Myrigalone G					
Triterpenoids	Oleanolic acid	Leaves		Li et al. (2015)	
	Betulinic acid				
	Friedelin			Kuiate et al., (2007); Haque, (2015)	
	3-nor-2,3-Secofriedelan	Stem bark, leaves		Haque, (2015)	
	B-Sitosterol	Stem bark		Lin et al., (2014); Haque, (2015)	
	B-Amyrin acetate			Kuiate et al. (2007)	
	Lupeol				
	Ursolic acid			Lin et al. (2014)	
	3-Acetyl-ursolic acid				
	Asiatic acid				
	Arjunolic acid				
	Morolic acid 3-o-caffeate			Ghareeb et al. (2017)	
	Phloroglucinol	Jambone A	Leaves		Li et al. (2015)
Jambone B					
Jambone C					
Jambone D					
Jambone E					
Jambone F					
Jambone G					
Ellagic acid and ellagitannins	Tellimagrandin	Leaves		Slowing et al. (1994)	
	Limagrandin I				
	Strictinin				
	Casuarictin			Yang et al. (2000)	
	2,3-hexahydroxydiphenoylglucose stachyurin			Slowing et al. (1994)	
	Casuarin	Stem bark, leaves			
	3,3',4'-tri-O-methylellagic acid	Leaves		Chakravarty et al. (1998)	
	3,3',4'-tri-O-methylellagic acid-4-O- β -d-glucopyranoside				
	1-O-galloylcastalagin			Yang et al. (2000)	
	Castalagin	Stem bark, leaves		Sobeh et al., (2018); Mahmoud et al., (2021)	
	Vescalagin				
	Phyllanthusin G	Stem bark		Mahmoud et al. (2021)	
	Ellagic acid pentoside				
Ellagic acid					
Methyl ellagic acid sulfate					
Phenolic acid	Gallic acid	Leaves, fruit	HPLC-PDA-MS/MS and GC-MS	Bonfanti et al., (2013), Nawwar et al., (2016) Ghareeb et al. (2017)	
	Cinnamic acid				
	3,4,5-Trihydroxybenzoic acid				
	Prenylbenzoic acid 4- β -d-glucoside				
	4'-hydroxy-3'-methoxyphenol- β -d-[6- O-(4"-hydroxy-3"-5"-dimethoxybenzoate)] glucopyranoside				
	Caffeic acid	Leaves			Bonfanti et al. (2013)
	Chlorogenic acid				
Rosmarinic acid rhamnoside			Sobeh et al. (2018)		
Organic acids	Citric acid	Leaves	GC-MS		
	Malic acid				
Volatile compounds	Phenylacetic acid			Khalaf et al. (2021)	
	Hexanal			Musthafa et al., (2017); Reis et al., (2021)	
	Geraniol				
	Citronellol				
	Hotrienol				
	(E)-cinnamyl alcohol				

(Continued on following page)

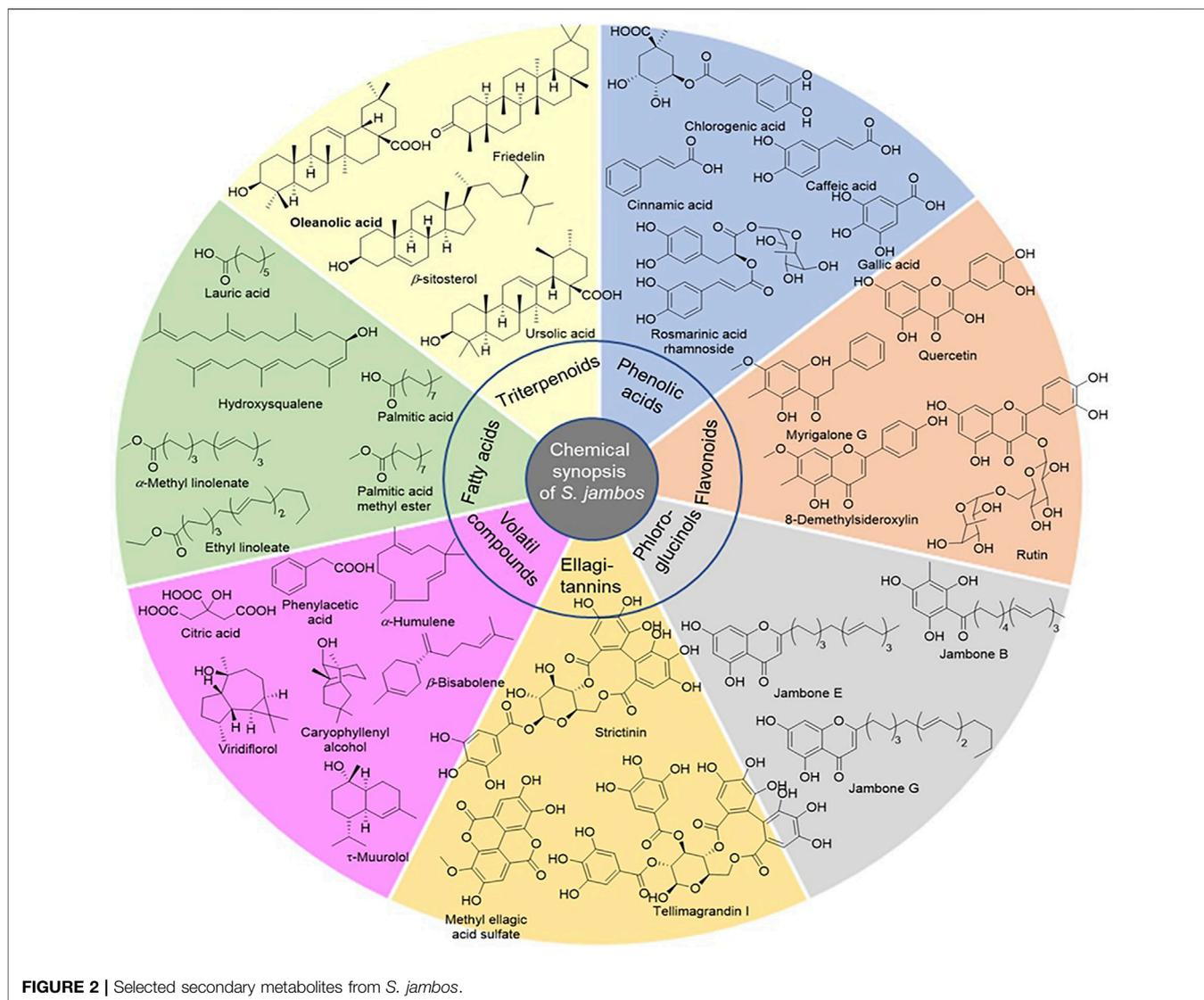


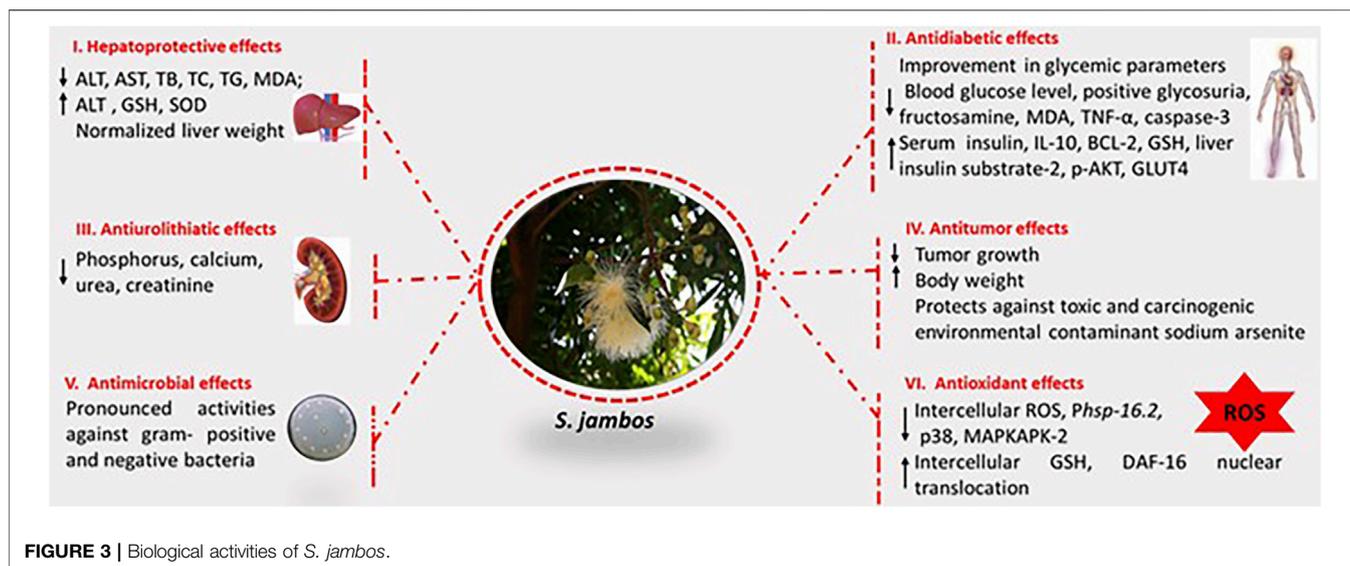
FIGURE 2 | Selected secondary metabolites from *S. jambos*.

including strains of *Escherichia coli* (AG100ATet, AG102), *Enterobacter aerogenes* (EA27, EA289), *Klebsiella pneumoniae* (KP55, KP63), *Providencia stuartii* (PS299645, NEA16) and *Pseudomonas aeruginosa* (PA01, PA124) (Wamba et al., 2018). Likewise, *S. jambos* leaf extracts demonstrated potent antiviral effects on the virus involved in vesicular stomatitis and against different types of herpes simplex virus (Abad et al., 1997; Athikomkulchai et al., 2008).

Isolated compounds friedelin, β -amyrin acetate, betulinic acid, and lupeol, from the bark extract, were tested for their antidermatophytic activity against three commonly dermatophyte species found in Cameroon namely *Microsporum audouinii*, *Trichophyton mentagrophytes* and *T. soudanense*. Betulinic acid and friedelolactone were the most active compounds with MIC ranging from 12.5 to 100 $\mu\text{g/ml}$ and the most sensitive fungi were *Trichophyton soudanense* (MIC = 25 $\mu\text{g/ml}$) and *Trichophyton mentagrophytes* (12.5 $\mu\text{g/ml}$) (Kuiate et al., 2007). The phenolic compounds, quercetin, rutin,

prenylbenzoic acid 4- O - β -D-glucopyranoside, morolic acid 3- O -caffeate, 5,4'-dihydroxy-7-methoxy-6-methylflavone, 3,4,5-trihydroxybenzoic acid, isetin-7- O - β -D-glucopyranoside, and (4'-hydroxy-3'-methoxyphenol- β -D-[6- O -(4''-hydroxy-3'',5''-dimethoxybenzoate)] glucopyranoside) also exhibited both antibacterial and antifungal potentials with a diameter of inhibition zones ranging from 9–19 mm (Ghareeb et al., 2017). Accordingly, the antimicrobial activity of *S. jambos* crude extracts have been related to the presence of an increased level of tannins in the preparation (Baliga et al., 2017).

Moreover, silver nanoparticles synthesized from leaves and bark extracts of *S. jambos* showed higher antiplasmodial activity against chloroquine sensitive and resistant strains of *Plasmodium falciparum* (Dutta et al., 2017). The fatty compounds, ethyl linoleate, methyl linolenate and phytol, inhibited the QS-dependent pigment production in *C. violaceum* and lowered pyoverdine production in *P. aeruginosa* as well. Results were also confirmed by docking



analysis (Musthafa et al., 2017). The above research confirmed the antimicrobial activity of *S. jambos*. However, it is worthy to note that the above studies focused on the *in vitro* evaluations. Consequently, these studies only give preliminary information about the activity of *S. jambos*. Therefore, further studies combining *in vivo* and *in vitro* need to be conducted to provide reliable basis for exploring new potentially and low toxic antimicrobial agents from the studied plant.

Antioxidant Activity

Several studies, both *in vitro* and *in vivo*, reported the antioxidant activity of *S. jambos* extracts and its phytochemicals. Bonfanti et al. (2013) demonstrated the potency of the leaf aqueous extract of *S. jambos* to inhibit the nitric oxide radical, the lipid peroxidation and the mitigation sodium-nitroprusside-induced oxidative stress in rats. The extract also showed a capacity to increase the GSH levels in rats (Sobeh et al., 2018). Furthermore, the bark extract inhibited lipid peroxidation and increased reduced glutathione (GSH) in pancreatic tissues of STZ-diabetic rats (Mahmoud et al., 2021). *S. jambos* leaf extract abolished ROS production by endothelin-1 in human polymorphonuclear and mononuclear cell migration (Inostroza-Nieves et al., 2021). On the other hand, *S. jambos* rich phenolic and flavonoid fractions demonstrated good antioxidant activities as shown in Table 3. The chalcones phloretin 4'-O-methyl ether, myrigalones B and G were assessed for their antioxidant activity using DPPH radical. As a result, myrigalone B showed a significant capacity of scavenging radicals with an IC_{50} of 3.8 $\mu\text{g/ml}$ while the other compounds showed low to moderate activity ($IC_{50} > 30 \mu\text{g/ml}$) (Jayasinghe et al., 2007). Moreover, 2,6-dihydroxy-4-methoxy-3,5-dimethyldihydrochalcone showed anti-DPPH activity with an IC_{50} value of 10.6 $\mu\text{g/ml}$ while, the flavones, 4'-methoxysideroxylin and 6-demethylsideroxylin, and phloroglucinols, jambones A-B, presented weak antioxidant

activities in FRAP and DPPH radical scavenging activities (Li et al., 2015).

Neurological Activity

There are relatively few studies on neuroprotective effect of *S. jambos*. Bonfanti et al. (2013) investigated the effects of *S. jambos* in the inhibition of both AChE and BuCE, the two main enzymes in the occurrence of Alzheimer. As a result, the aqueous leaves extract of *S. jambos* showed significant AChE ($IC_{50} = 16.5 \mu\text{g/ml}$) and BuCE ($IC_{50} = 15.2 \mu\text{g/ml}$) inhibition potentials in support with the uses of the plant to alleviate Alzheimer disorders. Considering these findings, further investigations may improve the neuroprotective effect of *S. jambos*.

Anticancer Activity

In vitro anticancer activity of isolates from *S. jambos* was determined towards various cancer cell lines, providing data on the bioactivity of both extract and single compounds, Table 3. Methanolic extract of *S. jambos* leaves showed cytotoxic effects against liver cancer cell line, Hep G2 cells, by inducing apoptotic pathways (Thamizh Selvam et al., 2016). Moreover, another study evaluated the anticancer effects of the leaves along with other extracts on human melanoma (A375), epidermoid carcinoma (A431), cervical epithelial carcinoma (HeLa) and human embryonic kidney cells (HEK-293). They found that the extract showed low toxicity against HEK-293 cells but better effects against A431 and HeLa cells ($IC_{50} = 34.90\text{--}56.20 \mu\text{g/ml}$) (Twilley et al., 2017). The hydrolysable tannins, 1-O-galloyl castalagin and casuarinin, exhibited significant cytotoxic activity against the human promyelocytic leukemia cell line HL-60 with IC_{50} of 10.8–12.5 μM and showed moderate to low cytotoxicity on the human adenocarcinoma SK-HEP-1, normal cell lines of human lymphocytes and liver cell lines. Results were confirmed by DNA fragmentation assay and microscopic investigation of cells (Yang et al., 2000). The cytotoxic effects of the phenolic compounds, *cis*-3-

TABLE 2 | Antimicrobial activity of *S. jambos* extracts.

Extract	Tested strains	Key results	Reference
Leaves			
Methanol extract	<i>Alcaligenes faecalis</i> <i>A. Hydrophilia</i> <i>Bacillus cereus</i> <i>S. aureus</i> <i>Aeromonas hydrophilia</i> , <i>Citrobacter freundii</i> , <i>E. coli</i> , <i>Klebsiella pneumoniae</i> , <i>Proteus mirabilis</i> , <i>P. fluorescens</i> , <i>Salmonella newport</i> , <i>Serratia marcescens</i> , <i>Shigella sonnei</i> , <i>S. epidermidis</i> and <i>Streptococcus pyogenes</i>	MIC = 797.5 µg/ml MIC = 384.6 µg/ml MIC = 182.6 µg/ml MIC = 46.5 µg/ml These bacteria were not susceptible by <i>S. jambos</i> leaf extract	Mohanty and Cock, (2010)
Ethanol extract	<i>Chromobacterium violaceum</i> DMST 21761	At 500 µg/ml, a highest inhibition in QS-dependent violacein pigment production was observed up to 90%	Musthafa et al. (2017)
Ethanol extract	<i>P. aeruginosa</i> ATCC 27853 <i>P. aeruginosa</i>	At sub-MIC (500 µg/ml), the extract showed significant reduction in QS-regulated virulence determinants The extract showed also 31.96% of decreases in biofilm formation of <i>P. aeruginosa</i>	Rajkumari et al. (2018a)
Ethanol extract	<i>P. acnes</i>	MIC = 31.3 µg/ml	Sharma et al. (2013)
Hydroethanol extract	<i>S. aureus</i> , <i>E. coli</i> , <i>A. niger</i> , <i>C. albicans</i>	<i>S. aureus</i> : MIC between 200 and 300 µg/ml No activity against <i>E. coli</i> , <i>A. niger</i> and <i>C. albicans</i> at 1,000 and 2000 µg/ml	Donatini et al. (2013)
Decoction	<i>P. vulgaris</i> (ATCC 6896) <i>S. saprophyticus</i> (ATCC 15305) <i>S. aureus</i> (ATCC 6341)	MIC = 31 µg/ml and MBC = 1.0 mg/ml MIC = 500 µg/ml and MBC = 2.0 mg/ml MIC = 500 µg/ml and MBC = 1.0 mg/ml	Luciano-Montalvo et al. (2013)
Aqueous and methanolic extracts	<i>C. albicans</i> (ATCC10231) Epidermophyton floccosum (ATCC 26072) Microsporium gypseum (ATCC7911) Trichophyton mentagrophytes BSL2 (ATCC 13996) Trichophyton rubrum (ATCC 22402)	IZ = 8–13 mm IZ = > 16 mm IZ = 12.3 mm IZ > 10 mm IZ > 10 mm	Noé et al. (2019)
Ethanol extract	<i>S. aureus</i> <i>E. coli</i> <i>C. albicans</i> <i>A. niger</i>	Φmm = 20 mm Φmm = 8 mm Φmm = 21 mm Φmm = 7 mm	Khalaf et al. (2021)
Acetone extract	<i>Staphylococcus aureus</i>	MIC = 128 µg/ml	Panthong and Voravuthikunchai, (2020)
85% MeOH Defatted 85% MeOH Petroleum ether Dichloromethane Ethyl acetate n-Butanol Aqueous	<i>S. aureus</i> , Methicillin-resistant, <i>S. aureus</i> , <i>P. aeruginosa</i> , <i>C. albicans</i> , and <i>A. niger</i>	Φ = 13.5, 11.0, 13.5, and 11.5 mm, respectively Φmm ranging between 10 and 13.5 mm Φmm ranging between 8.5 and 11.5 mm Φmm ranging between 9 and 11.5 mm Φmm ranging between 11.5 and 13.5 mm Φmm ranging between 9.5 and 14.5 mm Φmm ranging between 12.5 and 15.5 mm	Ghareeb et al. (2016)
Methanolic extract	26 strains of <i>S. aureus</i> <i>Enterobacter aerogenes</i> EA294 <i>Enterobacter cloacae</i> (ECC169) <i>Pseudomonas aeruginosa</i> (PA01, PA124) <i>Providencia stuartii</i> (NEA16, PS2636) <i>Klebsiella pneumoniae</i> K24 <i>E. coli</i>	MIC ranging between 32 and 512 µg/ml MIC = 64 µg/ml MIC = 512 µg/ml MIC = 512 µg/ml MIC = 128 and 256 µg/ml, respectively MIC = 64 µg/ml MIC range of 128 and 512 µg/ml	Wamba et al. (2018)
Bark, leaves and seeds			
Acetone extract Aqueous extract	<i>Staphylococcus aureus</i> <i>Bacillus subtilis</i> <i>Escherichia coli</i> <i>Klebsiella pneumoniae</i> <i>Proteus vulgaris</i> <i>Pseudomonas aeruginosa</i> <i>Salmonella typhi</i> <i>Vibrio cholera</i>	Φmm ranging between 7 and 12 mm Φmm ranging between 12 and 16 mm Φmm ranging between 6 and 17 mm Φmm ranging between 12 and 15 mm Φmm ranging between 9 and 12 mm Φmm ranging between 12 and 15 mm Φmm ranging between 8 and 12 mm Φmm ranging between 12 and 15 mm	Murugan et al. (2011)
Bark			
Acetone and aqueous extracts	<i>S. aureus</i> <i>Y. enterocolitica</i>	MIC ranged between 500 and 1,000 µg/ml MIC ranged between 250 and 750 µg/ml	Djija et al. (2000)

(Continued on following page)

TABLE 2 | (Continued) Antimicrobial activity of *S. jambos* extracts.

Extract	Tested strains	Key results	Reference
Leaves			
	<i>S. hominis</i> <i>S. cohnii</i> <i>S. warneri</i>	MIC ranged between 15 and 250 µg/ml MIC = 250 µg/ml, in both extracts MIC ranged between 15 and 750 µg/ml	
Flower			
85% MeOH	<i>S. aureus</i> , Methicillin-resistant, <i>P. aeruginosa</i> , <i>C. albicans</i> , <i>A. niger</i>	Φmm between 8.5 and 10.5 mm	Ghareeb et al. (2016)
Seeds			
Aqueous extract	<i>Microsporum gypseum</i> <i>Microsporum canis</i> <i>Candida albicans</i>	IZ = 28.75 mm IZ = 30.25 mm IZ = 16 mm	Sakander, et al. (2015)

p-coumaroylaliphitic acid and 4'-methoxysideroxylin, on melanoma SK-MEL-28 and SK-MEL-110 cell lines were assessed as well as that of the normal Vero cells, following the MTT assay. The compounds, displayed potent effects on the two melanoma cells with IC₅₀ ranging from 18.3–81.5 µM (Li et al., 2015). The cytotoxic effect of quercetin-3-O-β-D-xylofuranosyl-(1 → 2)-α-L-rhamnopyranoside and myricetin-3-O-β-D-xylofuranosyl-(1 → 2)-α-L-rhamnopyranoside isolated from the CH₂Cl₂/MeOH fraction of the plant was evaluated against RW 264.7 cell lines. Both flavonoids demonstrated a moderate activity (IC₅₀ = 1.68 and 1.11 µM, respectively) (Ticona et al., 2021). The cytotoxic effect of the nanoparticles synthesized from the leaf and bark extracts of *S. jambos* was assessed against HeLa and L6 cells using MTT assay. As a result, the nanoparticles were found to be non-toxic toward HeLa and L6 cell lines (Dutta et al., 2017). These investigations provided the anticancer potential of *S. jambos*, further *in vivo*, toxicological, and clinical studies are needed in future to guarantee efficiency and safety.

Anti-Inflammatory Effect

Inflammation and specifically low-grade inflammation play a vital role in many diseases. Natural products with anti-inflammatory effects are promising targets for drug discovery. *In vitro* and *in vivo* models were applied to determine the anti-inflammatory effects of crude extracts and pure compounds from *S. jambos*. *In vitro* studies showed that the ethanol leaf extract of *S. jambos* and the commercially available chemicals ursolic acid and myricitrin dramatically reduced the release of inflammatory cytokines IL 8 and TNF-α by 74–99% indicating anti acne effects (Sharma et al., 2013). A more recent study on two isolated glycosylated flavonoids, the quercetin-3-O-β-D-xylofuranosyl-(1 → 2)-α-L-rhamnopyranoside and myricetin-3-O-β-D-xylofuranosyl-(1 → 2)-α-L-rhamnopyranoside, isolated from the chloroform/methanol fraction of *S. jambos* showed that they reduced the production of TNF-α, with IC₅₀ values of 1.68 and 1.11 M, respectively in the RAW 264.7 cell line. In addition, at a dose of 5 mg/kg, the flavonoids reduced the levels of TNF-α, C-reactive protein, and fibrinogen in murine models (Apaza Ticona et al., 2021). *In vivo* studies showed that the ethanol extract of the leaves also exerted potent anti-

inflammatory effects at a dose of 400 mg/kg in carrageenan and histamine edema rat models (Hossain et al., 2016). The soluble fraction of polysaccharide fraction of the plant also expressed a capacity to increase the secretion of TNF-α, IL-1β and IL-10 in a concentration-dependent manner (10–100 µg/ml). The aqueous extract of the plant attenuated the inflammatory response induced by LPS at a concentration of 100 µg/ml (Tamiello et al., 2018b). Furthermore, the bark extract inhibited pancreatic inflammation in STZ diabetic rat model where it dose-dependently suppressed the pro-inflammatory, TNF-α and increased the anti-inflammatory IL-10 levels (Mahmoud et al., 2021).

Hepatoprotective Activities

Liver is one of the largest and important organs in human body and performs numerous interrelated vital functions, such as metabolism, biotransformation, and detoxification of toxins. Consequently, liver diseases resulting from liver damage is a global problem. Herbal medicine has been used traditionally for the prevention of liver diseases (Islam et al., 2012). Preclinical studies have shown that extracts from different parts of *S. jambos* possess beneficial effect in liver related diseases, **Table 4**. The methanol extract of the leaves of the plant significantly modulated the levels of liver biochemical parameters ALT, AST, MDA, TB, TC, TG, GSH and SOD) in comparison with the positive control, silymarin, **Table 4** (Sobeh et al., 2018). Isolation of the compounds of the extract may led to the discovery of promising active constituents.

Antidiabetic Activity

Diabetes and diabetic complications are global health problem. Although many medicinal plants were investigated for their possible antidiabetic activities, there are relatively few studies on antidiabetic effect of *S. jambos* extracts. An *in vitro* study compared the inhibitory effects of ethanol extract of different organs of *S. jambos* on α-glycosidase and α-amylase activities, enzymes related to diabetes, and showed that the inhibitory effects against yeast and mice intestinal α-glucosidase activity was on the following order: seed > stem > leaf > root > flower > flesh > acarbose, while the inhibitory effect on α-amylase activity was

TABLE 3 | *In vitro* effects of *S. jambos* extracts.

Extract	Activity	Used method	Country	Effects	Reference
Whole plant					
ethanol extract	Antioxidant	DPPH and NO scavenging assay	South Africa	DPPH (IC ₅₀ = 14.10 µg/ml) NO scavenging assay (Low activity)	Twilley et al. (2017)
	Anti-inflammatory	COX-2		IC ₅₀ of 3.79 µg/ml	
	Cytotoxic	A375, A431, HeLa and HEK-293 cell lines		IC ₅₀ ranged between 56 and 198 µg/ml	
	Antiviral	Anti-herpes simplex virus type-1 assay		The extract exhibited potential anti-viral activity at 50.00 µg/ml 100% viral inhibition when tested at the highest viral dose	
Leaves					
Hydroethanol	Antioxidant	DPPH MDA	Brazil	EC ₅₀ = 5.68 µg/ml IC ₅₀ = 0.17 µg/ml	Donatini et al. (2009)
Methanolic extract	Anti-inflammatory	Hyaluronidase inhibition assay	India	60.80% inhibition at 1 µg/ml	Reddy et al. (2014)
	Antioxidant	DPPH assay Nitric oxide assay lipid peroxidation		IC ₅₀ = 41 ± 1.8 µg/ml IC ₅₀ = 63 ± 1.6 µg/ml IC ₅₀ = 48 ± 20 µg/ml	
Ethanol extract	Antioxidant	ABTS	Bangladesh	IC ₅₀ = 57.80 µg/ml	Hossain et al. (2016)
Methanolic extract	Antioxidant	DPPH FRAP	Egypt	IC ₅₀ = 5.7 ± 0.45 µg/ml IC ₅₀ = 19.77 ± 0.79 mM	Sobeh et al. (2018)
Ethanol extract	Anticancer	XXT	South Africa	IC ₅₀ < 60 µg/ml against the HeLa and A431 cell line	Twilley et al. (2017)
	Antiviral	Cytopathic effect (CPE) inhibition assay		Potential antiviral activity with 100% viral inhibition for both (10 and 100 TCID ₅₀) viral doses against HSV-1	
Methanolic, hexane and dichloromethane extract	Antioxidant	DPPH	Thailand	IC ₅₀ = 1.17 ± 0.30 µg/ml	Athikomkulchai et al. (2008)
	Antiviral	Plaque Reduction Assay		At 100 µg/ml, extracts of hexane and dichloromethane exhibited HSV-1/HSV-2 inhibitory activity greater than 50% inhibition	
70% aqueous acetone extract	Cytotoxicity	MTT assay	Taiwan	IC ₅₀ = 10.2 µg/ml strongest cytotoxic effect on human promyelocytic leukemia cells (HL-60)	Yang et al. (2000)
Methanol extract	Cytotoxicity	SRB assay	Egypt	At 100 µg/ml, the extract exhibited an increase of MCF-7 cell proliferation	Rocchetti et al. (2019)
85% MeOH Deffated 85% MeOH Petroleum ether Dichloromethane Ethyl acetate n-Butanol Aqueous	Antioxidant	Phosphomolybdenum assay	Egypt	538.20 mg AAE/g extract	Ghareeb et al. (2016)
				619.51 mg AAE/g extract	
				147.96 mg AAE/g extract	
				222.76 mg AAE/g extract	
				460.15 mg AAE/g extract	
				643.90 mg AAE/g extract	
				315.44 mg AAE/g extract	
Ethanol extract	Antioxidant	DPPH	Bangladesh	IC ₅₀ = 14.10 µg/ml	Islam et al. (2012)
Methanolic and ZnO-NPs extract	Antiuroliathitic	Single diffusion gel growth technique	India	PI = 19.63–30.56% of inhibition at 2% of extract PI = 16.28–24.68% of inhibition at 0.5% of extract for ZnO-NPs extract, PI = 25.60 at 0.5 and 35.27% at 5%	Deka et al. (2021)
			Egypt	IC ₅₀ = 48.13 µg/ml	Khalaf et al. (2021)
Ethanol extract	Antioxidant	DPPH	India	IC ₅₀ = 38.73 µg/ml	Rajkumari et al. (2018b)
Aqueous ethanolic extract	Antioxidant	DPPH ORAC assay	Egypt	EC ₅₀ = 13.52 ± 0.69 µg/ml EC ₅₀ = 34.35 ± 12.45 µg/ml	Nawwar et al. (2016)
	Cytotoxicity	Neutral red uptake assay		HaCaT (IC ₅₀ = 106.74 ± 10.89 µg/ml) Bladder carcinoma cells (IC ₅₀ = 55.24 ± 2.67 µg/ml)	
Fruit					
Methanolic extract	Antioxidant	DPPH	United States	IC ₅₀ = 92.0 ± 8.24 µg/ml	Reynertson et al. (2008)
Hydroalcoholic extract	Antioxidant	DPPH	Pahang	IC ₅₀ = 24.44 µg/ml	Yunus et al. (2021)
Ethanol extract	Antioxidant	DPPH	Malaysia	Lowest activity, IC ₅₀ = 24.44 µg/ml	

(Continued on following page)

TABLE 3 | (Continued) *In vitro* effects of *S. jambos* extracts.

Extract	Activity	Used method	Country	Effects	Reference
n-Hexane, DCM and MeOH	Antidiabetic	α -Glucosidase inhibition assay		Low inhibition activity, $IC_{50} = 0.67 \pm 0.04$	
	Cytotoxicity	HeLa and Vero cell lines	Bangladesh	Not active	Nesa et al. (2021)
Seed					
Methanolic extract	Antioxidant	DPPH and ORAC	Brazil	112.06 and 489.62 μ mol/g Trolox equivalent, respectively	Vagula et al. (2019)
Ethanol extract	Antioxidant	ABTS	China	$IC_{50} = 45.79 \pm 1.02 \mu$ g/ml	Zheng et al. (2011)
		Hydroxyl radical activity DPPH		$IC_{50} = 65.22 \pm 0.93 \mu$ g/ml $IC_{50} = 95.21 \pm 1.78 \mu$ g/ml	
85% MeOH	Antioxidant	Phosphomolybdenum assay	Flowers Egypt	560.97 mg AAE/g extract	Ghareeb et al. (2016)

AAE: ascorbic acid equivalent; PI: percentage inhibition of the struvite crystals.

acarbose > seed > stem > root > leaf > flesh > flower (Wen et al., 2019). *In vivo* studies showed that the infusion of the combined leaves of *S. jambos* and *S. cumini* had no significant effect on blood glucose levels in a randomized double-blind clinical trial in non-diabetic and diabetic subjects (Teixeira et al., 1990). However a more recent study showed that the ethanol extract of leaves at two dose levels (374.5 mg/kg and 749 mg/kg, Po) lowered blood glucose levels in alloxan induced diabetic rabbits (Prastiwi et al., 2019). Moreover, an aqueous leaf extract from the plant showed better blood modulation potential of glucose over time, in diabetes genetic mouse models (Gavillán-Suárez et al., 2015). Recent studies have shown the protective effect of the bark extract on pancreatic β cells against streptozotocin-induced diabetes. The extract have also improved insulin signaling pathway in the liver and glycemic parameters and have suppressed pancreatic oxidative stress (Mahmoud et al., 2021). However, further studies need to be conducted to confirm the potential of *S. jambos* as a natural antidiabetic agent, as it can be incorporated into functional foods and nutraceutical products.

Antiurolithiatic Activity

The antiurolithiatic activity of the leaf extract of *S. jambos*, collected in India, was evaluated both *in vitro* and *in vivo* using ethylene glycol induced urolithiatic model in rats. Results showed a capability of the extract to prevent the growth of urinary stones. However, further studies should be done to understand the mechanism and pharmacological action in preventing urolithiasis in susceptible populations (Deka et al., 2021).

DISCUSSION

The main chemicals found in *S. jambos* were phenolic compounds and triterpenoids. Phenolic compounds were the major constituents of the plant. They are made up of glycosylated flavonoid and ellagitannin derivatives. Plant extracts showed significant antibacterial activity, improving the

potency of strong antibiotics like tetracycline, ciprofloxacin, erythromycin, or chloramphenicol. Likewise, both water-soluble fraction and organic extracts have shown significant capabilities in reducing radicals and heavy metal ions. *In vivo* anti-inflammatory activity of plant extracts has also been demonstrated with considerable endpoints. These biological characteristics of the plant could be related to their main chemical constituents. Flavonoids and ellagitannins are excellent free radical scavengers (Koagne et al., 2020). For this reason, they protect cells from aging and stress, and exerted anti-nociceptive activities. Indeed, *S. jambos* plant extracts have shown considerable anti-inflammatory activity towards some models. The analgesic potential has been ascribed to two glycosylate flavonols occurring in rose apple namely, myricetin-3-*O*- β -D-xylofuranosyl-(1 \rightarrow 2)- α -L-rhamnopyranoside and quercetin 3-*O*- β -D-xylopyranosyl-(1 \rightarrow 2)- α -L-rhamnopyranoside. However, no mechanism of action of the recorded biological activity was proposed yet. Nevertheless, both antioxidant and anti-inflammatory activities encountered for *S. jambos* extracts and compounds are closely related. The anti-inflammatory potency of rose apple extracts is a key point in the uses of plant extracts to alleviate different illnesses. More importantly, the major constituents of *S. jambos* extracts, flavonoids and ellagitannins, are mostly glycosylated. They can then be found in large extent in the blood because of their water solubility. This parameter is quite important in drug development as it improves the therapeutic action of a drug. Accordingly, *S. jambos* constitutes a potential candidate to the development of potent traditional drugs against ROS and inflammation-induced illness.

CONCLUSION AND PERSPECTIVES

This review provides an up-to-date summary of *S. jambos* from the perspectives of its phytochemistry, pharmacology, traditional uses as well as toxicology. Phytochemical investigations have been focused on different organs of the plant, prepared with various organic and water solvents. These studies revealed the presence of flavonoids (flavones, chalcones, anthocyanins and

TABLE 4 | *In vivo* effects of *S. jambos* extracts.

Extract	Doses	Route	Model	Activity	Country	Effects	Reference
Aerial parts							
Hydro-alcoholic	100–300 mg/kg	Intraperitoneal injection	Male Sprague–Dawley rats	Anti-inflammatory	Venezuela	Analgesic effect on inflammatory cutaneous and deep muscle pain	Ávila-Peña et al. (2007)
Leaves							
Hydroethanolic	400 mg/kg	Oral	Gastric injury induced by HCL/ethanol to rats	Anti-ulcerogenic	Brazil	Reduction of the subchronic ulcer	Donatini et al. (2009)
Ethanolic	400 mg/kg	Oral	Rats, induced with acute inflammation	Anti-inflammatory	Bangladesh	Acute anti-inflammatory activity	Hossain et al. (2016)
Methanolic	200 mg/kg	Oral	Rats, CCl ₄ acute induced hepatic injury	Hepatoprotective	Egypt	The extract decreased the levels of all measured liver makers, including ALT, AST, TB, TC, TG, and MDA, while increasing GSH and SOD.	Sobeh et al. (2018)
	200 µg/ml	Juglone induced oxidative stress	<i>Caenorhabditis elegans</i>	Antioxidant		Decrease the intracellular ROS level in a dose dependent manner by 59.22%, the survival activity was also very low and dose dependent	
Methanolic	100–200 mg/kg	Oral	Paracetamol-induced hepatic damage in Wistar albino rats	Hepatoprotective	-	The extract caused a significant decrease in the serum hepatic enzyme levels, SGOT, SGPT, ALKP, and serum Bilirubin in dose-dependent manner	Selvam et al. (2013)
Ethanolic	300 mg/kg	Intraperitoneal injection/oral	Rats, CCl ₄ induced hepatic injury	Hepatoprotective	Bangladesh	Gradual normalization of serum markers enzyme (SGPT, SGOT, ALP), total bilirubin, total protein, and liver weight	Islam et al. (2012)
Methanolic	250 mg/kg	NS	Rats, Ethylene glycol-induced urolithiasis model	Antiurolithiatic	India	reduced the phosphorus, calcium, urea, and creatinine levels in the serum	Deka et al. (2021)
Ethanolic	500 µg/ml	NS	<i>S. cerevisiae</i> (wild type and mutant strain)	Antioxidant	India	H ₂ O ₂ scavenging potential	Rajkumari et al. (2018b)
Decoction	220 mg/kg	Oral	C57BL/J ob/ob Mice	Hypoglycemic	Puerto Rico	Better blood glucose modulation over time	Gavillán-Suárez et al. (2015)
Bark							
Aqueous	100–200 mg/kg	Oral	Streptozotocin-induced diabetes in rats	Antidiabetic	Egypt	Protective effects against STZ-induced diabetes Improvement in glycemic parameters Suppression of pancreatic oxidative stress, inflammation, apoptosis, and insulin signaling pathway in the liver	Mahmoud et al. (2021)
Fruit							
Pectic polysaccharides	150, 250 mg/kg	Intraperitoneal injection	Mice bearing Ehrlich solid tumor	Antitumor	Brazil	Reduced tumor growth and improved the body weight of tumor bearing mice	Tamiello et al. (2018a)

Ns: Not specified.

proanthocyanins), ellagitannins, phenolic acids, triterpenoids, volatiles compounds and fatty analogues. Compounds were either isolated following chromatographic techniques or identified by online methods like HPLC-MS/MS and GC-MS. Flavonoids and saponins as well as phenolic acids are the main constituents of the plant.

Activities of the plant towards pathogens and cells are also diverse and rich, consecutive to the broad spectrum of applications of the plant in traditional medicine to alleviate some illnesses. Plant extracts showed considerable anti-inflammatory activity and a synergistic effect to antibiotics activity of some popular drugs correlating the uses of the plant to relieve pains and infection. Extracts have also antiviral, anti-dermatophyte, hepatoprotective, and anticancer effects. Numerous compounds were isolated and initially screened for their bioactive potential. Further investigations are needed to complete the phytochemical profile, pharmacology mechanisms and pharmacokinetics studies of

the plant. In the same line, toxicity study of *S. jambos* is indispensable in the future to assess the safety of the plant and its bioactive compounds to support possible future medicinal applications and before proceeding to the development of pharmaceutical formulations.

AUTHOR CONTRIBUTIONS

MAO and WBB drafted the manuscript; GTMB and MFM reviewed the manuscript; MS revised the manuscript and designed and conceived the study. All authors approve the final version.

FUNDING

The APC was paid by UM6P.

REFERENCES

- Abad, M. J., Bermejo, P., Villar, A., Sanchez Palomino, S., and Carrasco, L. (1997). Antiviral Activity of Medicinal Plant Extracts. *Phytother. Res.* 11 (3), 198–202. doi:10.1002/(sici)1099-1573(199705)11:3<198:aid-ptr78>3.0.co;2-1
- Apaza Ticona, L., Souto Pérez, B., Martín Alejano, V., and Slowing, K. (2021). Anti-inflammatory and Anti-arthritis Activities of Glycosylated Flavonoids from *Syzygium Jambos* in Edematogenic Agent-Induced Paw Edema in Mice. *Rev. Bras. Farmacogn.* 31 (4), 429–441. doi:10.1007/s43450-021-00167-0
- Athikomkulchai, S., Lipipun, V., Leelawattayanont, T., Khanboon, A., and Ruangrunsi, N. (2008). Anti-herpes Simplex Virus Activity of *Syzygium Jambos*. *J. Health Res.* 22 (1), 49–51.
- Ávila-Peña, D., Peña, N., Quintero, L., and Suárez-Roca, H. (2007). Antinociceptive Activity of *Syzygium Jambos* Leaves Extract on Rats. *J. Ethnopharmacology* 112 (2), 380–385. doi:10.1016/j.jep.2007.03.027
- Baliga, M. S., Ranganath Pai, K. S., Saldanha, E., Ratnu, V. S., Priya, R., Adnan, M., et al. (2017). “Rose Apple (*Syzygium Jambos* (L.) Alston),” in *Fruit and Vegetable Phytochemicals: Chemistry and Human Health*. Editor E. M. Yahia. Second Edition 2 (Hoboken, NJ, USA: John Wiley and Sons), 1235–1242.
- Bonfanti, G., Bitencourt, P. R., Bona, K. S., Silva, P. S., Jantsch, L. B., Pigatto, A. S., et al. (2013). *Syzygium Jambos* and *Solanum Guaranicum* Show Similar Antioxidant Properties but Induce Different Enzymatic Activities in the Brain of Rats. *Molecules* 18 (8), 9179–9194. doi:10.3390/molecules18089179
- Chakravarty, A. K., Das, B., Sarkar, T., Masuda, K., and Shiojima, K. (1998). ChemInform Abstract: Ellagic Acid Derivatives from the Leaves of *Eugenia Jambos* Linn. *ChemInform* 30 (25), no. doi:10.1002/chin.199925211
- Chua, L. K., Lim, C. L., Ling, A. P. K., Chye, S. M., and Koh, R. Y. (2019). Anticancer Potential of *Syzygium* Species: a Review. *Plant Foods Hum. Nutr.* 74 (1), 18–27. doi:10.1007/s11130-018-0704-z
- Cock, I. E., and Cheesman, M. (2018). “Bioactive Compounds of Medicinal Plants,” in *Bioactive Compounds of Medicinal Plants: Properties and Potential for Human Health*. Editors M. R. Goyal and A. O. Ayeleso (Williston: Apple Academic Press), 35–84.
- Daly, J., Hamrick, D., Gary, G., and Guinn, A. (2016). *Maize Value Chains in East Africa*. London, United Kingdom: International Growth Centre, 1–50.
- Deka, K., Kakoti, B. B., and Das, M. (2021). Antirolithiatic Activity of Leaf Extracts of *Syzygium Jambos* (L.) Alston and its Zinc Nanoparticles: an *In-Vitro* and *In-Vivo* Approach. *Int. J. Pharm. Sci. Res.* 12 (1), 336–346. doi:10.13040/IJPSR.0975-8232.12(1).336-46
- Dhanabalan, R. M. P., and Devakumar, J. (2014). *In Vivo* antiplasmodial Activity of Four Folklore Medicinal Plants Used Among Tribal Communities of Western Ghats, Coimbatore, Tamil Nadu. *J. Pharm. Res.* 8 (6), 751–759.
- Djipa, C. D., Delmée, M., and Quetin-Leclercq, J. (2000). Antimicrobial Activity of Bark Extracts of *Syzygium Jambos* (L.) Alston (Myrtaceae). *J. Ethnopharmacol.* 71 (1-2), 307–313. doi:10.1016/s0378-8741(99)00186-5
- Donatini, R. S., Ishikawa, T., Barros, S. B. M., and Bacchi, E. M. (2009). Atividades antiúlcera e antioxidante Do extrato de folhas de *Syzygium jambos* (L.) Alston (Myrtaceae). *Rev. Bras. Farmacogn.* 19, 89–94. doi:10.1590/s0102-695x2009000100018
- Donatini, R. S., Kato, E., Ohara, M. T., and Bacchi, E. M. (2013). Morphoanatomy and Antimicrobial Study of *Syzygium Jambos* (L.) Alston (Myrtaceae) Leaves. *Lat. Am. J. Pharm.* 32 (4), 518.
- Dutta, P. P., Bordoloi, M., Gogoi, K., Roy, S., Narzary, B., Bhattacharyya, D. R., et al. (2017). Antimalarial Silver and Gold Nanoparticles: Green Synthesis, Characterization and *In Vitro* Study. *Biomed. Pharmacother.* 91, 567–580. doi:10.1016/j.biopha.2017.04.032
- Gavillán-Suárez, J., Aguilar-Perez, A., Rivera-Ortiz, N., Rodríguez-Tirado, K., Figueroa-Cuilan, W., Morales-Santiago, L., et al. (2015). Chemical Profile and *In Vivo* Hypoglycemic Effects of *Syzygium Jambos*, *Costus Speciosus* and *Tapeinochilos Ananassae* Plant Extracts Used as Diabetes Adjuvants in Puerto Rico. *BMC Complement. Altern. Med.* 15, 244. doi:10.1186/s12906-015-0772-7
- Ghareeb, M. A., Hamed, M. M., Abdel-Aleem, A.-a. H., Saad, A. M., Abdel-Aziz, M. S., and Hadad, A. (2017). Extraction, Isolation, and Characterization of Bioactive Compounds and Essential Oil from *Syzygium Jambos*. *Asian J. Pharm. Clin. Res.* 10 (8), 194. doi:10.22159/ajpcr.2017.v10i8.18849
- Ghareeb, M. A., Saad, A. M., Abdel-Aleem, A. H., Abdel-Aziz, M. S., Hamed, M. M., and Hadad, A. H. (2016). Antioxidant, Antimicrobial, Cytotoxic Activities and Biosynthesis of Silver and Gold Nanoparticles Using *Syzygium Jambos* Leave Growing in Egypt. *Der Pharm. Chem.* 8, 277–286.
- Guedes, C. M., Pinto, A. B., Moreira, R. F. A., and De Maria, C. A. B. (2004). Study of the Aroma Compounds of Rose Apple (*Syzygium Jambos* Alston) Fruit from Brazil. *Eur. Food Res. Technol.* 219 (5), 460–464. doi:10.1007/s00217-004-0967-5
- Haque, M. (2015). Investigation of the Medicinal Potentials of *Syzygium Jambos* (L.) Extract and Characterization of the Isolated Compounds. *Am. J. BioScience* 3 (2), 12. doi:10.11648/j.ajbio.s.2015030201.13
- Harsha, P. V., Ashoka, S. M., Karunakar, H., and Shabaraya, A. R. (2021). *Syzygium Jambos*: A Brief Review. *World J. Pharm. Pharm. Sci.* doi:10.20959/wjpps20214-18583
- Hossain, H., Rahman, S. E., Akbar, P. N., Khan, T. A., Rahman, M. M., and Jahan, I. A. (2016). HPLC Profiling, Antioxidant and *In Vivo* Anti-inflammatory Activity of the Ethanol Extract of *Syzygium Jambos* Available in Bangladesh. *BMC Res. Notes* 9, 191. doi:10.1186/s13104-016-2000-z
- Inostroza-Nieves, Y., Valentin-Berrios, S., Vega, C., Prado, G. N., Luciano-Montalvo, C., Romero, J. R., et al. (2021). Inhibitory Effects of *Syzygium*

- Jambos Extract on Biomarkers of Endothelial Cell Activation. *Complement. Med. Therapies*. doi:10.21203/rs.3.rs-926922/v1
- Islam, M. R., Parvin, M. S., and Islam, M. E. (2012). Antioxidant and Hepatoprotective Activity of an Ethanolic Extract of *Syzygium Jambos* (L.) Leaves. *Drug Discov. Ther.* 6 (4), 205–211. doi:10.5582/ddt.2012.v6.4.205
- Iwu, M. M. (1993). *Handbook of African Medicinal Plants*. London: CRC Press, 183–184.
- Jayasinghe, U. L., Ratnayake, R. M., Medawala, M. M., and Fujimoto, Y. (2007). Dihydrochalcones with Radical Scavenging Properties from the Leaves of *Syzygium Jambos*. *Nat. Prod. Res.* 21 (6), 551–554. doi:10.1080/14786410601132238
- Koagne, R. R., Annang, F., Cautain, B., Martín, J., Pérez-Moreno, G., Bitchagno, G. T. M., et al. (2020). Cytotoxicity and Antiplasmodial Activity of Phenolic Derivatives from *Albizia Zygia* (DC.) J.F. Macbr. (Mimosaceae). *BMC Complement. Med. Ther.* 20 (1), 8. doi:10.1186/s12906-019-2792-1
- Koteswara, A., Sakander, H., and Akhilesh, B. (2015). Evaluation of Antifungal Potential of Selected Medicinal Plants against Human Pathogenic Fungi. *Int. J. Green. Pharm.* 9 (2), 110–117. doi:10.4103/0973-8258.155058
- Kuiate, J. R., Mouokey, S., Wabo, H. K., and Tane, P. (2007). Antidermatophytic Triterpenoids from *Syzygium Jambos* (L.) Alston (Myrtaceae). *Phytother. Res.* 21 (2), 149–152. doi:10.1002/ptr.2039
- Li, G. Q., Zhang, Y. B., Wu, P., Chen, N. H., Wu, Z. N., Yang, L., et al. (2015). New Phloroglucinol Derivatives from the Fruit Tree *Syzygium Jambos* and Their Cytotoxic and Antioxidant Activities. *J. Agric. Food Chem.* 63 (47), 10257–10262. doi:10.1021/acs.jafc.5b04293
- Lin, D. D., Liu, J. W., Li, W. G., Luo, W., Cheng, J. L., and Chen, W. W. (2014). Chemical Constituents from Stems of *Syzygium Jambos* Var. *Jambos* and Their *In Vitro* Cytotoxicity. *Chin. Trad. Herb. Drugs* 45 (17), 1993–1997. doi:10.7501/j.issn.0253-2670.2014.14.006
- Luciano-Montalvo, C., Boulogne, I., and Gavillán-Suárez, J. (2013). A Screening for Antimicrobial Activities of Caribbean Herbal Remedies. *BMC Complement. Altern. Med.* 13, 126. doi:10.1186/1472-6882-13-126
- Mabberley, D. J. (2017). *Mabberley's Plant-Book: A Portable Dictionary of Plants, Their Classification and Uses*. 4 ed. Cambridge, United Kingdom: Cambridge University Press.
- Mahmoud, M. F., Abdelaal, S., Mohammed, H. O., El-Shazly, A. M., Daoud, R., El Raey, M. A., et al. (2021). *Syzygium Jambos* Extract Mitigates Pancreatic Oxidative Stress, Inflammation and Apoptosis and Modulates Hepatic IRS-2/AKT/GLUT4 Signaling Pathway in Streptozotocin-Induced Diabetic Rats. *Biomed. Pharmacother.* 142, 112085. doi:10.1016/j.biopha.2021.112085
- Mangini, L. F. K., Valt, R. B. G., Ponte, M. J. J. d. S., and Ponte, H. d. A. (2020). Vanadium Removal from Spent Catalyst Used in the Manufacture of Sulfuric Acid by Electrical Potential Application. *Separat. Purif. Technol.* 246, 116854. doi:10.1016/j.seppur.2020.116854
- Maskey, K., and Shah, B. B. (1982). Sugars in Some Nepalese Edible Wild Fruits. *J. Nepal Chem. Soc.* 2, 23–30.
- M. Khalaf, O., Abdel-Aziz, M. S., El-Hagrassi, A. M., Osman, A. F., and Ghareeb, M. A. (2021). Biochemical Aspect, Antimicrobial and Antioxidant Activities of *Melaleuca* and *Syzygium* Species (Myrtaceae) Grown in Egypt. *J. Phys. Conf. Ser.* 1879 (2), 022062. doi:10.1088/1742-6596/1879/2/022062
- Mohanty, S., and Cock, I. E. (2010). Bioactivity of *Syzygium Jambos* Methanolic Extracts: Antibacterial Activity and Toxicity. *Pharmacognosy Res.* 2 (1), 4–9. doi:10.4103/0974-8490.60577
- Morton, J. F. (1987). *Fruits of Warm Climates*. Miami, FL: Creative Resource Systems, 33189.
- Murugan, S., Devi, P. U., Parameswari, N. K., and Mani, K. R. (2011). Antimicrobial Activity of *Syzygium Jambos* against Selected Human Pathogens. *Int. J. Pharm. Pharm. Sci.* 3 (2), 44–47.
- Musthafa, K. S., Sianglum, W., Saising, J., Lethongkam, S., and Voravuthikunchai, S. P. (2017). Evaluation of Phytochemicals from Medicinal Plants of Myrtaceae Family on Virulence Factor Production by *Pseudomonas aeruginosa*. *Apmis* 125 (5), 482–490. doi:10.1111/apm.12672
- Nawwar, M. A., Hashem, A. N., Hussein, S. A., Swilam, N. F., Becker, A., Haertel, B., et al. (2016). Phenolic Profiling of an Extract from *Eugenia Jambos* L. (Alston)-The Structure of Three Flavonoid Glycosides-Aantioxidant and Cytotoxic Activities. *Pharmazie* 71, 162–168. doi:10.1691/ph.2016.5747
- Nesa, F., Shoeb, M., Islam, M. M., and Islam, M. N. (2021). Studies of Physico-Chemical Properties and Cytotoxicity of Fruits of *Syzygium Jambos* L. Against HeLa and Vero Cell Lines. *Bangla Pharma J.* 24 (2), 111–116. doi:10.3329/bpj.v24i2.54709
- Noé, W., Murhekar, S., White, A., Davis, C., and Cock, I. E. (2019). Inhibition of the Growth of Human Dermatophytic Pathogens by Selected Australian and Asian Plants Traditionally Used to Treat Fungal Infections. *J. Mycol. Med.* 29 (4), 331–344. doi:10.1016/j.mycmed.2019.05.003
- Panthong, K., and Voravuthikunchai, S. P. (2020). Eugejambones A–D from Leaves of *Eugenia Jambos*. *Phytochemistry Lett.* 38, 49–54. doi:10.1016/j.phytol.2020.05.011
- Prastiwi, M., Kartika, R., and Hindryawati, N. (2019). *Jurnal Atomik* 4 (1), 14–16.
- Rajkumari, J., Dyavaiah, M., Sudharshan, S. J., and Busi, S. (2018b). Evaluation of *In Vivo* Antioxidant Potential of *Syzygium Jambos* (L.) Alston and *Terminalia Citrina* Roxb. Towards Oxidative Stress Response in *Saccharomyces cerevisiae*. *J. Food Sci. Technol.* 55 (11), 4432–4439. doi:10.1007/s13197-018-3355-z
- Rajkumari, J., Borkotoky, S., Murali, A., and Busi, S. (2018a). Anti-Quorum Sensing Activity of *Syzygium Jambos* (L.) Alston against *Pseudomonas aeruginosa* PAO1 and Identification of its Bioactive Components. *South Afr. J. Bot.* 118, 151–157. doi:10.1016/j.sajb.2018.07.004
- Reddy, Y. N., Vinil Kumar, V., and Naresh Chandra, R. N. B. S. (2014). *In Vitro* antioxidant and Anti-inflammatory Activity of Hydro Methanolic Extract of Leaves of *Syzygium Jambos* (L.) Alston. *Int. J. Pharm. Life Sci.* 2 (2), 71–82.
- Reis, A. S., Silva, L. de S., Martins, C. F., and de Paula, J. R. (2021). Analysis of the Volatile Oils from Three Species of the Gender *Syzygium*. *Res. Soc. Dev.* 10 (7), e13510716375. doi:10.33448/rsd-v10i7.16375
- Reynertson, K. A., Yang, H., Jiang, B., Basile, M. J., and Kenedly, E. J. (2008). Quantitative Analysis of Antiradical Phenolic Constituents from Fourteen Edible Myrtaceae Fruits. *Food Chem.* 109 (4), 883–890. doi:10.1016/j.foodchem.2008.01.021
- Rocchetti, G., Lucini, L., Ahmed, S. R., and Saber, F. R. (2019). *In Vitro* cytotoxic Activity of Six *Syzygium* Leaf Extracts as Related to Their Phenolic Profiles: An Untargeted UHPLC-QTOF-MS Approach. *Food Res. Int.* 126, 108715. doi:10.1016/j.foodres.2019.108715
- Selvam, N. T., Venkatakrishnan, V., Dhamodharan, R., Murugesan, S., and Kumar, S. D. (2013). Hepatoprotective Activity of Methanolic Extract of *Syzygium Jambos* (Linn.) Leaf against Paracetamol Intoxicated Wistar Albino Rats. *Ayu* 34 (3), 305–308. doi:10.4103/0974-8520.123133
- Sharma, R., Kishore, N., Hussein, A., and Lall, N. (2013). Antibacterial and Anti-inflammatory Effects of *Syzygium Jambos* L. (Alston) and Isolated Compounds on *Acne Vulgaris*. *BMC Complement. Altern. Med.* 13 (1), 292. doi:10.1186/1472-6882-13-292
- Slowing, K., Söllhuber, M., Carretero, E., and Villar, A. (1994). Flavonoid Glycosides from *Eugenia Jambos*. *Phytochemistry* 37 (1), 255–258. doi:10.1016/0031-9422(94)85036-4
- Slowing, K., Carretero, E., and Villar, A. (1996). Anti-inflammatory Compounds of *Eugenia Jambos*. *Phytother. Res.* 10 (1), 126–127.
- Sobeh, M., Braun, M. S., Krstin, S., Youssef, F. S., Ashour, M. L., and Wink, M. (2016). Chemical Profiling of the Essential Oils of *Syzygium Aqueum*, *Syzygium Samarangense* and *Eugenia Uniflora* and Their Discrimination Using Chemometric Analysis. *Chem. Biodivers.* 13 (11), 1537–1550. doi:10.1002/cbdv.201600089
- Sobeh, M., Esmat, A., Petruk, G., Abdelfattah, M. A. O., Dmirieh, M., Monti, D. M., et al. (2018). Phenolic Compounds from *Syzygium Jambos* (Myrtaceae) Exhibit Distinct Antioxidant and Hepatoprotective Activities *In Vivo*. *J. Funct. Foods* 41, 223–231. doi:10.1016/j.jff.2017.12.055
- Subbulakshmi, K., Satish, S., and Shabaraya, A. R. (2021). Rose Apple Fruit: A Pharmacological Review. *World J. Pharm. Pharm. Sci.* 10, 842–849. doi:10.20959/wjpps20214-18707
- Sun, Z., Huang, Q., and Feng, C. (2020). Complete Chloroplast Genome Sequence of the Rose Apple, *Syzygium Jambos* (Myrtaceae). *Mitochondrial DNA B* 5 (3), 3460–3462. doi:10.1080/23802359.2020.1826000
- Tamiello, C. S., Adami, E. R., de Oliveira, N. M. T., Acco, A., Iacomini, M., and Cordeiro, L. M. C. (2018a). Structural Features of Polysaccharides from Edible Jambo (*Syzygium Jambos*) Fruits and Antitumor Activity of Extracted Pectins. *Int. J. Biol. Macromol.* 118, 1414–1421. doi:10.1016/j.jbiomac.2018.06.164
- Tamiello, C. S., do Nascimento, G. E., Iacomini, M., and Cordeiro, L. M. C. (2018b). Arabinogalactan from Edible Jambo Fruit Induces Different Responses on Cytokine Secretion by THP-1 Macrophages in the Absence and Presence of

- Proinflammatory Stimulus. *Int. J. Biol. Macromol.* 107, 35–41. doi:10.1016/j.ijbiomac.2017.08.148
- Teixeira, C. C., Fuchs, F. D., Blotta, R. M., Knijnik, J., Delgado, I. C., Netto, M. S., et al. (1990). Effect of tea Prepared from Leaves of *Syzygium Jambos* on Glucose Tolerance in Nondiabetic Subjects. *Diabetes Care* 13 (8), 907–908. doi:10.2337/diacare.13.8.907
- Thamizh Selvam, N., Acharya, M., Venkatakrishnan, V., and Murugesan, S. (2016). Effect of Methanolic Extract of (Linn.) Alston Leaves at Intra *Syzygium Jambos* Cellular Level in Selective Liver Cancer Cell Line: Molecular Approach for its Cytotoxic Activity. *Adv. Pharm. J.* 1 (5), 139.
- Ticona, L. A., Pérez, B. S., Alejano, V. M., and Slowing, K. (2021). Anti-inflammatory and Anti-arthritis Activities of Glycosylated Flavonoids from *Syzygium Jambos* in Edematogenic Agent-Induced Paw Edema in Mice. *Rev. Bras. Farmacogn.* 31, 429–441. doi:10.1007/s43450-021-00167-0
- Twilley, D., Langhansová, L., Palaniswamy, D., and Lall, N. (2017). Evaluation of Traditionally Used Medicinal Plants for Anticancer, Antioxidant, Anti-inflammatory and Anti-viral (HPV-1) Activity. *South Afr. J. Bot.* 112, 494–500. doi:10.1016/j.sajb.2017.05.021
- Vagula, J. M., Visentainer, J. V., Lopes, A. P., Maistrovicz, F. C., Rotta, E. M., and Suzuki, R. M. (2019). Antioxidant Activity of Fifteen Seeds from Fruit Processing Residues by Different Methods. *Acta Sci. Technol.* 41, e35043. doi:10.4025/actascitechnol.v41i2.35043
- van Wyk, B-E., and Wink, M. (2015). *Phytomedicines, Herbal Drugs, and Poisons*. Chicago: The University of Chicago Press.
- Vernin, G., Vernin, G., Metzger, J., Roque, C., and Pieribattesti, J.-C. (1991). Volatile Constituents of the *Jamrosia AromaSyzygium jambos*L. Aston from Reunion Island. *J. Essent. Oil Res.* 3 (2), 83–97. doi:10.1080/10412905.1991.9697916
- Wamba, B. E. N., Nayim, P., Mbaveng, A. T., Voukeng, I. K., Dzotam, J. K., Ngalani, O. J. T., et al. (2018). *Syzygium Jambos* Displayed Antibacterial and Antibiotic-Modulating Activities against Resistant Phenotypes. *Evid. Based Complement. Alternat. Med.* 2018, 5124735. doi:10.1155/2018/5124735
- Wen, Z., Ling, M., Yu, S., Zhuang, Y., Luo, X., Pan, Z., et al. (2019). Study on Inhibitory Effects of Ethanol Extract of Different Medicinal Parts from *Syzygium Jambos* on the Activities of α -Glycosidase and α -Amylase. *China Pharm.*, 3246–3251.
- Wong, K. C., and Lai, F. Y. (1996). Volatile Constituents from the Fruits of Four *Syzygium* Species Grown in Malaysia. *Flavour Fragr. J.* 11 (1), 61–66. doi:10.1002/(sici)1099-1026(199601)11:1<61:aid-ffj539>3.0.co;2-1
- Yang, L. L., Lee, C. Y., and Yen, K. Y. (2000). Induction of Apoptosis by Hydrolyzable Tannins from *Eugenia Jambos* L. On Human Leukemia Cells. *Cancer Lett.* 157 (1), 65–75. doi:10.1016/S0304-3835(00)00477-8
- Yunus, S. N. M., Abas, F., Jaafar, A. H., Azizan, A., Zolkeflee, N. K. Z., and Abd Ghafar, S. Z. (2021). Antioxidant and α -glucosidase Inhibitory Activities of Eight Neglected Fruit Extracts and UHPLC-MS/MS Profile of the Active Extracts. *Food Sci. Biotechnol.* 30 (2), 195–208. doi:10.1007/s10068-020-00856-x
- Zheng, N. I., Wang, Z., Chen, F., and Lin, J. (2011). Evaluation to the Antioxidant Activity of Total Flavonoids Extract from *Syzygium Jambos* Seeds and Optimization by Response Surface Methodology. *Afr. J. Pharm. Pharmacol.* 5 (21), 2411–2419. doi:10.5897/ajpp11.691

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Copyright © 2022 Ochieng, Ben Bakrim, Bitchagno, Mahmoud and Sobeh. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.