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Review Article
Potential Therapeutic Use of *Sterculia quadrifida* R.Br and *Sterculia foetida* Linn.: Review

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Abstract

The Sterculiaceae family is known to have many benefits in the fields of food, medicine and industry. The *S. quadrifida* R.Br and *S. foetida* Linn. is a plant of the family Sterculiaceae which has utilization in the field of medicine. Empirically used to stamina booster, cure diarrhea, treat hepatitis, relieve infections and anti-cancer. In the research, antioxidants, antibacterial, immunomodulatory and cytotoxic activity of this plant were reviewed. After this study, it is expected to provide insight into the utilization of natural resources in the exploration of potential drugs from the *S. quadrifida* R.Br and *S. foetida* Linn plants. Much work remains to be done to ensure the safety, quality and effectiveness of the *S. quadrifida* R.Br and *S. foetida* Linn plants before used to treat diseases in humans.

Key words: *Sterculia quadrifida* R.Br, *Sterculia foetida* Linn., antioxidant, antibacterial, immunomodulatory and cytotoxic

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Indonesia is a country with the largest number of plant species in the world with 30,000 species and among them, there are around 7,500 species that are known to have herbal properties[1]. Sterculiaceae has been recognized as a family by most systematicians[2]. This family consists of 70 genera, numbering around 1500 species of tropical trees and shrubs. The most famous family product is chocolate and cocoa from *Theobroma cacao*[3].

Several species from the family Sterculiaceae have been used as a traditional medicine in various countries for decades to treat various diseases. A number of researchers have conducted studies to look for the chemical content and pharmacological effects of several species of the Sterculiaceae family. Plants of the family Sterculiaceae have long been used as a traditional medicine in several countries and tribes. Almost all parts of the plant including roots, bark and leaves of species from the family are reported to show various medicinal properties.

Sterculia quadrifida R.Br is one of the plants of the family Sterculiceae[4]. The plant grows in East Nusa Tenggara (Fig. 1). Faloak is a local name, especially Timorese. *S. quadrifida* has several local names, such as Bangilan (Manado), Bingiladu (Gorontalo), Kalimanaolimana (Tobelo), Kaita (Sula Island in Maluku), Lahea (Manga Island), Pani Wood (Buru Island), Susulangit (Seram Island)[5-6]. *S. quadrifida* activities are useful for the topic of antioxidant, antimicrobial, immunomodulatory and cytotoxic properties. These characteristics make it a very interesting target for herbal medicine (Fig. 2a-d).

Fig. 1: Map of *S. quadrifida* and *S. foetida* sampling location in Kupang, East Nusa Tenggara[4]

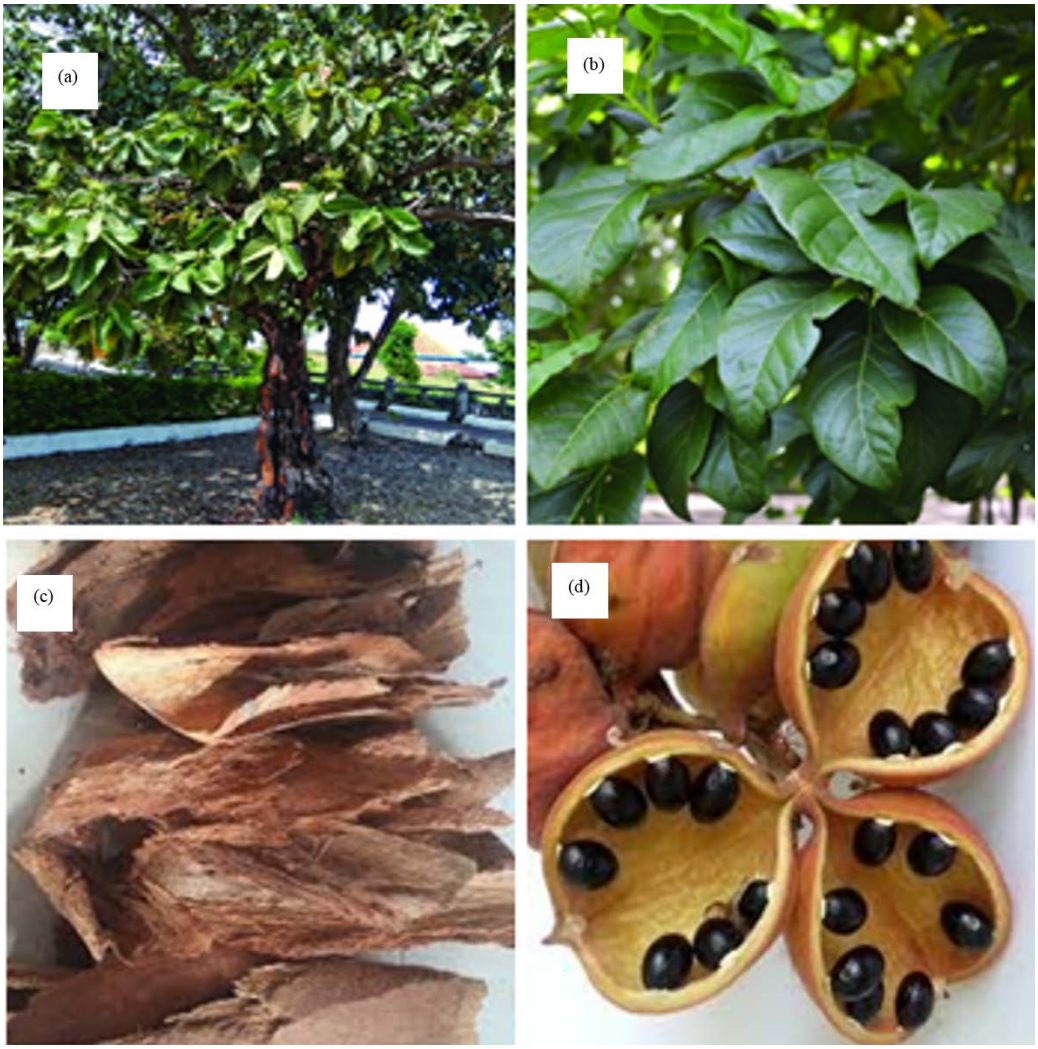

Fig. 2(a-d): (a) *S. quadrifida* R.Br. trees, (b) leaves, (c) bark, (d) fruits and seeds

The *S. foetida* L. known as "Nitas" (Fig. 3a-d) is one of the plants in the East Nusa Tenggara region that belongs to the Sterculiaceae family[6]. The *S. foetida* collection in the Kupang research (Fig. 1) and development environment forest originates from North Sulawesi. In Indonesia, this plant is spread in several areas including Sumatra, Java, Bali, Lombok, Sumbawa, Flores, Timor, Borneo, Sulawesi, Maluku and Irian Jaya[7].

S. quadrifida R.Br and *S. foetida* Linn. have been used as traditional medicines in various countries. A number of researchers have conducted studies on the chemical constituents and pharmacological properties. This review describes the pharmacological properties of species from *S. quadrifida* R.Br and *S. foetida* Linn. The phytochemical studies have resulted in the extraction and fractionation consisting of various classes of compounds including propanoids, flavonoids, terpenoids and alkaloids. However, the pharmacology of this family has not been widely investigated. Moreover, no toxicity studies of both the extracts and chemical constituents of this species have been analyzed. These gaps open up a great research opportunity to study more about the phytochemical and pharmacology of *S. quadrifida* R.Br and *S. foetida* Linn. considering the interesting medicinal properties possessed by species and the chemical constituents of this species. Since this species has not been explored yet, there are very significant opportunities to find novel compounds as well as promising medicinal and pharmacological properties from various extracts of the species. This can also lead to the possibility of finding new sources of drugs for future applications.

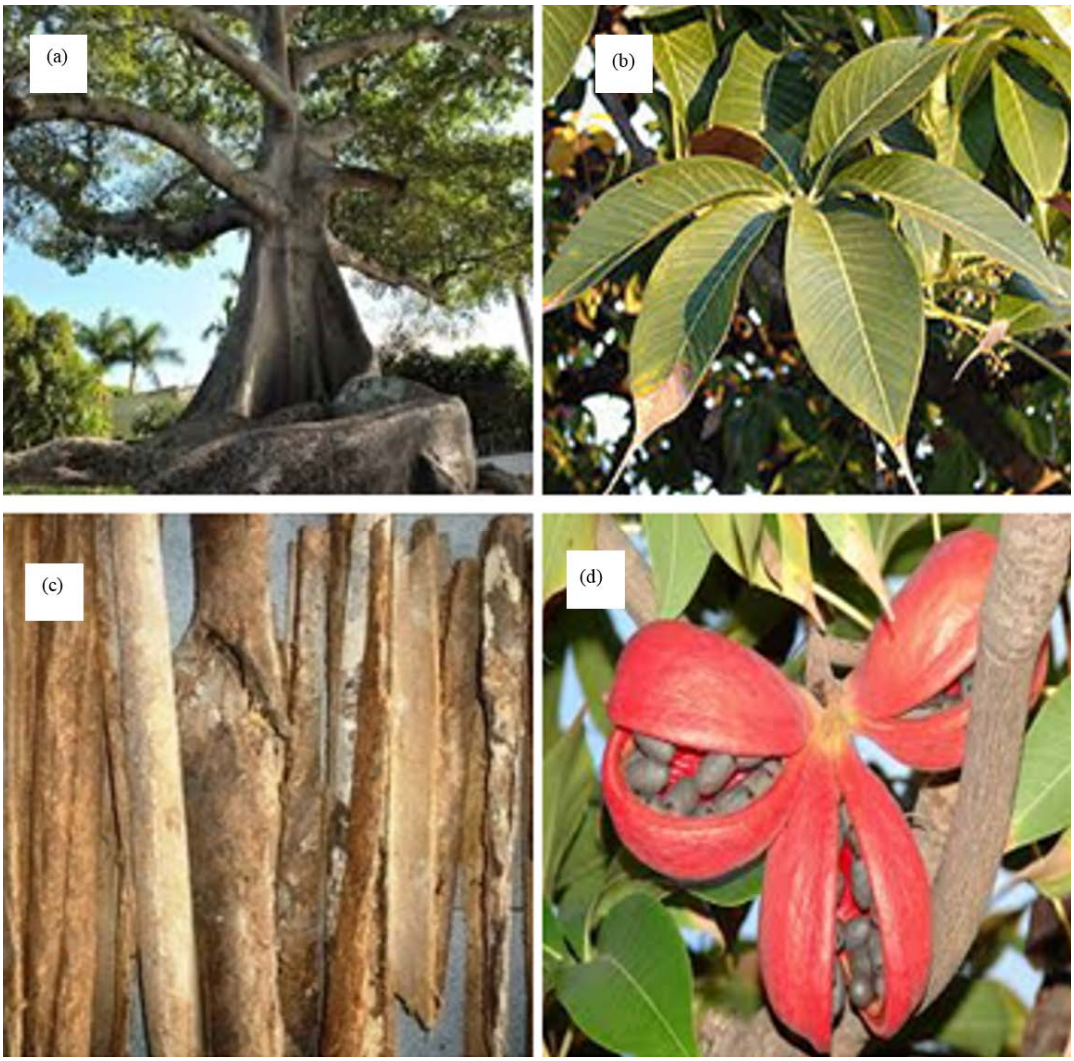

Fig. 3(a-d): (a) *S. foetida* Linn trees, (b) leaves, (c) bark, (d) fruits and seeds

MATERIALS AND METHODS

Relevant information in the field of natural product research, herbal medicine, antibacterial, antioxidant, immunomodulator and cytotoxic were investigated and assembled from several sources such as Google Scholar, Pubmed, Science Direct, SciFinder, Scopus and Web of Science. Supporting references sourced from journal articles, books, theses and scientific reports were accessed using facilities provided by Ma Chung University, Indonesia. The literature search was carried out between April and June 2020.

***Sterculia quadrifida* R.Br and *Sterculia foetida* biological activities:** Due to its diverse therapeutic properties and its composition chemical richness, *S. quadrifida* and *S. foetida* has become a focus of interest in many areas of scientific research, seeking to discover new therapies to treat many diseases like a tumor, bacterial infections, ulcers and diabetes. *S. quadrifida* and *S. foetida* active compounds have hepatoprotective, antiviral, antioxidant, anti-tumor, immunomodulatory, antifungal, antibacterial[7-8] (Fig. 4). *S. quadrifida* extract contains terpenoids, aromatic and aliphatic compounds that exhibit antibacterial activity and inhibits free radical[9]. Leaves of *S. foetida* ethanol extracts contains five compounds were identified as 5,7,8-tetrahydroxy-4'-methoxyflavone-8-O-beta-D-glucoside, apigenin-6, 8-di-C-beta-D-glucoside, puerarin, 5,7,8-tetrahydroxy-3',4'-dimethoxyflavone, 5,7,8-tetrahydroxy-4'-methoxyflavone[10]. In this review, the use of extract or fraction from bark, seed, leaves of *S. quadrifida* and *S. foetida* was observed, whether it is for therapeutic or for herbal medicine.

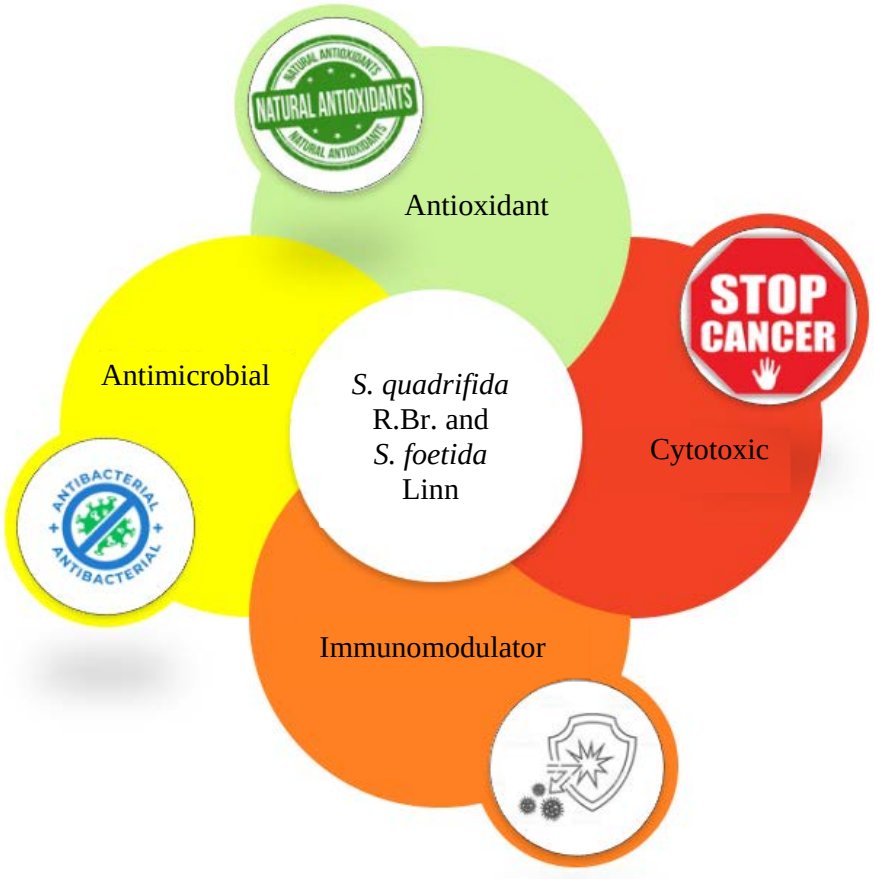

Fig. 4: *S. quadrfida* and *S. foetida* Linn. shown exert biological activities interesting for human health

The use of *S. quadrfida* and *S. foetida* and Its properties are discussed in Table 1, such as antioxidant, antimicrobial, immunomodulator and cytotoxic activities.

Antioxidant properties: Free radicals are groups of compounds that have one or more unpaired electrons in their groups. Molecules that have unpaired electrons tend to be reactive in order to achieve more stable conditions. These reactive properties allow free radical compounds to react with proteins, lipids and DNA, triggering oxidative stress. Untreated oxidative stress will cause a decrease in function on the substrate being attacked[11].

Antioxidants work through two main mechanisms, namely Hydrogen Atom Transfer (HAT) and Single Electron Transfer (SET). In the HAT mechanism, free radical compounds will attract one hydrogen atom from antioxidant compounds. As a result of the transfer process will produce radical antioxidant compounds. The binding process of hydrogen atoms is influenced by the enthalpy of bond dissociation, where the smaller the enthalpy value of hydrogen atom donors (antioxidants) will produce better activity[12].

A study conducted by another author[13] showed that the concentrations of flavonoids in *S. quadrifida* extracts from different plant parts varied from 0.58±0.13-1.25±0.10 mg QE g^{-1}. The TPC in the extracts of different plant parts ranged between 8.61±0.09 and 10.43±0.08 mg GAE g^{-1}. Branch bark has the highest total flavonoids and phenolic content. The extract of new regrown stem bark exhibited the potential antioxidant activity with inhibitory concentration (IC_{50}) values of 2.51±0.03 µg mL^{-1}. From this study concluded extracts from different plant parts of *S. quadrifida* exhibited strong antioxidant activity. However, the total phenolic and flavonoid contents in *S. quadrifida* only indicated a weak correlation with its antioxidant activity.

In addition, a study conducted by Lulan *et al.*[14] found that methanol extract of *S. quadrifida* R. Br. root exhibited the highest DPPH radical scavenging activity with IC_{50} value of 3.11 µg mL^{-1} and also showed the highest ABTS radical scavenging activity with IC_{50} value of 7.29 µg mL^{-1}, respectively. The *S. quadrifida* extract showed high flavonoids and phenolic content with 661.85 mg of GAE and 116.84 mg of QE per 100 g of extract.

Table 1: Biological activity of extracts and fractions of *S. quadrifida* and *S. foetida*

Species	Bioactivity	Description	References
S. quadrifida R.Br	Antioxidant	The antioxidant activity of root and stem bark of faloak extract was classified as very strong	Amin *et al.*[2]
		The extract of new regrown stem bark exhibited potent antioxidant activity with inhibitory concentration (IC_{50}) values of 2.51±0.03 μg mL^{-1}	Njurumana[3]
		The methanol extract of *S. quadrifida* R. Br. root exhibited the highest DPPH radical scavenging activity with IC_{50} value of 3.11 μg mL^{-1} and also showed the highest ABTS radical scavenging activity with IC_{50} value of 7.293.11 μg mL^{-1}	Dillak *et al.*[15]
	Antimicrobial	The ethanol extract of *S. quadrifida* tree bark with a concentration of 22.5% w/v, 45% w/v, 75% w/v and 100% w/v have antibacterial activity against the growth of *Staphylococcus aureus* bacteria	Tenda *et al.*[21]
		The fraction 3 showed high antibacterial activity in *B. subtilis* bacteria (90.51 μg mL^{-1}), *E. coli* (80.12 μg mL^{-1}), *S. aureus* (77.87 μg mL^{-1})	Susanto[22]
		The diethyl ether fraction has the highest inhibitory activity, The fraction has inhibition of 14.33 mm and MIC of 30.34 μg mL^{-1}	Ranta *et al.*[23]
	Immunomodulatory	The aqueous extract, 50% ethanolic extract and 96% ethanolic extract of *S. quadrifida* bark proved to have immunomodulatory activity *in vitro*	Hertiani *et al.*[29]
		The highest phagocytic capacity of macrophages is ethyl acetate fraction at a concentration of 250 μg mL^{-1} of 51.94±4.67%	Munawaroh *et al.*[30]
		The syrup dosage form of *S. quadrifida* and *P. niruri* extract modulating TNFα, NF-κB and increasing macrophage capacity were 535.98±8.15%, 57.86±1.46% and 98.45±0.23%	Rollando *et al.*[31]
	Cytotoxic activities	The ethyl acetate fraction of *S. quadrifida* bark able to inhibit the development of T47D breast cancer cell line with IC_{50} 24.88 μg mL^{-1} and selectivity index 15.58	Rolando and Prilianti[4]
		The ethanol extract from *S. quadrifida* bark can inhibit the development of T47D breast cancer cell line with IC_{50} of 32.45 μg mL^{-1}	Rollando and Siswadi[35]
		The ethanol extract of *S. quadrifida* bark on Hela cell line and reported ethanol extract had an IC_{50} of 2,221,849 μg mL^{-1}	Novitasari[36]
		The 2,3-dihydro-6-hydroxy-2-methylenenaphtho [1,2-b] furan-4,5-dione with IC_{50} in breast cancer cells was 9.88 μg mL^{-1} and with an index selectivity value of 30.23	Rollando and Alfanaar[37]
S. foetida Linn.	Antioxidant	The methanol extract of *S. foetida* leaves has the free radical scavenging activity of 1-diphenyl-2-picrylhydrazyl (DPPH) with IC_{50} of 13.14 μg / ml and from the nitric oxide radical inhibition test obtained IC_{50} of 14.53 μg mL^{-1}	Kavitha *et al.*[16]
		The hexane and methanolic extracts with IC_{50} values of 51.26 and 66.84, respectively, Flavonoid levels were 86.93±1.98 mg g^{-1} and phenol levels were 142.31±3.43 mg g^{-1}	Khatoon *et al.*[17]
	Antimicrobial	The n-hexane extract has a high activity against bacteria *Shigella flexneri*, *Klebsiella pneumoniae* and *Salmonella enterica ser typhi*	El-Sherei *et al.*[24]
		Lectin from seeds has a high activity against *Salmonella enterica ser typhi* and *Klebsiella pneumoniae* with MIC of 12.34 μg mL^{-1} and 11.23 μg mL^{-1}, respectively	Braga *et al.*[25]
	Cytotoxic activities	The ethanol extract of *S. foetida* seeds was able to inhibit the development of MG-63 osteosarcoma cell lines by 51.33%	Jafri *et al.*[38]
		The HeLa cell proliferation was significantly inhibited (>90%) by Ag-PL NPs at the concentration of 16 μg mL^{-1}	Rajasekharreddy and Rani *et al.*[40]

Dillak *et al.*[15] on his study found that the highest total flavonoid content was found in stem barks extract (62.76±4.84 mg g^{-1}), while the lowest was in seeds extract (1.55±1.44 mg g^{-1}). The highest phenols (82.90±2.50 mg g^{-1}) and tannins (71.26±10.21 mg g^{-1}) compound content were found in the roots while the smallest phenols were in the seeds (2.89 mg g^{-1}) and tannins were found in leaves (10.52±3.61 mg g^{-1}). Based on IC_{50} values, the antioxidant activity of root and stem bark of faloak extract was classified as very strong (IC_{50} value <50 μg mL^{-1}), while the leaves, fruit and seed extract were classified as strong (IC_{50} value 50-100 μg mL^{-1}).

Research conducted by Kavita *et al.*[16] reported that the methanol extract of *S. foetida* leaves had the activity of capturing 1-diphenyl-2-picrylhydrazyl (DPPH) free radicals with IC_{50} of 13.14 μg mL^{-1} and from the nitric oxide radical inhibition test obtained IC_{50} of 14.53 μg mL^{-1}. In the study reported that methanol extract had a phenol level of 83.09±1.03 mg g^{-1} and a flavonoid level of 103.11±1.41 mg g^{-1}.

Other antioxidant activity tests were also reported by Khatoon *et al.*[17], the results of antioxidant activity tests of *S. foetida* bark reported the antioxidant activity by DPPH scavenging method which resulted in the significant antioxidant potential of n-hexane and methanolic extracts with IC_{50} values of 51.26 and 66.84 respectively. Flavonoid levels were 86.93±1.98 mg g^{-1} and phenol levels were 142.31±3.43 mg g^{-1}.

From the *in vitro* verification, it can wisely be concluded that the bark and roots of *S. quadrifida* and *S. foetida* have the potential to be treated for traditional drugs. Faloak bark extract is reported to have polyphenol and flavonoid compounds[18]. Polyphenols and flavonoids can also act by different antioxidant mechanisms, including to chelate trace elements (free iron or copper), which are potential enhancers of the generation of free radicals, or to act even as stabilizers of these radicals involved in oxidative processes by forming complexes with them and inhibition of the enzymes involved in the formation of reactive oxygen species (xanthine oxidase, protein kinase C, lipoxygenase and cyclooxygenase)[19].

Antimicrobial activities: Ethanol extract of *S. quadrifida* bark was reported to have antimicrobial activity in gram-positive and gram-negative bacteria[20]. The study conducted by Tenda *et al.*[21] reported ethanol extract of faloak tree bark with a concentration of 22.5% w/v; 45% w/v; 75% w/v and 100% w/v have antibacterial activity against the growth of *Staphylococcus aureus* bacteria.

Recently, Susanto[22] in his study reported that ethanol extracts of *S. quadrifida* bark have phenol, flavonoid and terpenoid compounds. The results of fractionation showed that fraction number 3 showed high antibacterial activity in *B. subtilis* (90.51 μg mL^{-1}), *E. coli* (80.12 μg mL^{-1}), *S. aureus* (77.87 μg mL^{-1}). Other works have shown that some components of may be crucial for its antifungal activity, such as reported by Ranta *et al.*[23]. In their research, they conducted tests on human parasite fungi, namely *C. albicans*. The bark, leaves and seeds of *S. quadrifida* are extracted using various solvents. The test results showed the diethyl ether fraction had the highest inhibitory activity. The fraction has inhibition of 14.33 mm and MIC of 30.34 μg mL^{-1}.

A study conducted by El-Sherei *et al.*[24] reported that n-hexane extract had high activity against parasitic bacteria in humans such as *Shigella flexneri*, *Klebsiella pneumoniae* and *Salmonella enterica ser typhi*. However, it has intermediate activity in the bacteria *Bacillus subtilis*, *Streptococcus mitis* and *Staphylococcus aureus*. The study reported that n-hexane extract contained phenolic and flavonoid compounds.

Research carried out by Braga *et al.*[25] conducted isolation of pectin from *S. foetida* seeds. The pectin was purified using HPLC and tested on *Salmonella enterica ser typhi*, *Staphylococcus aureus*, *Escherichia coli* and *Klebsiella pneumoniae* bacteria. The results of the study showed that pectin had a high activity against *Salmonella enterica ser typhi* and *Klebsiella pneumoniae* bacteria with MIC of 12.34 μg mL^{-1} and 11.23 μg mL^{-1}, respectively.

The antibacterial mechanism is caused by the compounds in *S. quadrifida* and *S. foetida* extracts, it is said that the extract has polyphenol, flavonoid and alkaloid compounds[26]. Flavonoids and polyphenols, are reported to have mechanisms by inhibiting membrane disruption, antibiofilm, inhibition of cell envelope synthesis, inhibition of nucleic acid synthesis and inhibition of bacterial toxins[27]. Alkaloids are reported to have a mechanism through efflux pump inhibition; efflux inhibition is thought to occur due to downregulation and inhibition of efflux pump ATPases[28].

Immunomodulatory activities: It has been suggested that the use of *S. quadrifida* in immunomodulators may be beneficial, not only because of its antioxidant properties but also for the maintain endurance (Fig. 4). Utilization of faloak bark for various kinds of treatment allows the effect of treatment through an immunomodulatory mechanism. Herbs or plants that have been used extensively in ethnopharmacology are a potential source of immunomodulators. Water extract, 50% ethanolic extract and 96% ethanolic extract of *S. quadrifida* bark proved to have immunomodulatory activity *in vitro*, which can increase the activity of macrophage phagocytosis but cannot increase lymphocyte proliferation[29].

Other works have shown that some components of *S. quadrifid* may be crucial for its immunomodulatory activity, such as reported by Munawaroh *et al.*[30]. In his study reported ethyl acetate fraction has the highest phagocytic capacity of macrophages and total flavonoid levels compared to other fractions. The highest phagocytic capacity of macrophages was ethyl acetate fraction at a concentration of 250 μg mL^{-1} of 51.94±4.67%, the total flavonoid content of ethyl acetate fraction determined by the aluminum chloride method was 4.290±0.029 mg equivalent to quercetin/g fraction. There is a positive and strong correlation between total flavonoid extract and *S. quadrifida* fraction with the phagocytic capacity of macrophages.

More impressively, in a specific formulation, the combination of *S. quadrifida* and *P. niruri* was able to induce TNF-α and NF-κB, to *Mus musculus*[31]. The syrup dosage form of *S. quadrifida* and *P. niruri* extract modulating TNFα, NF-κB and increasing macrophage capacity were 535.98± 8.15%, 57.86±1.46% and 98.45±0.23%, respectively. Flavonoids have specific immunomodulatory effects, flavonoids on the immune system and then their impact on the mTOR pathway. Flavonoids can suppress mTOR activity and are consequently able to induce the T regulatory subset[32]. Flavonoids such as quercetin inhibited LPS-induced expression of TNF-α, IL-1β

and IL-6 by suppressing the activation of ERK and p38 MAP kinases in macrophages[33]. Many flavonoids exert their immunomodulatory effects by either inducing or decreasing the expression of pro-inflammatory cytokines such as TNF-α, IL-12, IL-6, IL-1β, TNF-α and IFN-as well as expression of surface activation molecules such as CD80, CD86 and MHC Class I and II[34]. This response of the innate immune system forms the first line of defense against pathogens and also plays a critical role in initiating the adaptive immune response.

Cytotoxic activities: Several studies have shown extracts and fractions of *S. quadrifida* to have cytotoxic activity. Rollando and siswadi[35] reported that ethanol extracts from *S. quadrifida* stem bark were able to inhibit the development of T47D breast cancer cell line with IC_{50} of 32.45 μg mL^{-1}. In addition, the fraction separated by preparative TLC showed that fraction number 4 had an IC_{50} of 21.89 μg mL^{-1}. In addition, another study reported that ethyl acetate fraction from *S. quadrifida* bark was able to inhibit the development of T47D breast cancer cell line with IC_{50} 24.88 μg mL^{-1} and selectivity index of 15.58. The ethyl acetate fraction was also able to induce cell arrest in the S phase, with a percentage of 27.43% and induce an apoptosis process of 11.88%[4].

Novita Sari[36] studied the effect of ethanol extract of *S. quadrifida* bark on the Hela cell line and it was reported that ethanol extract had an IC_{50} of 2,221,849 μg mL^{-1}. The active compound from *S. quadrifida* bark was only published by Rollando and Alfanaar[37], studied *S. quadrifida* bark having naptokuinon compounds, 2,3-dihydro-6-hydroxy-2-methylenenaphtho [1,2-b] furan-4,5 -dione with IC_{50} in breast cancer cells was 9.88 μg mL^{-1} and with an index selectivity value of 30.23. Studies of active compounds from *S. quadrifida* bark are still not widely explored and it is hoped that many studies will examine this active compound.

The *S. foetida* is reported to have cytotoxic activity in several cancer cell lines. Jafri *et al.*[38] in their study reported that ethanol extracts of *S. foetida* seeds were able to inhibit the development of MG-63 osteosarcoma cell lines by 51.33%. The ethanol extract of *S. foetida* seeds has the compound 3-Hydroxybutanoic acid Phenol, 2-methoxbenzene, 1-methoxy-4- (2-propenyl) 2,3-Dihydro-benzofuran2-Methoxy-4-vinylphenoPhenol, 2,6-dimethoxy-Cymen-7-ol. In addition, Stercufoetin A was isolated from the ethanol extract of *S. foetida* leaves. The compound has cytotoxic activity against MCF-7 and HepG2 cell lines with IC_{50} of 10.09±2.72 and 10.88±7.86[39].

Recently, Rajasekharreddy and Rani[40] in their study of the fabrication of Ag nanoparticles from ethanol extracts of *S. foetida* seeds (Ag-PL NPs). It was reported that there is an increased effect when extracts are made in Ag nanoparticles. The results show HeLa cell proliferation was significantly inhibited (>90%) by Ag-PL NPs at the concentration of 16 μg mL^{-1}.

Reportedly *S. quadrifida* bark has polyphenol and flavonoid compounds[41]. Some phenolic compounds and flavonoids from plants are used as chemotherapy drugs either in the form of original structures or after undergoing structural modification. It has been reported that phenolic compounds and flavonoids act as strong anticancer compounds by modulating the genes responsible for the transformation or growth and development of normal cells into cancer, metastasis and angiogenesis[42]. More specifically, phenolic compounds and flavonoids act on cell cycle pathway signaling molecules (Cyclin-Dependent Kinases (CDKs), angiogenesis factors (VEGF, FGFR1 and MIC-1), cell proliferation regulators (Erk1/2), oncogenic survival kinases (PI3K, Actions), transcription factors (NF-kβ, NRF2, STATs), death receptors (TRAIL), cytochrome c mitochondria, tumor suppressor proteins (p53, PTEN, p21) to control cancer development and metastasis. In addition, natural products are increasingly important in some last day due to reduced side effects[43-45].

S. quadrifida and *S. foetida* have the potential to be used as herbal medicines. However, there are still a few things missing. For instance, it is still unknown extracts of *S. quadrifida* and *S. foetida* have hepatotoxic activity and can cause damage to the kidneys, so further research is needed. In addition there have never been studies of teratogenic testing, to test the safety of using *S. quadrifida* and *S. foetida* for pregnant women. This still has great potential for research. On the other hand, the antioxidants, antibacterial, immunomodulatory and antitumor activities of *S. quadrifida* and *S. foetida* may be more effectively used in the development of new research. Especially for traditional medicine industries that can utilize these plants to make pharmaceutical products that have good bioactivity and have low side effects.

CONCLUSION

In vitro and *in vivo* studies of *S. quadrifida* R.Br and *S. foetida* Linn have provided evidence of its antioxidant, antibacterial, immunomodulatory and cytotoxic activity. Antioxidant activity studies show that the leaves, bark and seeds of the *S. quadrifida* R.Br and *S. foetida* Linn. have a high ability to inhibit DPPH free radicals and reduce FRAP. Investigation of antibacterial activity showed ethanol extract

from the stem bark of *S. quadrifida* R.Br inhibited the growth of gram-positive and negative bacteria. *S. foetida* Linn seeds contain pectin compounds that inhibit the growth of *Salmonella enterica* ser typhi and *Klebsiella pneumoniae* bacteria with MIC of 12.34 and 11.23 μg mL^{-1}. Immunomodulatory activity studies show ethyl acetate fraction of the stem bark of *S. quadrifida* R.Br has the highest phagocytic capacity of macrophages. The combination of *S. quadrifida* and *P. niruri* extracts increases TNFα, NF-κB and macrophage capacity. Cytotoxic test on *S. quadrifida* bark extract reported being able to inhibit the growth of T47D and Hela cells. Ethanol extract from *S. foetida* leaves inhibits the growth of MCF-7 and HepG2 cells.

SIGNIFICANCE STATEMENT

This study discovered the antioxidant, antibacterial, immunomodulatory and cytotoxic activity of *S. quadrifida* R.Br and *S. foetida* Linn. It can be beneficial for scientific information and the development of both plants for medical use. This study will help the researchers to uncover the critical areas of using natural substances as drugs that many researchers were not able to explore. Thus a new theory on activities *in vitro* and *in vivo* may be arrived at.

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