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Review on Phytochemicals and Pharmacological Activities of *Syzygium aromaticum*

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ABSTRACT

Backgrounds: *Syzygium aromaticum L* (*S. aromaticum,* clove) is a plant species belonging to the *Myrtaceae* family. It is cultivated in many African and Asian countries. Folk medicine practitioners use different parts of this plant to treat gastrointestinal problems, diarrhea, dental pain, ulcer, and other chronic diseases. Experimental data on phytochemicals and pharmacological activities of this plant are scattered or unsystematic. Therefore, this review aimed to explore the available data on phytochemicals and pharmacological activities of *S. aromaticum* essential oil and extracts with various polarities.

Materials & Methods: The literature review showed that only a few studies were conducted on this plant; consequently, there is not enough documented information about its bioactive phytochemicals and pharmacological activities.

Findings: Most previous studies reviewed reported significant bioactive phytochemical contents, namely eugenol (49.7%), caryophyllene (18.9%), benzene, and 1-ethyl-3-nitro (11.1%), along with minor amounts of phytochemicals including carotenoids, gallic acid, flavonoids, oxalic acid, tannins, amino acids, fatty acids, and cyanidin glycoside. Sugars, coumarins, oleanolic acid, saponins, glycosides, and lipids were also identified in this species. The methanol extract of this plant and its different polar fractions were shown to exhibit significant antimicrobial, antioxidant, anti-allergic, antidiabetic, antihypertensive, anti-inflammatory, antifungal, and anticancer activities. Furthermore, the plant extracts were also shown to have chemoprotective and hepatoprotective properties.

Conclusion: This review provides comprehensive data on botanical aspects, phytochemicals, and pharmacological activities of this plant to researchers to explore traditional/ medicinal uses and commercial drug production from *S. aromaticum*.

Keywords: *S. aromaticum,* Phytochemicals, Pharmacological activity, Traditional use, Drug discovery..

CITATION LINKS

[1] Batiha GE, Alkazmi LM, Wasef LG, Besh ... [2] Shi QW, Li LG, Huo CH, Zhang ML, Wang ... [3] Fabricant DS, Farnsworth NR. The valu ... [4] Alves RR, Rosa IM. Biodiversity, trad ... [5] Rahman MM, Uddin MJ, ... [6] Hossain MA*, Alrashdi YBA, Al-Touby SSJ. A review on... [7] Akkol EK, Tatlı II, Karatoprak GŞ, Ağ ... [8] Bari MS, Khandokar L, ... [9] Chowdhury KH, Chowdhury R, Hasan M, U ... [10] Gusain P, Uniyal DP, ... [11] Kaur K, Kaushal S. Phytochemistry and ... [12] Alma MH, Ertas M, Nitz S, Kollmannsbe ... [13] Banerjee S, Panda CK, Das S. Clove ... [14] Mishra RK, Singh SK. Reproductive eff ... [15] Board N. Handd book on spices. India, D ... [16] Schmid R. A resolution ... [17] Hossain MA, Al-Hashmi RA, Weli AM, Al ... [18] Kamatou GP, Vermaak I, Viljoen... [19] Kasai H, Shirao M, Ikegami-Kawai M. A ... [20] Komuraiah B, Chinde S, Kumar AN, Srin ... [21] Nigam V, Nigam R. Distribution and me ... [22] Sobeh M, Mahmoud MF, Petruk G, Rezq S ... [23] Chagas VT, França LM, Malik S, Paes A ... [24] Mittal M, Gupta N, Parashar P, Mehra ... [25] Bhakta S, Das SK. In praise of... [26] Rojas DF, de Souza CR, Oliveira WP. C ... [27] Burt S. Essential oils: their antibacterial... [28] Choi D, Roh HS, Kang DW, Lee JS... [29] Al-Shabibi MHS, Al-Touby SSJ, Hossain MA... [30] Chaieb K, Hajlaoui H, Zmantar T, Kahl ... [31] Kim HM, Lee EH, Hong SH, Song HJ, Shi ... [32] Pino JA, Marbot R, ... [33] Gopalakrishnan N, Narayanan CS, Mathe ... [34] Hossain MA, ... [35] Amri FS, Hossain MA. Comparison of to ... [36] Maisa SS, Al-Touby SS... [37] Al-Qassabi JS, Weil AM, Hossain MA. C ... [38] Adefegha SA, Oboh G, Oyeleye SI. Osun ... [39] Shah MD, Hossain MA. Total flavonoids ... [40] Hossain MA, Akhtar MS, Said S, Al-Abr ... [41] Adaramola B, Onigbinde A. Effect of e ... [42] Wahyulianingsih W, Handayani S, Malik ... [43] Sharma S, Mehta BK, Mehta D, Nagar H, ... [44] Ediriweera ER, Ratnasooriya WD. A rev ... [45] Toda M, Kawabata J, Kasai T. Alpha-gl ... [46] Park MJ, Gwak KS, Yang I, Choi... [47] Radünz M, ... [48] Jimoh SO, Arowolo LA, Alabi KA. Phyto ... [49] Mohamed SG, Badri AM. Antimicrobial a ... [50] Saikumari D, Shiva Rani SK, Saxena N. ... [51] Hina S, Rehman K, Shahid M, Jahan N. ... [52] Abd El Azim MH, El-Mesallamy... [53] Kumar PS, Febriyanti RM, Sofyan FF, L ... [54] Regards JF, Baldovini N, Vidal N, Pie ... [55] Dwivedi V, Shrivastava R, Husain S, G ... [56] Jirovetz L, Buchbauer G, Stoilova I, Stoyanova A, Krastanov A, Schmidt... [57] Kuroda M, Mimaki Y, Ohtomo T, Yamada ... [58] Prasad RC, ... [59] Adefegha SA, Oboh G, Adefegha OM, Bol ... [60] Roman RR, ... [61] Araujo AF, Ribeiro-Paes JT, Deus JT, ... [62] Warikoo R, Ray A, Sandhu JK, Samal R, ... [63] Fayemiwo KA, Adeleke MA, Okoro OP, Aw ...

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Introduction

Natural products, namely plant parts, animal organs, microorganisms, and marine resources, have been used in different alternative healing systems to prevent, relieve, and treat diseases since ancient times [1]. According to previous records, people used plants and their derived products as medicines in different alternative systems 60,000 years ago [2, 3]. Drugs derived from natural products are used to treat various diseases in Chinese medicine, Ayurveda, aromatherapy, acupuncture, and Korean and Unani medicine [2].

Natural resources are a crucial source of alternative safe medicines. They play a primary role in health sectors due to their healing and medicinal values [2-6]. Plants and their derived products are used as medicines in primary health care in most developing countries due to their better acceptability, compatibility, adaptability to the human body, and negligible adverse effects [7-9]. For decades, plants have been widely used as medicines due to their bioactive ingredients isolated from plant parts and used to treat human diseases. In addition, some medicinal plants have edible fruits, and others have attractive flowers [2, 4].

Plant-based medicines have always played a vital role in human health care, and their therapeutic role in different cultures is often well documented [4, 5]. According to the International Union for Conservation of Nature and the World Wildlife Fund, there are between 50,000 and 80,000 flowering plant species used for medicinal purposes worldwide [10]. It is estimated that more than 25% of prescription drugs available worldwide are derived from medicinal plants. Many studies have been conducted on medicinal plants and their active ingredients. Even in the allopathic treatment system, interest in medicinal plants has recently increased [11-13].

Syzygium aromaticum is a medicinal plant. Its common name is clove. It has several common names based on its geographical distribution, namely Cengkih, Kronfol, Chengkeh, Clove, Chingkeh, 丁香, and many others [14]. The selected plant species belongs to the *Syzygium* genus and the *Myrtaceae* family. A brief scientific classification of *S. aromaticum* is presented in Table 1.

Table 1) Scientific classification of *S. aromaticum*

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperms
Clade	Eudicots
Clade	Rosids
Order	Myrtales
Family	Myrtaceae
Genus	*Syzygium*
Species	*S. aromaticum*

The plant species is indigenous to North Maluku Islands in Indonesia. The largest clove-producing countries are Indonesia, Madagascar, and the United Republic of Tanzania. Some wild varieties of clove are found in Bacan, Ternate, Motor, Tidore, Makian, and Irian Jaya in Indonesia. Clove is cultivated commercially in Karnataka, Tamil Nadu, and Kerala states. India is the second largest clove consumer after Indonesia [15].

Morphology: The selected *S. aromaticum* species is endemic to North Maluku Islands, Indonesia. It belongs to the *Syzygium* genus [16], the largest genus of the *Myrtaceae* family. Clove is only one of the many species of the *Syzygium* genus, which has outstanding economic and medicinal values. Its scientific name is *Syzygium aromaticum* [17]. The selected plant is cultivated in humid tropical or subtropical countries. The clove tree is a large evergreen tree that grows up to 8–12 meters in height. It has large leaves and clusters of red flowers at the end of the branches. Initially, the buds are pale in col-

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or, then they change to green and finally, the buds become bright red as they mature. The buds are customarily harvested when they are about 1.5–2 cm long. A bud consists of a long calyx with four spreading sepals and four unopened petals with a small ball in the center. The plant could be propagated by cutting, grafting, seeding, and air-layering. The oppositely arranged leaves are usually 15 inches long and 5 inches wide [18]. Its flowering period is from early April to August, and the plant has yellowish flowers, which are 2.5 cm in diameter. A flower usually consists of more than 20 petals. The calyx is green and turns to yellow color during maturity. The trees of this plant bring their first flowers at the age of seven and continue to do so for more than 80 years [19]. Their juicy and sweet purple fruits contain two cotyledons.

Geographical distribution: Due to its economic and medicinal values, the selected plant is one of the most valuable spices worldwide. Various synonymous names are used for the clove, like *Caryophyllus aromaticus, Caryophyllus silvestris, Eugenia caryophyllus, Jambosa caryophyllus,* and *Myrtus caryophyllus.* The plant species *S. aromaticum* is native to Indonesia but has spread to other countries such as India, Malaysia, Sri Lanka, Tanzania, and many others [16]. This tree grows well throughout the Asian sub-continent and several other tropical or subtropical countries [20, 21].

Traditional uses: *S. aromaticum* is one of the most popular spices in the world. It is used in both savory dishes and desserts worldwide [22]. Furthermore, it is a frequent component of herbal teas and perfumes. Traditionally, clove has been used in Western, Chinese, and Ayurveda medicine for centuries. Due to their eugenol content, clove extracts and essential oil are widely used as analgesics, especially for dental problems. In this review, many reports were published about the antidiabetic properties of this plant crude extracts and essential oil [23]. In addition, they are also used as a natural stimulant and anthelmintic. Some reviewed studies reported antidepressant, antithrombotic, and antiulcer properties of this plant [24, 25]. Crude extracts and essential oil of *S. aromaticum* are frequent components of various pharmaceutical preparations due to their carminative, anti-inflammatory, and antifungal properties [26, 27].

Phytochemicals: The major group of compounds in the selected plant is the group of flavonoids. They are naturally occurring polyphenols. They have significant antioxidant, antimicrobial, antiviral, anti-inflammatory, cytotoxic, antidiabetic, antifungal, antihypertensive, and anti-allergic activities. In addition, these compounds also show potential anticancer, antiulcer, antidiarrheal, antipyretic, and gastro-protective activities [28-31]. More than 100 chemical compounds are present in crude extracts of *S. aromaticum* with various polarities. Among them, there are about 20 chemical compounds in significant amounts. The rest are minor chemical compounds based on LC-MS/MS (liquid chromatography–tandem mass spectrometry) analysis. Polar extracts such as methanol, chloroform, ethyl acetate, and butanol extracts contain most of the bioactive flavonoids and their glycoside derivatives. The major chemical compounds are flavonoids, namely myricetin rhamnoside (flavonoids glycoside), myrigalone glycoside, quercetin glycoside, myrigalone-B, and myrigalone-G [29, 32, 33]. In addition, three flavonoids benzaldehyde-4-hydroxy, 3,5,7-trihydroxy-3-O-rhamnoside, and pentahydroxy-3-O-rhamnoside are also isolated from the ethanol extract of the selected plant leaves. According to LC-MS/MS analysis, the plant extracts contain more than 100 compounds; however, only significant phytochemicals are presented in Table 2.

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Essential oil: According to GC-MS/MS analysis, *S. aromaticum* essential oil contains more than 73 compounds. Most of which are monoterpenes, sesquiterpenes, and their oxygenated derivatives [29-33]. A total of 10 major compounds representing 92% of the total *S. aromaticum* essential oil include: eugenol (49.7%), α-pinene (6%), chavibetal (9.7%), α-penten-3- ol (13%), β-caryophyllene (6.5%), camphene (11%), eugenol acetate (8.01%), β-pinene (2.19%), trisiloxane 1, 1, 1, 5, 5, 5-hexamethyl-3,3-bis [(trimethylsilyl)oxy] (1.7%), limonene (1.28%.), menthone (1.99%), and cis-2-octenal (1.29%) (Table 3). Other chemical constituents such as α-cadinol, myristicin, δ-cadinene, and τ-muurolol are also detected in small concentrations (less than <1%) [29-34].

Total phenol content: In some reviewed studies, the total phenol content of the plant extracts with different polarities and concentrations was determined by spectroscopic method using Folin-Ciocalteu reagent (FCR) as described by several authors [35-37]. The gallic acid standard curve was used to calculate the total phenol contents expressed as mg gallic acid equivalents per gram of extract. In this review, previous studies on this plant crude extracts showed that all polar extracts, namely hexane, chloroform, ethyl acetate, butanol, and water extracts, had significantly high phenol contents. It was also noticed that the most polar extract (water extract) had the highest total phenol content compared to the other extracts, while the hexane extract contained the lowest total phenol content. It means that most of the phenolic ingredients of the selected plant are soluble in water solvent. The order of total phenol content in different extracts was reported to be as follows: water> butanol> ethyl acetate> chloroform>hexane extract [38]. However, in this study, no report on the total phenol content of the selected plant essential oil was found in the literature. Generally, the total phenol content varied from region to region, which could be due to geographical or genetic differences [38].

Total flavonoid content: In some reviewed studies, the total flavonoid content of the plant extracts with different polarities and concentrations was determined by spectroscopic method using aluminum chloride ($AlCl_3$) as described by several authors [39, 40]. The quercetin standard curve was used to calculate the total flavonoid contents expressed as mg quercetin equivalents per gram of extract. In this review, previous studies on this plant crude extracts showed that all polar extracts had moderate total flavonoid contents in the range of 1.25-2.33 mg/g [41, 42]. It was also shown that the total flavonoid content was higher in the water extract than in the other extracts, while the hexane extract contained the lowest total flavonoid content. The order of total flavonoid content in different extracts was reported to be as follows: water> butanol> ethyl acetate> chloroform> hexane extract [42]. However, in this study, no report on the total flavonoid content of the selected plant essential oil was found in the literature. Generally, the total flavonoid content varied from region to region, possibly due to geographical or genetic differences [39-42].

Biological activities: Generally, biological activities depend on the chemical ingredients of the plant. The selected plant extracts and essential oil were shown in reviewed studies to have promising activities, namely antifungal, antibacterial, diuretic, anti-nociceptive, anticancer, antitumor, cardioprotective, antioxidant, kidney reinforcement, antiseptic, anesthetic, hypothermic, anti-inflammatory, chemoprotective, antiviral, anti-vomiting, analgesic, antispasmodic, and repellent activities [43-46]. Some of the specific biological activities of the selected plant essential oil and extracts with various polarities are described in detail below.

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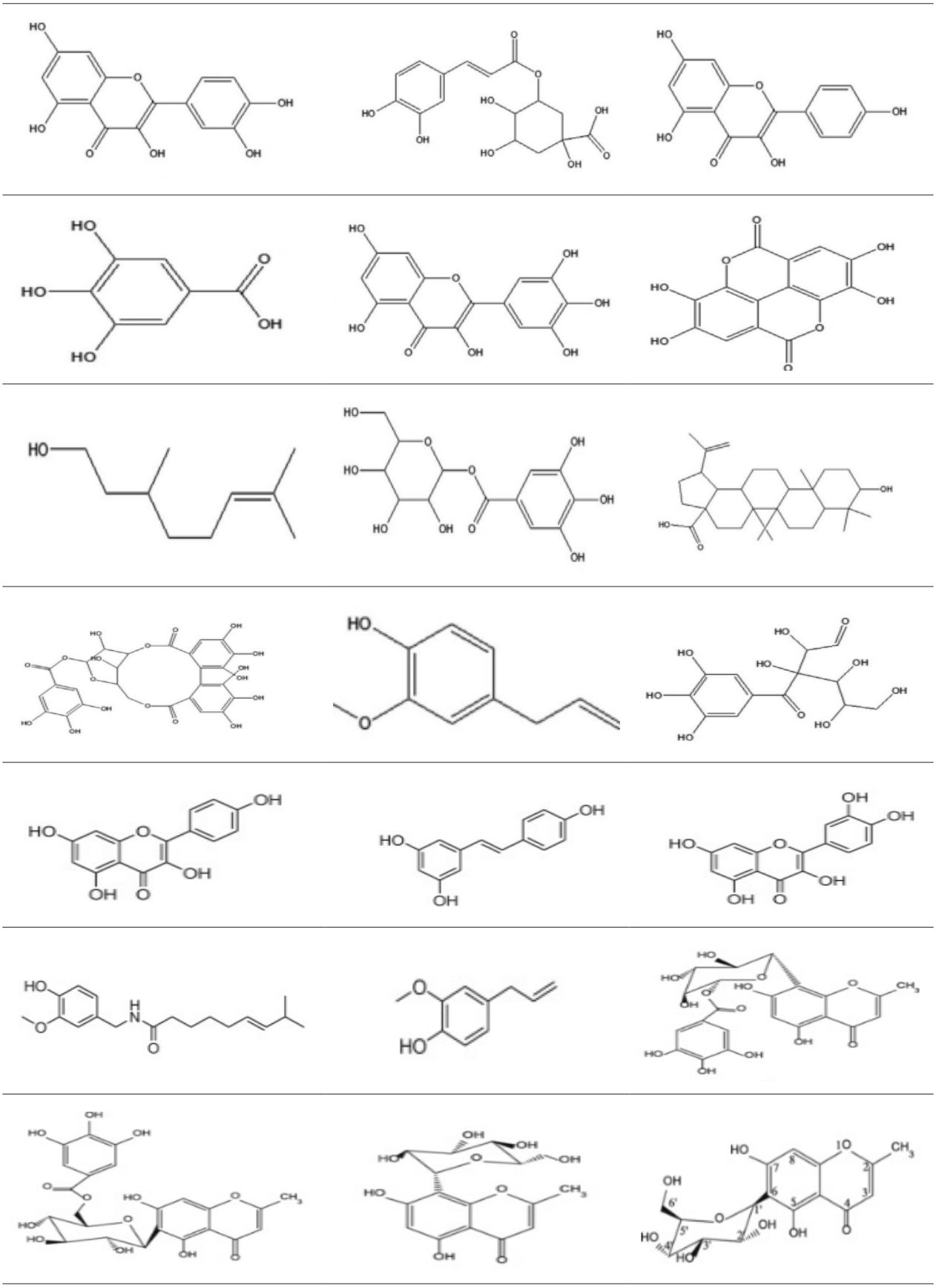
Table 2) Major phenolic derivatives in the extracts of S. *aromaticum*



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Antibacterial activity: In this review, the antibacterial activity of *S. aromaticum* essential oil and extracts with different polarities and concentrations was investigated in several studies using the agar gel diffusion method [47-50]. Previous reports reviewed in this study showed good antibacterial activity for the essential oil isolated from cloves [48, 49]. The antibacterial effects of clove essential oil at different concentrations was investigated [48, 49] against Gram-positive (*Listeria innocua, Carnobacterium divergens,* and *Staphylococcus aureus*) and Gram-negative (*Salmonella typhimurium, Escherichia coli, Serratia liquefaciens,* and *Shewanella putrefacians*) bacteria in some studies, the results showed the promising growth inhibitory activity against all the applied bacteria. According to the literature, the promising antimicrobial activity of this essential oil is due to the presence of chemical ingredients, mainly eugenol, eugenol acetate, kaempferol, gallic acid, iso-eugenol, and oleanolic acid [48]. The mentioned ingredients are denatured proteins that change the absorption capacity of the cell membrane. Similarly, some reviewed studies investigated the antifungal activities of clove essential oil against five human foodborne pathogenic fungi, namely *Candida albicans*, *Epidermophyton floccosum*. *Microsporum audouinii*, *Trichophyton mentagrophytes*, and *T. rubrum*. The results showed the outstanding antifungal activity of this essential oil at various concentrations. On the contrary, moderate antimicrobial activity was reported in these studies for clove extracts with different polarities and concentrations against Gram-positive and Gram-negative bacterial and fungal strains [49,50].

Antioxidant activity: Antioxidants are responsible for protecting the human body against diseases associated with the attack of free radicals. Therefore, daily consumption of plant-derived antioxidants could protect or prevent diseases such as cancer, Parkinson's disease, Alzheimer's disease, or atherosclerosis as they are triggered by oxidative stress [47, 51]. Several electron transfer methods such as Trolox equivalent antioxidant capacity (TEAC) decolorization, ferric reducing antioxidant power (FRAP), 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging, and copper (II) reduction capacity are used to evaluate the antioxidant activity of plant extracts and essential oils. The antioxidant activity of the selected plant extracts was evaluated in some reviewed studies using ferric reducing antioxidant power (FRAP), DPPH free radical scavenging, and copper (II) reduction capacity methods [51, 52]. In these studies, all the applied methods yielded almost similar results within the range of 89 to 94% (compared to the gallic acid standard) for the antioxidant activity of these extracts [51], and the water extract showed the highest antioxidant activity, while the hexane extract showed the lowest antioxidant activity. The order of antioxidant activity of different extracts was reported to be as follows: water> butanol> ethyl acetate> chloroform> hexane extract [51, 52]. These findings are directly correlated with the total phenol and flavonoid contents. In conclusion, these findings show that the antioxidant activity of the essential oil and crude extracts with various polarities and concentrations is influenced by the total phenol and flavonoid contents of *S. aromaticum*.

Anticancer activity: *In vitro* anticancer activity of different concentrations of hexane, chloroform, ethyl acetate, butanol, methanol, and water extracts and essential oil of *S. aromaticum* was evaluated in some reviewed studies using brine shrimp lethality test (BSL) and MCF-7 breast cancer cell line [52-56]. In these studies, the essential oil at various concentrations in both methods showed significant cytotoxic effects. Banerjee et al.

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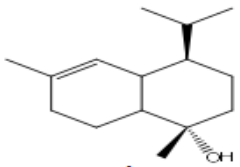
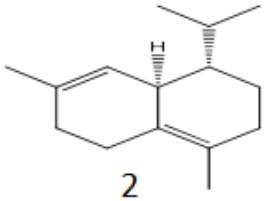
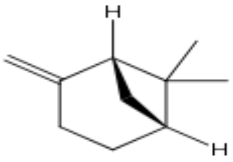
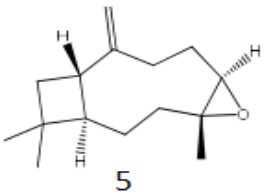
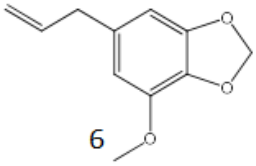
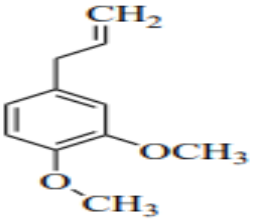
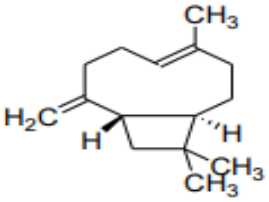
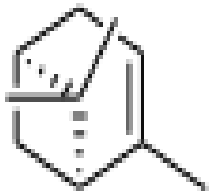
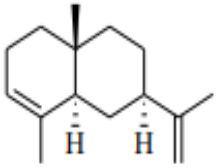
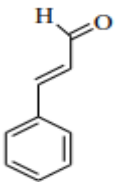
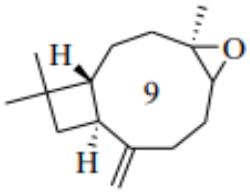
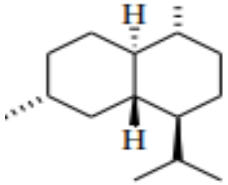
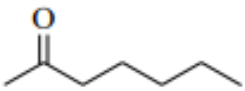
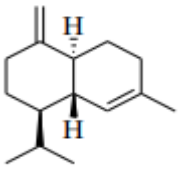
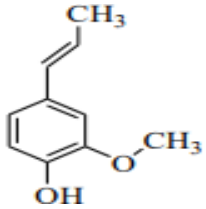
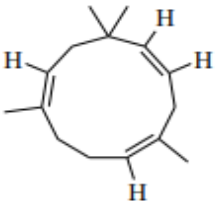
Table 3) Major chemical constituents in the essential oil of S. aromaticum

 1	 2	 3	 5
 6	 7	 8	 9
 10	 11	 12	 13
 14	 15	 16	 17

(2006) [56] reported that polyphenols and terpenoid ingredients showed antitumor and anticancer activities in both cell lines and tumors; in addition, the crude extracts of the selected plant species also showed promising *in vitro* cytotoxic activity in the BSL method [55]. In their study, most polar extracts, namely acetate, butanol, methanol, and water extracts, showed almost maximum similar cytotoxic activity [55, 56]. However, the literature showed that the hexane and chloroform extracts had minimum anticancer activity in the BSL method [56]. Therefore, all polar extracts contain toxic ingredients that could kill shrimp nauplii. These results are directly correlated with the total phenol and flavonoid contents. Therefore, the cytotoxic activity of essential oil and crude extracts with different polarities and concentrations is influenced by the combined effect of the total phenol and flavonoid contents of *S. aromaticum*. In conclusion, polar extracts could be used to isolate toxic ingredients, which may treat cancer cells.

Antidiabetic activity: Currently, several medicinal plants are traditionally used to treat diabetic patients. In alternative treatment systems, plants and plant extracts are used as medicine. Scientists have recently been looking for new plant ingredients

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to treat diabetic patients, and as a result, various plants have been reported to have promising antidiabetic activity. *S. aromaticum* is one of these plants that may serve as a safe and natural source for developing novel oral hypoglycemic drugs. The *in vitro* method was used in some reviewed studies to determine the antidiabetic activity of the plant crude extracts with different polarities against alpha-glucosidase and alpha-amylase enzymes [57-60]. In these studies, all polar extracts, such as methanol, water, ethyl acetate, and butanol extracts, showed the maximum activity against alpha-glucosidase and alpha-amylase enzymes [60], and fasting blood sugar and glycosylated hemoglobin levels were rapidly reduced (compared to the control group) when the polar extract of the selected plant (250 mg/kg body weight concentration) was administered to alloxan-induced mice [57-60]. The above experiments show that *S. aromaticum* extracts with different polarities exhibit potential hypoglycemic activity. Therefore, the potential hypoglycemic activity of the plant extracts and essential oil at different concentrations is influenced by the direct combined effect of the total phenol and flavonoid contents. In conclusion, polar extracts could be used to isolate effective ingredients to treat diabetic patients.

Larvicidal Activity: Mosquitoes are carriers of various diseases, namely dengue fever, chikungunya, encephalitis, and malaria [61]. In most countries, harmful chemicals are usually used to kill larvae. As a result, many other species are also killed, and even worse, mosquitoes have developed resistance against insecticides. Therefore, one of the best options is to use a larvicidal plant extract instead of insecticides to kill harmful insects [62, 63]. In this review, different extracts of *S. aromaticum,* namely hexane, dichloromethane, chloroform, ethyl acetate, butanol, methanol, and water extracts, were used in some studies to evaluate their larvicidal activity against mosquito vectors [63]. In addition, the larvicidal activity of the leaf essential oil was also tested. In these studies, the extracts and the essential oil caused 100% mortality in larvae [63]. These results show that the extracts and essential oil of *S. aromaticum* could be used as a potent natural source for manufacturing safe larvicidal agents.

Conclusion

Traditionally, all parts of *S. aromaticum* and its extracts are used as medicine in different traditional treatment systems to treat diabetes, inflammation, allergies, viral infection, and gastric ulcer. The literature review showed that the plant extracts and essential oil contain biologically active compounds used globally as prescription drugs. In addition, the plant extracts and essential oil were shown in some studies to exhibit significant pharmacological activities, including antifungal, antibacterial, diuretic, anti-nociceptive, anticancer, antitumor, cardioprotective, antioxidant, kidney reinforcement, antiseptic, anesthetic, hypothermic, anti-inflammatory, chemoprotective, antiviral, anti-vomiting, analgesic, antispasmodic, and repellent activities. The following phytochemicals were isolated from the selected plant extracts and essential oil: eugenol, β-caryophyllene, pinene, myricetin rhamnoside, myrigalone glycoside, quercetin glycoside, myrigalone-B, and myrigalone-G. All phytochemicals showed significant pharmacological activities, so that they are currently used as medicine in different treatment systems to treat different ailments. According to previous reports, the plant extracts and phytochemicals could be use as a good source for the development of new pharmaceutical drugs. Animal studies on phytochemicals and their specific pharmacological activities are still pending. Therefore, the present re-

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view will help future generations investigate the pharmacological activities of the plant extracts and isolated pure compounds. This review also helps better use phytochemicals in the pharmaceutical, agrochemical, and cosmetics industries.

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References

1. Batiha GE, Alkazmi LM, Wasef LG, Beshbishy AM, Nadwa EH, Rashwan EK. *Syzygium aromaticum* L. (Myrtaceae): Traditional uses, bioactive chemical constituents, pharmacological and toxicological activities. Biomolecular. 2020;10(2):202-18.
2. Shi QW, Li LG, Huo CH, Zhang ML, Wang YF. Study on natural medicinal chemistry and new drug development. Chin Tradit Herb Drugs. 2010;41(10):1583–9.
3. Fabricant DS, Farnsworth NR. The value of plants used in traditional medicine for drug discovery. Environ Health Perspect. 2001;109(Suppl 1):69–75.
4. Alves RR, Rosa IM. Biodiversity, traditional medicine and public health: Where do they meet? J Ethnobiol Ethnomed. 2007;3:14-23.
5. Rahman MM, Uddin MJ, Reza AA, Tareq AM, Emran TB, Simal-Gandara J. Ethnomedicinal value of antidiabetic plants in Bangladesh: A comprehensive review. Plants. 2021;10(4):729.
6. Hossain MA*, Alrashdi YBA, Al-Touby SSJ. A review on essential oil analyses and biological activities of the traditionally used medicinal plant Thymus vulgaris L. Int J Second Metabol. 2022; 9(1): 103–111.
7. Akkol EK, Tatlı II, Karatoprak GŞ, Ağar OT, Yücel Ç, Sobarzo-Sánchez E, et al. Is emodin with anticancer effects completely innocent? Two sides of the coin. Cancers. 2012;13(11):2733.
8. Bari MS, Khandokar L, Haque E, Romano B, Capasso R, Seidel V, et al. Ethnomedicinal uses, phytochemistry, and biological activity of plants of the genus Gynura. J Ethnopharmacol. 2021;271:113834.
9. Chowdhury KH, Chowdhury R, Hasan M, Uddin MJ, Hasan Z, Nasrin S, et al. Xylia xylocarpa (Roxb.) Taub. leaves ameliorates inflammation and pain in experimental mice and computer-aided model. Walailak J Sci Technol. 2021;18(15):1-13.
10. Gusain P, Uniyal DP, Joga R. Conservation and sustainable use of medicinal plants. In: Preparation of phytopharmaceuticals for the management of disorders. The Netherlands, Amsterdam: Elsevier; 2021, p. 409-427.
11. Kaur K, Kaushal S. Phytochemistry and pharmacological aspects of Syzygium aromaticum: A review. J Pharmacogn Phytochem. 2019;8(1):394-406.
12. Alma MH, Ertas M, Nitz S, Kollmannsberger H. Chemical composition and content of essential oil from the bud of cultivated Turkish clove (Syzygium aromaticum L.). Bioresources. 2007;2(2):265-9.
13. Banerjee S, Panda CK, Das S. Clove (Syzygium aromaticum L.), a potential chemopreventive agent for lung cancer. Carcinogenesis. 2006;27(8):1645-54.
14. Mishra RK, Singh SK. Reproductive effects of lipid-soluble components of Syzygium aromaticum flower bud in male mice. J Ayurveda Integr Med. 2013;4(2):94-8.
15. Board N. Handbook on spices. India, Delhi: Asia Pacific Business Press Inc; 2010, p. 199-213.
16. Schmid R. A resolution of the Eugenia–Syzygium controversy (Myrtaceae). Am J Bot. 1972;59(4):423–36.
17. Hossain MA, Al-Hashmi RA, Weli AM, Al-Riyami Q, Al-Sabahib JN. Constituents of the essential oil from different brands of Syzygium caryophyllatum L by gas chromatography-mass spectrometry. Asian Pac J Trop Biomed. 2012;2(3):S1446–9.
18. Kamatou GP, Vermaak I, Viljoen AM. Eugenol-from the remote Maluka Islands to the international market place: A review of a remarkable and versatile molecule. Molecules. 2010;17(6):6953-81.
19. Kasai H, Shirao M, Ikegami-Kawai M. Analysis of volatile compounds of clove (Syzygium aromaticum) buds as influenced by growth phase and investigation of antioxidant activity of clove extract. Flavour Fragr J. 2016;31(2):178-84.
20. Komuraiah B, Chinde S, Kumar AN, Srinivas K, Venu C, Kumar JK, et al. Isolation of phytochem-

[DOI: 10.52547/iem.9.1.87]

icals from anticancer active extracts of Syzygium alternifolium Walp. Leaf. Pharmacogn J. 2014;6(4):83–5.
21. Nigam V, Nigam R. Distribution and medicinal properties of Syzygium species. Curr Res Pharm Sci. 2012;2(2):73–80.
22. Sobeh M, Mahmoud MF, Petruk G, Rezq S, Ashour ML, Youssef FS, et al. Syzygium aqueum: A polyphenol-rich leaf extract exhibits antioxidant, hepatoprotective, pain-killing, and anti-inflammatory activities in animal models. Front Pharmacol. 2018;9:566-70.
23. Chagas VT, França LM, Malik S, Paes AM. Syzygium cumini (L.) skeels: A prominent source of bioactive molecules against cardiometabolic diseases. Front Pharmacol. 2015;6:259-64
24. Mittal M, Gupta N, Parashar P, Mehra V, Khatri M. Phytochemical evaluation and pharmacological activity of Syzygium aromaticum: A comprehensive review. Int J Pharm Pharm Sci. 2014;6(8):67-72.
25. Bhakta S, Das SK. In praise of the phytogenic medicinal plant Syzygium aromaticum: A review. Turk J Agric Food Sci Technol. 2021;9(10):1863-8.
26. Rojas DF, de Souza CR, Oliveira WP. Clove (Syzygium aromaticum): A precious spice. Asian Pac J Trop Biomed. 2014;4(2):90-6
27. Burt S. Essential oils: their antibacterial properties and potential applications in foods-a review. Int J Food Microbiol. 2004;94:223–253.
28. Choi D, Roh HS, Kang DW, Lee JS. The potential regressive role of Syzygium aromaticum on the reproduction of male golden hamsters. Dev Reprod. 2014;18(1):57~64.
29. Al-Shabibi MHS, Al-Touby SSJ, Hossain MA. Isolation, characterization and prediction of biologically active glycoside compounds quercetin-3-rutinoside from the fruits of Ficus sycomorus. Carbohy Res. 2022; 511: 108483.
30. Chaieb K, Hajlaoui H, Zmantar T, Kahla-Nakbi AB, Rouabhia M, Mahdouani K, et al. The chemical composition and biological activity of clove essential oil, Eugenia cryophyllata (Syzygium aromatricum L. Myrtaceae): A short review. Phytother Res. 2007;21(6):501-6.
31. Kim HM, Lee EH, Hong SH, Song HJ, Shin MK, Kim SH, et al. Effect of Syzygium aromaticum extract on immediate hypersensitivity in rats. J Ethnopharmacol. 1998;60(2):125-31.
32. Pino JA, Marbot R, Aguero J, Fuentes V. Essential oil from buds and leaves of clove (Syzygium aromaticum (L.) Merr. et Perry) grown in Cuba. J Essent Oil Res. 2001;13(4):278-9.
33. Gopalakrishnan N, Narayanan CS, Mathew AG. Sesquiterpene hydrocarbons from clove oil. Lebensm Wiss Technol. 1984;17(1):42-3.
34. Hossain MA, Harbi SR, Weli AM, Al-Riyami Q, Al-Sabahi JN. Comparison of chemical constituents and antimicrobial activities of three essential oils from three different brands' clove samples collected from Golf region. Asian Pac J Trop Dis. 2014;4(4):262-8.
35. Amri FS, Hossain MA. Comparison of total pheo nols, flavonoids, and antioxidant potential of local and imported ripe bananas. Egypt J Basic Appl Sci. 2018;5(4):245-51.
36. Maisa SS, Al-Touby SS, Hossain MA. Total phenols content and antioxidant activity of different polarity crude extracts of Dodonaea viscosa. Indian Drugs, 2021;58(08):79-83.
37. Al-Qassabi JS, Weil AM, Hossain MA. Comparison of total phenols content and antioxidant potential of peel extracts of local and imported lemons samples. Sustain Chem Pharm. 2018;8:71–5.
38. Adefegha SA, Oboh G, Oyeleye SI. Osunmo K. Alteration of starch hydrolyzing enzyme inhibitory properties, antioxidant activities, and phenolic profile of clove buds (Syzygium aromaticum L.) by cooking duration. Food Sci Nutr. 2015;4(2):250-60.
39. Shah MD, Hossain MA. Total flavonoids content and biochemical screening of the leaves of tropical endemic medicinal plant Merremia borneensis. Arab J Chem. 2014;7(6):1034-8.
40. Hossain MA, Akhtar MS, Said S, Al-Abri TH. Two new flavonoids from Adenium obesum grown in Oman. J King Saud Univ Sci. 2017;29(1):62-9.
41. Adaramola B, Onigbinde A. Effect of extraction solvent on the phenolic content, flavonoid content, and antioxidant capacity of clove bud. IOSR J Pharm Biol Sci. 2016;11(3):33-8.
42. Wahyulianingsih W, Handayani S, Malik A. Penetapan kadar flavonoid total ekstrak daun cengkeh (Syzygium aromaticum (L.) Merr & Perry). J Fitofarmaka Indones. 2016;3(2):188-93.
43. Sharma S, Mehta BK, Mehta D, Nagar H, Mishra A. A review on pharmacological activity of Syzygium cumini extract using different solvents and their effective dose. Int Res J Pharm. 2012;3(12):54-8.
44. Ediriweera ER, Ratnasooriya WD. A review on herbs used in treatment of diabetes mellitus by Sri Lankan Ayurvedic and traditional physicians. Ayu. 2009;30(4):373-91.
45. Toda M, Kawabata J, Kasai T. Alpha-glucosidase inhibitors from clove (Syzgium aromaticum). Biosci Biotechnol Biochem. 2000;64(2):294–8.
46. Park MJ, Gwak KS, Yang I, Choi WS, Jo HJ, Chang JW, et al. Antifungal activities of the essential oils in Syzygium aromaticum (L.) Mar. Et Perry and Leptospermum petersonii Bailey and their constituents against various dermatophytes. J Microbiol. 2007;45(5):460–5.
47. Radünz M, da Trindade ML, Camargo TM, Radünz AL, Borges CD, Gandra EA, et al. Antimicrobial and antioxidant activity of unencapsulated and

[DOI: 10.52547/iem.9.1.87]

encapsulated clove (Syzygium aromaticum, L.) essential oil. Food Chem. 2019;276:180–6.
48. Jimoh SO, Arowolo LA, Alabi KA. Phytochemical screening and antimicrobial evaluation of Syzygium aromaticum extract and essential oil. Int J Curr Microbiol Appl Sci. 2017;6:4557-67.
49. Mohamed SG, Badri AM. Antimicrobial activity of Syzygium aromaticum and citrus aurantifolia essential oils against some microbes in Khartoum, Sudan. EC Microbiol. 2017;12:253-9.
50. Saikumari D, Shiva Rani SK, Saxena N. Antibacterial activity of Syzygium aromaticum L. (Clove). Int J Curr Microbiol Appl Sci. 2016;5(11):484-9.
51. Hina S, Rehman K, Shahid M, Jahan N. In vitro antioxidant, hepatoprotective potential, and chemical profiling of Syzygium aromaticum using HPLC and GC-MS. Pak J Pharm Sci. 2017;30(3):1031–9.
52. Abd El Azim MH, El-Mesallamy AM, El-Gerby M, Awad A. Antitumor, antioxidant, and antimicrobial and the phenolic constituents of clove flower buds Syzygium aromaticum. J Microb Biochem Technol. 2014;10:s8-007.
53. Kumar PS, Febriyanti RM, Sofyan FF, Luftimas DE, Abdulah R. Anticancer potential of Syzygium aromaticum L. in MCF-7 human breast cancer cell lines. Pharmacogn Res. 2014;6(4):350-4.
54. Regards JF, Baldovini N, Vidal N, Pietri S. Anticancer activities of essential oils constituents and synergy with conventional therapies: A review. Phytother Res. 2014;28(10):1423-46.
55. Dwivedi V, Shrivastava R, Husain S, Ganguly C, Bharadwaj M. Comparative anticancer potential of clove (Syzygium aromaticum) – an Indian species – against cancer cell lines of various anatomical origin. Asian Pac J Cancer Prev. 2011;12(8):1989-93.
56. Jirovetz L, Buchbauer G, Stoilova I, Stoyanova A, Krastanov A, Schmidt E. Chemical composition and antioxidant properties of Clove leaf essential oil. J Agric Food Chem. 2006;54:6303–6307.
57. Kuroda M, Mimaki Y, Ohtomo T, Yamada J, Nishiyama T, Mae T, et al. Hypoglycemic effects of clove (Syzygium aromaticum flower buds) on genetically diabetic KK-ay mice and identification of the active ingredients. J Nat Med. 2012;66:394–9.
58. Prasad RC, Herzog B, Boone B, Sims L, Waltner-Law M. An extract of Syzygium aromaticum represses genes encoding hepatic gluconeogenic enzymes. J Ethnopharmacol. 2005;96(1-2):295–301.
59. Adefegha SA, Oboh G, Adefegha OM, Boligon AA, Athayde ML. Antihyperglycemic, hypolipidemic, hepatoprotective, and antioxidative effects of dietary clove (Syzygium aromaticum) bud powder in a high-fat diet/streptozotocin-induced diabetes rat model. J Sci Food Agric. 2014;94(13):2726–37.
60. Roman RR, Flores-Saenz JL, Alarcon-Aguilar FJ. Anti-hyperglycemic effect of some edible plants. J Ethnopharmacol. 1995;48(1):25–32.
61. Araujo AF, Ribeiro-Paes JT, Deus JT, Cavalcanti SC, Nunes RDS, Alves PB, et al. Larvicidal activity of Syzygium aromaticum (L.) Merry and Citrus sinensis (L.) Osbeck essential oils and their antagonistic effects with temephos in resistant populations of Aedes aegypti. Mem Inst Oswaldo Cruz. 2016;111(7):443–9.
62. Warikoo R, Ray A, Sandhu JK, Samal R, Wahab N, Kumar S. Larvicidal and irritant activities of hexane leaf extracts of Citrus sinensis against dengue vector Aedes aegypti. Asian Pac J Trop Biomed. 2012;2(2):152–5.
63. Fayemiwo KA, Adeleke MA, Okoro OP, Awojide SH, Awoniyi IO. Larvicidal efficacies and chemical composition of essential oils of Pinus sylvestris and Syzygium aromaticum against mosquitoes. Asian Pac J Trop Biomed. 2014;4(1):30–4.

[DOI: 10.52547/iem.9.1.87]