RJC

RASĀYAN *J. Chem.*
Vol. 15 | No. 1 |1-11| January - March | 2022
ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
http://www.rasayanjournal.com
http://www.rasayanjournal.co.in

A REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF *Syzygium caryophyllatum*

Ramadevi Pemmereddy[1], K. S. Chandrashekar[1,✉], Sreedhara Ranganath K. Pai[2], Vasudev Pai[1], Anna Mathew[1] and B. Venkatesh Kamath[3]

[1]Department of Pharmacognosy, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, Karnataka, India
[2]Department of Pharmacology, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, Karnataka, India
[3]Department of Pharmaceutical Biotechnology, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal-576104, Karnataka, India
✉Corresponding Author:cksbhat@yahoo.co.in

ABSTRACT

Syzygium caryophyllatum, widely known as wild black plum, belongs to Myrtaceae. The tender leaves of *Syzygium caryophyllatum* are commonly used by folklore practitioners, particularly for stomatitis, diarrhea, blood-mucous stools, wounds, and ulcers. The plant contains numerous bioactive constituents like terpenoids, carotenoids, flavonoids, coumarins, saponins, glycosides, amino acids, sugars, fatty acids, lipids in significant amounts. The plant has reported anti-microbial effects, antioxidant, antidiabetic, and anticancer activities. The present review describes the botanical aspects, phytochemical constituents, pharmacological actions of *Syzygium caryophyllatum* to authenticate its use as a multipurpose medicinal herb.

Keywords: *Syzygium caryophyllatum*, Folkloric Herb, Essential Oils, Phytoconstituents, Pharmacological Activities
RASĀYAN *J. Chem.*, Vol. 15, No.1, 2022

INTRODUCTION

Plants are a reservoir of chemical compounds that can combat many human diseases. Natural products have traditionally been utilized as a valuable source of novel medicinal agents. Many plant-based compounds are used as lead molecules to generate synthetic molecular analogs. The genus *Syzygium* consists of 1200 species, and these plants are native to the tropics, mainly tropical America and Australia.[1] Plants of the *Syzygium* family are considered rich in volatile oils. These plant species have different biological properties such as antifungal, antibacterial, antiviral, anticarcinogenic antioxidant, anesthetic, and repellent activity.[2] Tender *Syzygium caryophyllatum* leaves, widely used by Paniya tribes in the community of Waynad, Kerala, to treat multiple ailments.[3]

The endangered evergreen tree, *Syzygium caryophyllatum,* is a member of the Myrtaceae family. This tree is indigenous to Srilanka and India; India's distribution is confined to the forests of the Kerala, Karnataka, and Tamilnadu regions of the Western Ghats. The tree is named in Hindi as Jangli Jamun, Kunta nerale in Karnataka, and Kattunjara or Jnarapazham in Malayalam. The plant grows 6 to 30 meters tall, found in the forests or rice fields, from low to higher elevations. This tree is indexed in IUCN Red List Endangered Class, based on the belief that its habitat loss and biotic strain pose a threat.[4]

The present review article emphasizes the pharmacognostical study of the plant, chief chemical constituents, essential oils present in the plant *Syzygium caryophyllatum*, and its pharmacological properties. The principal chemical components present in *S. caryophyllatum* fruit includes primary metabolites like fructose, asparagine, cysteine, serine, betalamic acid, dopaxanthin, palmitic acid, linolenic acid, linoleic acid, stearic acid, and decanoic acid, and the secondary metabolites include betulin, phytol, beta citronellal, friedelin, crocetin, nicotine, nornicotine, ambellin, mevalonic acid, lupic acid, azelaic acid, pipecolic acid, quercetin, kaempferol, caffeic acid, ferulic acid, gallic acid, xanthotoxin, jambolin.[5] The

http://dx.doi.org/10.31788/ RJC.2022.1516421

plant is rich in essential minerals such as sodium, iron, manganese, and potassium.[6] Research reports on the plant *Syzygium caryophyllatum* reveal its anti-microbial, larvicidal, antioxidant, anticancer, antidiabetic, and antifeedant properties.

Botanical Description of the Plant

Leaves are opposite, simple without stipules, the glabrous, obovate-oblong, petiole is short, leaf apex is obtuse, and the base is acute or attenuate. Lamina dimensions include 3-8 x 1.3-3.5 cm. The leaf consists of marginally looped prominent lateral nerves, which form intramarginal nerves.[7] Flowers are white, bisexual. And moderately dense, characterized by growing in corymbs, ascending branches of inflorescence. Persistent calyx tube length is 2-2.5, turbinate disc is absent. Numerous stamens are present. The ovary is two-celled, Inferior comprising several ovules; it comprises one style and simple stigma8: a single-seeded berry fruit, up to 5 mm around the globe. Edible, black globose fruits, unripe fruit is green in color, and it turns to pale pink, pink, and purplish-black upon maturity.[9] The bark is grey, smooth, blaze brown, branches subterete and glabrous.[10] Table-1 describes the taxonomic classification.

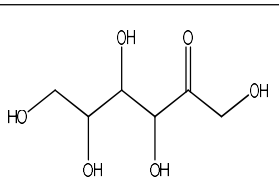
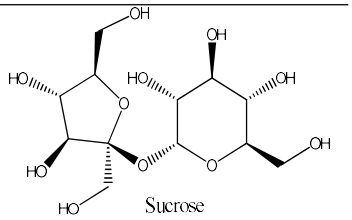
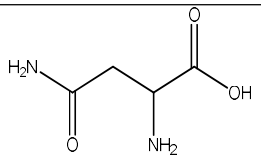
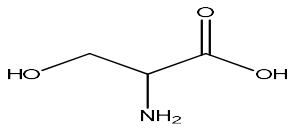
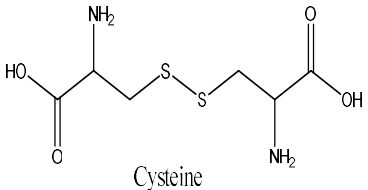
Table-1: Taxonomical Classification

Kingdom	Plantae
Phylum	Tracheophyte
Class	Magnoliopsida
Order	Myrtales
Family	Myrtaceae
Genus	*Syzygium*
Species	*Syzygium caryophyllatum*

Chemical Constituents in Fruit Pulp and Seed

Primary and secondary metabolites are many organic compounds produced by plants. Primary metabolites play an essential role in plants' metabolism, whereas secondary metabolites are functionally defensive and lower the risk of many diseases. *Syzygium caryophyllatum* fruit comprises various primary metabolites like sucrose, cysteine, fatty acids, and lipids. Secondary metabolites present in the plant include betulin, phytol, citronellal, friedelin, crocetin, nicotine, hydroquinidine, quercetin, isoquercetin, kaempferol, ferulic acid, scopoletin, xanthotoxin, wedelolactone, and saponins. Table-2 and Table-3 illustrate the primary and secondary metabolites present in fruit pulp and seed.[11]

Table:2- Primary Metabolites present in *s. caryophyllatum* Fruit and Seed

Type	In pulp	In Seeds	Chemical Structures
Sugars	Fructose	Sucrose	 Fructose  Sucrose
Amino acids	Aspargine	Cysteine Serine	 Aspargine  Serine  Cysteine

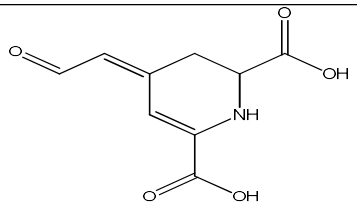
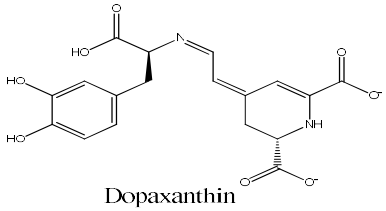
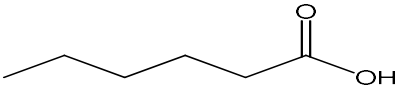
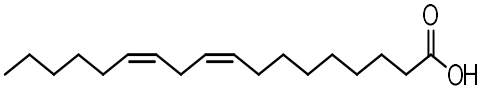
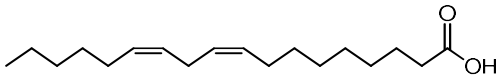
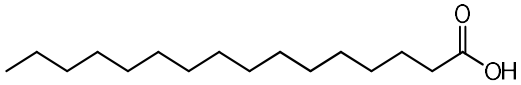
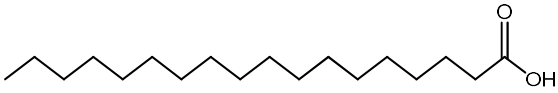
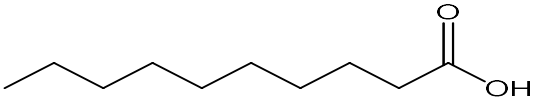
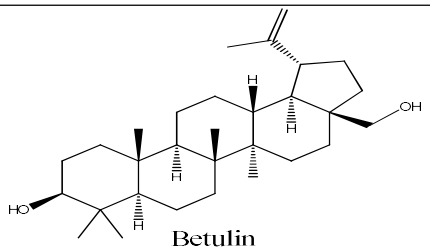
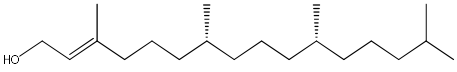
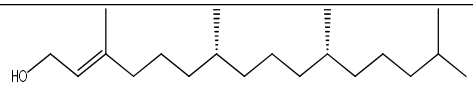
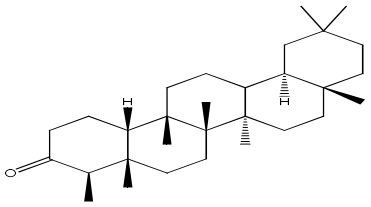
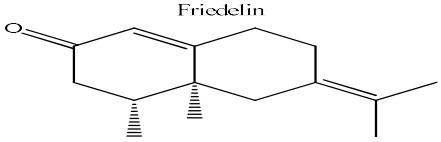
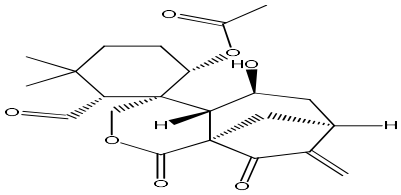
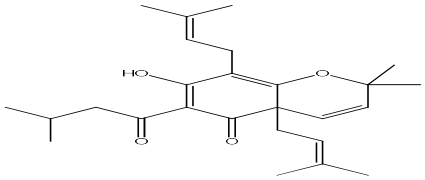
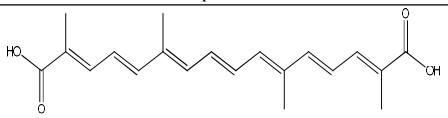
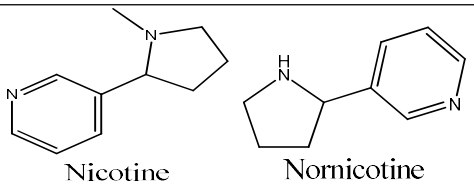
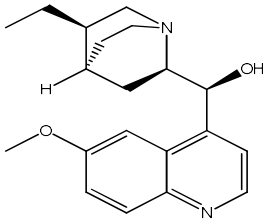
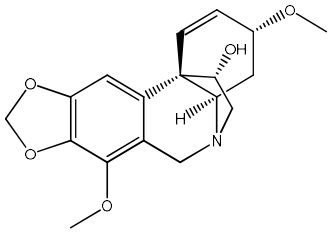
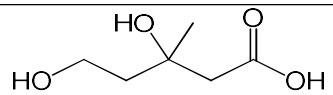
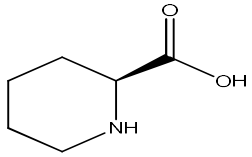
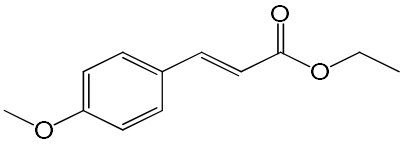
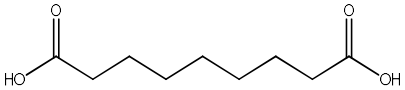
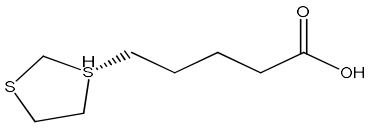
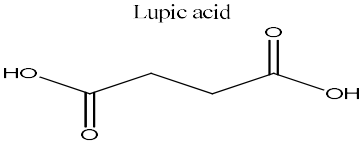
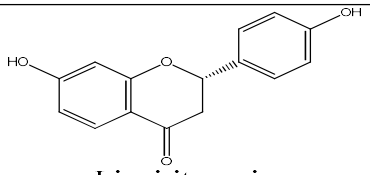
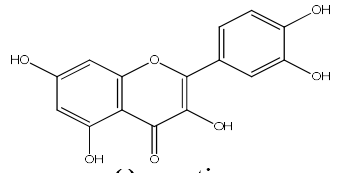
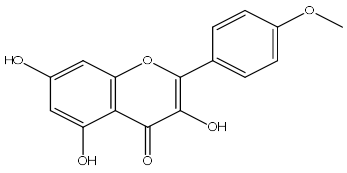
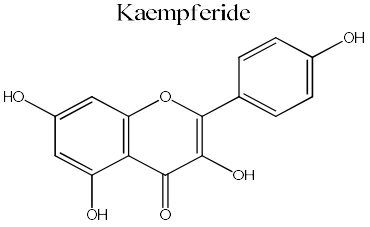
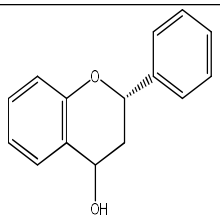
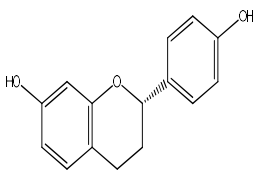
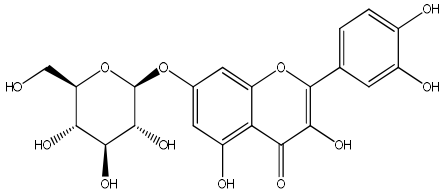
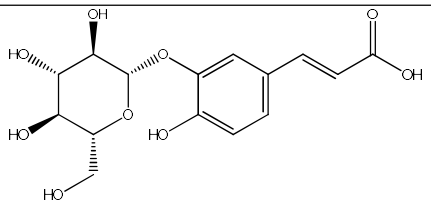
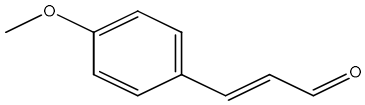
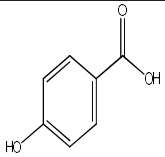
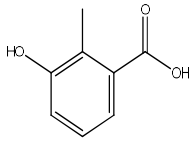
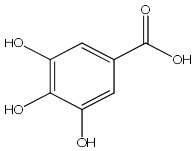
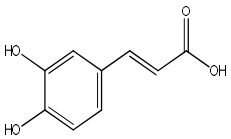
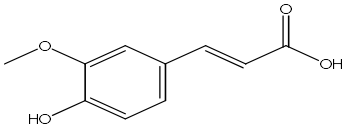
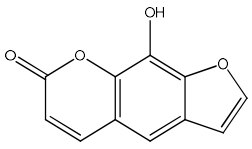
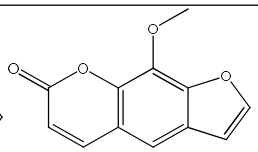
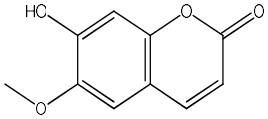
Amino acid-related compounds	Betalamic acid	Dopaxanthin	 Betalamic acid  Dopaxanthin
Fatty acids and lipids	Hexanoic acid Linoleic acid Linolenic acid Palmitic acid	Alpha-linolenic acid Palmitic acid Stearic acid Decanoic acid	 Hexanoic acid  Linoleic acid  Linolenic acid  Palmitic acid  Stearic acid  Decanoic acid

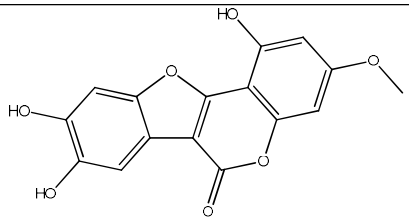
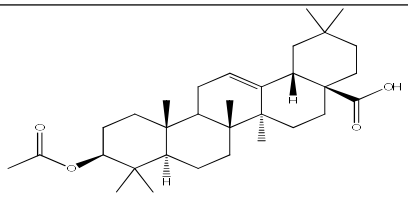
Table-3: Secondary Metabolites present in *s. caryophyllatum* Fruit and Seed

Type	In Pulp	In Seeds	Chemical Structures
Terpenoids	Betulin Phytol Citronellal Friedelin	alpha-Vetivone Isodonal Lupulone Citronellal Friedelin	 Betulin  Phytol

			 Citronellal  Friedelin  alpha-Vetivone  Isodonal  Lupulone
Carotenoids	Crocetin	-	 Crocetin
Alkaloids	Nicotine Nornicotine	Hydroquinidine Ambellin	 Nicotine Nornicotine  Hydroquinidine  Ambellin

Carboxyllic acids	Mevalonic acid Ethyl para methoxycinnamate Pipecolic acid Azelaic acid	Lupic acid Succinic acid	 Mevalonic acid  Pipecolic acid  Ethyl paramethoxy cinnamate  Azelaic acid  Lupic acid  Succinic acid
Flavanoids	Liquiritogenin Quercetin Kaempferol	Quercetin Isoquercetin Dihydroxyflavan Kaempferide Quercemeritrin Hydroxyflavan	 Liquiritogenin  Quercetin  Kaempferide  Kaempferol

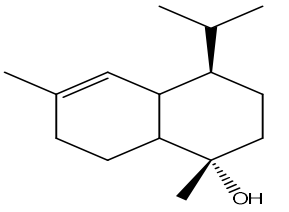
			 Hydroxyflavan  Dihydroxyflavan  Quercimeritrin
Phenyl propanoids	Caffeic acid glycoside	Methoxy cinnamaldehyde	 Caffeic acid glucoside  Methoxy cinnamaldehyde
Phenolic acids	Para hydroxy benzoic acid Hydroxymethyl benzoic acid Ferulic acid Caffeic acid Gallic acid	Ferulic acid	 Para hydroxy benzoic acid  Hydroxy methyl benzoic acid  Gallic acid  Caffeic acid  Ferulic acid
Coumarins	Xanthatoxol Scopoletin	Xanthotoxin Xanthotoxol Wedelolactone	 Xanthatoxol  Xanthotoxin  Scopoletin

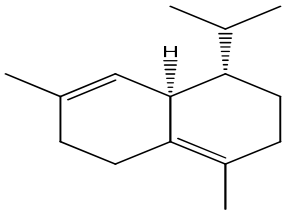
			 Wedelolactone
Saponins	Acetyl oleonolic acid	Acetyl oleonolic acid	 Acetyl oleonolic acid

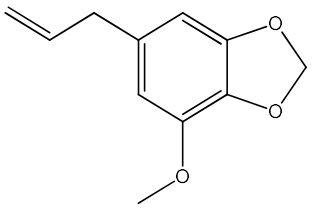
Leaf Essential Oils

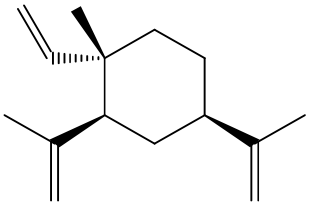
Leaf essential oils extracted from different species of the *Syzygium* genus showed different antimicrobial and pharmacological activities such as antifungal, antibacterial, anticancer and antitumor, antioxidant, anesthetic, antiviral and repellent activity.[12]

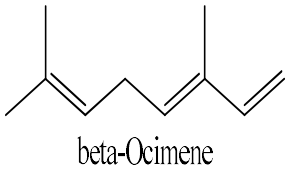
The chemical constituents of *S. caryophyllatum* leaves procured during the winter as well as summer seasons are analyzed. The primary chemical components isolated in the winter season are α-cadinol, myristicin, δ-cadinene, τ-muurolol. In the summer season, the main chemical constituents are cadin-4-en-10-ol, caryophyllene oxide, α-pinene, 4,8,13-duvatrene-1,3-diol. Leaf essential oils were tested using the agar disc diffusion techniques against 6 microorganisms. The findings show that, due to the presence of alpha-cardinol, alpha-pinene, and caryophyllene oxide as key constituents, the *S. caryophyllatum* leaf essential oils demonstrated strong antibacterial activity.[13,14] The *S. caryophyllatum* leaf essential oil consists of significant amounts of antioxidants such as glutathione reductase, glutathione-S-transferase, and superoxide dismutase.[15]

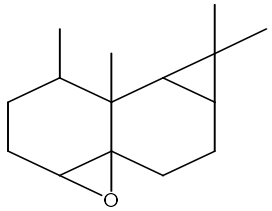

alpha- Cadinol

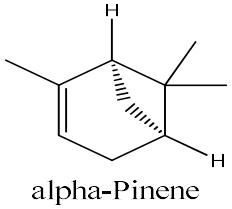

tau-Muurolol

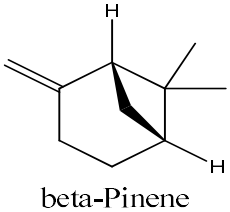

Myristicin

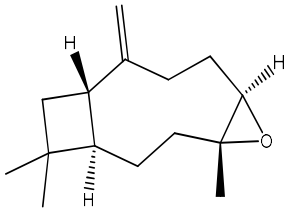

beta-Elemene


beta-Ocimene


Calarene epoxide


alpha-Pinene


beta-Pinene


Caryophyllene oxide

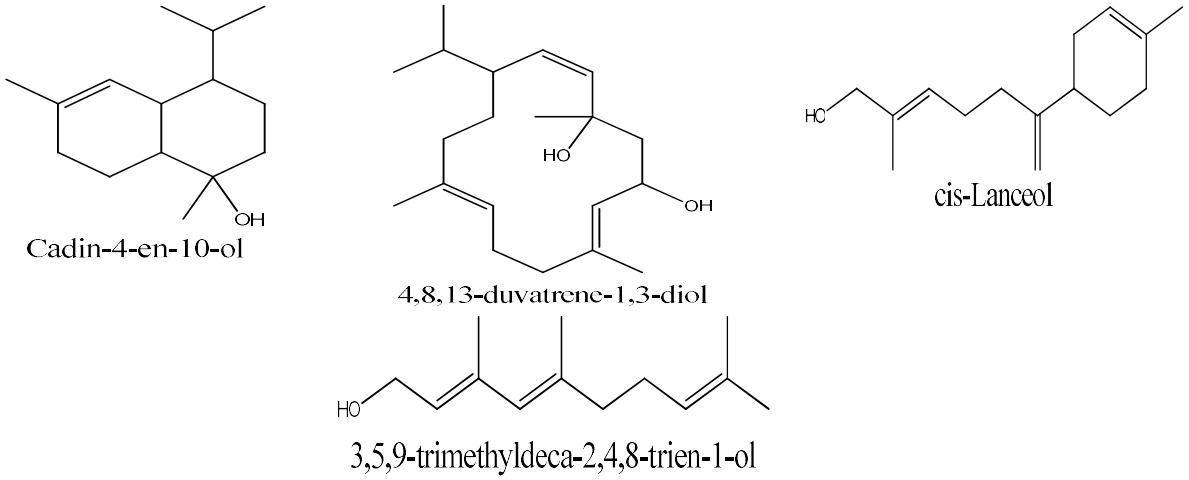


Fig.-1: Structures of Chief Chemical Constituents in Leaf

Pharmacological Actions

Anti-microbial Activity

After the "golden age" revolution, when almost all groups of essential antibiotics such as tetracyclines, aminoglycosides, cephalosporins, and macrolides were discovered, significant concerns were solved in 1960s; these antibiotics are currently at risk of losing potency due to multidrug-resistant microbes. Therefore, the development of new antibiotics is an explicitly important objective. Natural products are also one of today's primary sources of new drug molecules.[16]

The anti-microbial activity of *Syzygium caryophyllatum* ethyl acetate leaf extract was evaluated against four bacterial strains such as *Staphylococcus aureus, Aeromonas hydrophila*, *Bacillus substilis,* and *Enterococcus faecalis* and fungal strains, namely *Aspergillus niger*, *Alternaria alternata,* and *Penicillium chrysogenum* species by micro-broth dilution assay. The results of the plant extract revealed the maximum inhibition zone for *Staphylococcus aureus* (11 mm) and minimum for *Enterococcus faecalis* and *Penicillium chrysogenum.*[1]

The nutritional, fermentation and antibacterial activity of *Syzygium caryophyllatum* fruit methanol and the aqueous extracts were assessed against various strains of gram-positive bacteria (*Bacillus substilis, Staphylococcus aureus*) and gram-negative bacteria (*Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*) by microdilution assay. *Syzygium caryophyllatum* methanol extract recorded maximum efficacy with an active Minimum Inhibitory Concentration value of 8-10 mg/ml against all bacterial strains.[17]

The anti-microbial activity of methanolic extracts of various parts of *Syzygium caryophyllatum* by disc diffusion assay was performed with six bacterial strains (*Staphylococcus hominis*, *Bacillus cereus*, *Escherichia coli*, *Bacillus licheniformis*, *Aerococcus viridans*, and *Staphylococcus aureus*). Methanolic bark extract demonstrated strong antibacterial activity against *Staphylococcus hominis* with a zone diameter of 12.3 mm, followed by *Bacillus licheniformis* with a zone diameter of 12 mm and *Aerococcus viridians* with a zone diameter of 11.3 mm. *S. caryophyllatum* leaf extract exhibited significant antibacterial activity to *Escherichia coli*, *Bacillus cereus* and *Staphylococcus aureus* with zone diameters of 14.3 mm, 14 mm, and 12.3 mm respectively. The extract of methanol seed exhibited strong antibacterial activity against *Aerococcus viridians* (12 mm), *Bacillus cereus* (13 mm), and *Staphylococcus aureus* (10 mm). The plant fruit pulp extract exhibited a medium antibacterial effect.[5]

The antibacterial properties of aqueous leaf extract and ethanolic leaf extract of *Syzygium caryophyllatum* plant were studied against *Vibrio cholerae*, *Staphylococcus aureus*, *Shigella flexneri*, *Escherichia coli*, and *Salmonella typhi* by time-kill assay and agar dilution method. The ethanolic leaf extract demonstrated stronger anti-microbial activity towards *Staphylococcus aureus* and *Salmonella typhi* than the aqueous extract.[18]

The anti-microbial assay of leaf essential oil of the plant, *S. caryophyllatum* compared with standard Streptomycin and fluconazole, when performed, showed good microbial inhibition against gram-positive bacteria, *Bacillus cereus* and *Bacillus substilis* and *Klebsiella pneumoniae* and *Proteus vulgaris* at 1:2

dilution with DMSO. The reports revealed that the leaf oil is effective against *Candida albicans* with MIC of 44.0 μg/ml. The reports suggest that the anti-microbial effect is due to the presence of oxygenated sesquiterpenes, namely δ-cadinol and selin-11-en-4-α-ol.[8]

Larvicidal Activity

Mosquitos are vectors of various diseases such as dengue, chikungunya, encephalitis, malaria, and filariasis; most countries use chemicals to kill larvae, but chemicals are harmful to the atmosphere and many species of mosquitoes have developed DDT resistance to other pyrethroid insecticides. Hence the best option is conventional larvicidal plants.[19]

The methanolic extracts of different parts of the plant *Syzygium caryophyllatum* were tested for larvicidal activity against two mosquito vectors, *Culex quinquefasciatus* and *Aedes aegypti*. Of all the extracts, *S. caryophyllatum* leaf essential oil demonstrated 100 percent mortality against *Aedes aegypti* larvae.[5] The study clearly showed that the essential oil of the *S. caryophyllatum* leaf could be considered a powerful source for the production of an eco-friendly larvicidal agent.

Antioxidant Activity

Antioxidant enzymes such as catalase, glutathione reductase, superoxide dismutase, glutathione peroxidase, antioxidants like selenium, zinc, and glutathione, arginine, tocopherol, Ascorbic acid, and retinol play a vital role in scavenging free radicals. Dietary antioxidants and phytochemicals play a crucial role in preventing many human ailments such as neurodegenerative disorders, atherosclerosis, rheumatoid arthritis, cancer, diabetes, and stroke.[20]

The ethyl acetate extract of *S. caryophyllatum* leaves has shown potent inhibition of DPPH free radical scavenging activity at a higher concentration (400 μg / ml) compared to BHT, a commercial antioxidant.[1]

The antioxidant activity of *S. caryophyllatum* plant parts was assessed using methanolic extract. The studies revealed that the methanolic bark, leaves, fruit, and seed had shown significant inhibition of DPPH and ABTS with a percentage inhibition of 88.15 percent, 81.31 percent, 75.24 percent, and 83.36 percent, respectively.[5]

The DPPH radical scavenging assay, Ferric reducing antioxidant potential assay (FRAP) assay, and nitric oxide (NO) assays against L-ascorbic acid were used to determine the total antioxidant activity of aqueous extract of *S. caryophyllatum*. The antioxidant activities were recorded in IC50 values of 59.23 μg / ml, 4.32 μg / ml, and 199.56 μg / ml for DPPH, FRAP, and NO assays, respectively.[21]

Ramasamy *et al*. conducted the phytochemical estimations of *S. caryophyllatum* and *S. densiflorum*. They found that the phenolic and flavonoid contents varied concerning solvents (Hexane, ethyl acetate, and methanol). *S.caryophyllatum* leaves methanol extract demonstrated the highest DPPH radical scavenging activity (81.97 %) and ferric reducing activity (0.978 %) followed by ethyl acetate, hexane extracts. Thus, the plant *S. caryophyllatum* consists of phenolic compounds and antioxidants, and the plant can be used as a natural antioxidant.[22]

The antioxidant activities have been conducted on the hexane, ethyl acetate and aqueous fractions obtained from the fruits and leaf extracts of *S. caryophyllatum.* The isolated fraction of hexane of fruit has shown the highest anti-amylase activity (IC_{50} Value: 2.27±1.81 μg/ml). Antiglycation activity was performed on the crude extracts of leaves and fruits of *S. caryophyllatum.* The crude leaf extract has shown significant anti-glycase activity[23] (IC_{50} Value: 57.83±7.91 μg/ml).

Antidiabetic Activity

Traditional antidiabetic plants may serve as a valuable source for developing novel oral hypoglycaemic drugs as a pharmaceutical entity or simple dietary supplements to existing therapies.[24]

Methanolic extracts of various plant parts of *S. caryophyllatum* were tested for antidiabetic activity by alpha-glucosidase inhibitory and invitro alpha-amylase inhibition assays. *S. caryophyllatum* seed extract at a concentration of 500 μg / ml has shown maximum alpha-amylase inhibitory activity. The *S. caryophyllatum* bark extract at a 100 μg / ml concentration has shown maximum alpha-glucosidase inhibitory activity.[5]

The orally administered *S. caryophyllatum* methanolic leaf extract (250 mg/kg body weight/day) in alloxan-induced diabetic mice significantly lowered the fasting blood glucose levels and glycosylated hemoglobin

levels compared with the control group.[15] According to this observation, the *S. caryophyllatum* extract exhibits potential hypoglycemic activity.

Anticancer Activity

The anticancer activity of *S. caryophyllatum* methanolic leaf extract was determined by MTT assay on cervical cancer cell lines. The acetone soluble fraction showed more anticancer activity than methanolic and acetone insoluble fractions. The anticancer activity of acetone soluble fraction is attributed mainly due to the presence of chemical constituents like quercetin, flavonoids, and chalcones.[25]

Antifeedant Activity

The primary strategy for pest control is synthetic pesticides. However, synthetic pesticides caused significant environmental problems, and resistance in the target species has grown. Antifeedant plants are the eco-friendly alternative approach to managing pests.[26] The methanolic extract of plant *Syzygium caryophyllatum* stem has shown significant antifeedant activity against fourth instar larvae of Mexican bean beetle, *Epilachna varivestis muls*, *Coccinellida* and thus potential antifeedant compound can be isolated in future from this plant.[27]

CONCLUSION

Syzygium caryophyllatum belongs to the family Myrtaceae; the plants belonging to this genus have a wide range of pharmacological properties attributed to the presence of flavonoids, tannins, polyphenolic derivatives, and anthocyanins. The review presents the multiple benefits of the plant *Syzygium caryophyllatum*, making it a rich natural potential. The plant can be an excellent resource for conducting studies on purification, isolation, and characterization of active principles responsible for anti-microbial, antioxidant, anticancer, and antidiabetic activities. The plant can be further investigated for antioxidant, antidiabetic and anticancer activities using various suitable animal models in the near future.

ACKNOWLEDGEMENT

The authors would like to acknowledge the facilities provided by the Manipal College of Pharmaceutical Sciences and Manipal Academy of Higher Education in executing this review article.

REFERENCES

1. G. Annadurai, B. Masilla, S. Jothiramshekar, E. Palanisami, S. Puthiyapurayil, A. Parida, *International Journal of Green Pharmacy*, **6(4)**, 285(2012), https://doi.org/10.4103/0973-8258.108210
2. Shodhganga@INFLIBNET: Phytochemical and Pharmacological Studies on the selected species of Syzygium [Internet]Available from https://shodhganga.inflibnet.ac.in/handle/10603/222649
3. R. Narayanan, V. Balakrishnan, N. Anilkumar, M. Sivadasan, H. Alfarhan, A. Al-Atarr, *Journal of Medicinal Plants Research*, **5(15)**, 3520(2011).
4. Syzygium Caryophyllatum-Wikipedia, 2015, 8235, Available from: https://en.wikipedia.org/wiki/Syzygium_caryophyllatum
5. N. Stalin, P. Sudhakar Swamy, *Clinical Phytoscience*, **4(1)**, 1(2018), https://doi.org/10.1186/s40816-017-0059-2
6. R. Subramanian, P. Subbramaniyan, V. Raj, *Asian Pacific Journal of Tropical Biomedicine*, **2(2)**,555(2012), https://doi.org/10.1016/S2221-1691(12)60273-1
7. P. Soman, M. Faisal, S. Prabhu. *Journal of Ayurveda Medical Sciences*, **3(1)**, 304(2018), https://doi.org/10.5530/jams.2018.3.3
8. G. Raj, N. S. Pradeep, V. George, M.G. Sethuraman, *Indian Journal of Chemstry - Sect B Organic and Medicinal Chemistry*, **55B(6)**, 747(2016), https://doi.org/10.1016/S2221-1691(12)60273-1
9. Syzygium Caryophyllatum-MYRTACEAE. Available from: https://www.biotik.org/india/species/s/syzycary/syzycary_en.html
10. Syzygium Caryophyllatum- South Indian Plum. Available from: https://www.flowersofindia.net/catalog/slides/South Indian Plum.html

11. V.T. Antony, A. Saji, *International Journal of Pharmaceutical Sciences and Research*, **36(42)**, 239(2016), https://doi.org/10.1016/S2221-1691(12)60273-1
12. S. Nadarajan, S. S. Pujari, *Journal of Essential Oil-Bearing Plants*,**17(3)**, 371(2014), https://doi.org/10.1016/S2221-1691(12)60273-1
13. T. H. Khanh, P. H. Ban, *Journal of Essential Oil-Bearing Plants*, **23(3)**, 548(2020), https://doi.org/10.1080/0972060X.2020.1790429
14. S. Siddique, Z. Perveen, S. Nawaz , K. Shahzad, Z. Ali, *Journal of Essential Oil-Bearing Plants*, **18(4)**, 950(2015), https://doi.org/10.1016/j.jpha.2015.11.005
15. C. S. Rabeque, S. Padmavathy, *Asian Journal of Pharmaceutical and Clinical Research*, **6(4)**, 203(2013)
16. M. Balouiri, M. Sadiki, S. K. Ibnsouda, *Journal of Pharmaceutical Analysis*, **6(2)**, 71(2016), https://doi.org/10.1016/j.jpha.2015.11.005
17. K. J. Shilpa, G. Krishnakumar, *Cogent Food and Agriculture*, **1(1)**, 1(2015), https://doi.org/10.1080/23311932.2015.1018694
18. R. Pendru, J. Nadipelly, J. Kothapalli, S. Kotigadde, *Asian Journal of Pharmaceutical and clinical Research*, **11(2)**, 235(2018), https://doi.org/10.22159/ajpcr.2018.v11i2.21687
19. O. N. Maurya. *Mintage Journal of Pharmaceutical and Medical Sciences*, **7(3)**, 1(2018)
20. Y. Z. Fang, S. Yang, G. Wu. *Nutrition*, 18(10), 872(2002), https://doi.org/10.1016/S0899-9007(02)00916-4
21. A. P. Attanayake, K. Jayatilaka, C. Pathirana, L.K.B. Mudduwa, *African Journal of Traditional, Complementary and Alternative Medicine*, **12(4)**, 28(2015), https://doi.org/10.4314/ajtcam.v12i4.5
22. R. Subramanian, P. Subbramaniyan, V. Raj, *Journal of Biologically Active Products from Nature*, **4(3)**, 224(2014), https://doi.org/10.1080/22311866.2014.936900
23. H. P. Wathsara, H. D. Weeratunge, M. N. Mubarak, P. I. Godakumbura, P. Ranasinghe, *Evidence-Based Complementary and Alternative Medicine* (2020), https://doi.org/10.1155/2020/9529042
24. Bailey, J. Clifford, C. Day, *Diabetes Care*, **12(8)**, 553(1989), https://doi.org/10.2337/diacare.12.8.553
25. R. Raj, K. S. Chandrashekar, V. Pai, *Latin American Journal of Pharmacy*, **37(5)**, 1046(2018)
26. U. L. B. Jayasinghe, B. M. M. Kumarihamy, A. G. D. Bandara, J. Waiblinger, W. Kraus, *Natural Product Research*, **17(1)**, 5(2013), https://doi.org/10.1080/10575630290034285
27. M. Isman. *Pesticide Outlook*, **13(4)**, 152(2002), https://doi.org/10.1039/b206507j

[RJC-6421/2021]