ALKALOIDAL DIVERSITY ACROSS *SYZYGIUM* SPECIES: A COMPREHENSIVE REVIEW UNRAVELING SECONDARY METABOLITE PROFILING

A Dissertation Submitted

in Partial Fulfillment of the Requirements

for the Degree of

MASTER OF SCIENCE

in

Chemistry

by

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May, 2024

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CANDIDATE'S DECLARATION

I, Ambika Singh (2k22/MSCCHE/01) hereby certify that the work which is being presented in the dissertation entitled "Alkaloidal Diversity across *Syzygium* Species: A Comprehensive review unravelling Secondary Metabolite Profiling" in partial fulfillment of the requirements for the award of the Degree of Master of Science, submitted in the Department of Applied Chemistry , Delhi Technological University is an authentic record of my own work carried out during the period under the supervision of Dr. Ram Singh.

Candidate's Signature

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CERTIFICATE

Certified that **Ambika Singh** (2k22/MSCCHE/01) has carried out their search work presented in this dissertation entitled **"Alkaloidal Diversity across Syzygium Species: A Comprehensive review unraveling Secondary Metabolite Profiling"** for the award of **Master of Science** from Department of Applied Chemistry, Delhi Technological University, Delhi, under my supervision. The dissertation embodies results of original work, and studies are carried out by the student herself and the contents of dissertation do not form the basis for the award of any other degree to the candidate or to anybody else from this or any other University.

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ABSTRACT

Genus *Syzygium* consists of wide variety of species which are known for their pharmacological significance. This review delves into the phytochemical landscape of various *Syzygium* species, utilizing structured data to analyse present phytochemical compound structure, their distribution within different plant parts, and the reported pharmacological activities. By documenting phytochemicals from species such as *S. cumini*, *S. aromaticum*, and *S. caryophyllatum*, it seeks to elucidate their chemical composition and associated pharmacological effects. Among secondary metabolites, alkaloids are most effective against protective agents of metabolic operations. Alkaloids have demonstrated varied pharmacological actions, including antidiabetic and antimicrobial properties, underscoring their importance in drug discovery and development. This review serves as a comprehensive reference, facilitating exploration of the phytochemical and pharmacological aspects of *Syzygium* secondary metabolites for interested researchers. Thus, offering valuable insights and guidance for future research directions and potential applications in medicine and drug development.

CHAPTER 1

INTRODUCTION

The genus *Syzygium* comes derived from the Greek word "syzgios," which means "paired." This is due to the leaves and twigs grow at the same time. [1] The Myrtaceae family, which includes the genus *Syzygium*, has around 1800 species distributed worldwide. It is the world's largest genus of flowering plants composed entirely of wood. Medium-sized to large evergreen trees comprise the majority of *Syzygium's* species. Some species—like *S. jambos*, *S. aromaticum*, S. *aqueum*, and *S. cumini*, for instance—produce edible fruits that can be eaten raw or utilized for producing jams and jellies for commercial purposes. [2] *Syzygium* species are essential to ecosystems because they give a variety of creatures, such as insects and birds, a place to live and food. They are important elements of both urban and forest environments due to their dense greenery and flexibility in varying environmental circumstances.
Pharmacological characteristics of *Syzygium* have drawn interest; multiple species showed antibacterial, antidiabetic, anti-inflammatory and anticancer capabilities.

Extracts from *Syzygium* plants are used by traditional medical systems around the world to treat a variety of illnesses, from respiratory infections to digestive issues. *Syzygium* plant parts including seeds, leaves, bark, pulp and flower are rich in phytochemical components such flavonoids, terpenoids, tannins, steroids, alkaloids, phenols and glycosides.[3] Secondary metabolites are mostly used by plants to shield themselves from environmental dangers such as pollution, drought, UV radiation and pathogens. Research has demonstrated that phytochemicals can protect plants from illnesses that are harmful to people. [4]
Alkaloids are organic molecules found in nature that contain one or more nitrogen atoms and exhibit a variety of pharmacological properties, including antibacterial, anticancer, analgesic, antihyperglycemic, and antimalarial effects. [5]
Alkaloids contribute to the ecological interactions of *Syzygium*, serving as chemical defence against herbivores and pathogens.

Figure 1.1 Syzygium caryophyllatum, aqueum, cumini

1.1: - Taxonomical Details [6]

Table 1.1 Taxonomical classification of *Syzygium*

Kingdom	Plantae
Clade	Eudicots (Plants with two seeds)
Clade	Tracheophytes (Vascular plants)
Clade	Rosids (Plants that shared a same progenitor)
Clade	Angiosperms (Flowering plants)
Order	Myrtales (Includes myrtle family and related plants)
Family	Myrtaceae (Myrtle family)
genus	*Szygium*

1.2: - Geographical Distribution

The genus is indigenous to Asia – India, China, Thailand, Nepal, Malaysia, Bangladesh, Afghanistan, Indonesia, Sri Lanka, Philippines, Myanmar; Africa – Ghana, South Africa, Tanzania, Algeria, Sudan, Kenya; Oceania – Cook Islands,

Guam, Niue, Tonga, Christmas Island, Australia, French Polynesia, Hawaii, Palau, Fiji; North America – Cuba, Guatemala, Mexico, Panama, Jamaica, Guadeloupe, Barbados, Antigua and Barbuda, Nicaragua, Bahamas, Montserrat, Florida, Grenada, Dominica, Guyana, Netherlands Antilles, Trinidad and Tobago, Saint Kitts and Nevis, United States of America, Saint Lucia, Saint Vincent and the Grenadines; South America – Caribbean, Brazil and Colombia. [7]

CHAPTER 2

TRADITIONAL USES OF SOME *SYZYGIUM* SPECIES

Table 2.2 An inventory of *Syzygium* species, their plant components and applications

Species Name	**Part**	**Application in disease**
Syzygium cumini	Fruit Leaf Stem bark	Cough, diabetes, inflammation, gastrointestinal complaints [8] Stomach pains and diabetes [8] Dysentery, wounds and bleeding gums [8]
Syzygium aromaticum	Flower bud	Disinfectant, anti-inflammatory and reliving odor [9] Cough and cold, toothache, inflammation in gums [8]
Syzygium samarangense	Flower	Fever, Diarrhea [10]
Syzygium malaccense	Bark Leaf	Mouth ulcers [10] Irregular menstruation [10]
Syzygium caryophyllatum		Diabetes mellitus [11]
Syzygium calophyllifolium	Leaf Fruit and bark	Skin disease [12] Aching tooth and inflammation [12]

Syzygium polyanthum	Leaf	Hypertension, ulcers, diabetes mellitus, diarrhea, gastritis [13]
Syzygium alternifolium	Leaf, tender shoots Fruits	Bacillary dysentery [14] Diarrhea and diabetes [14]
Syzygium aqueum	Leaf	Antibiotic and childbirth pain [15]
Syzygium myrtifolium		Stomach aches [16]
Syzygium zeylanicum	Leaf Stem bark	Headache, arthritis, fever [17] Diabetes mellitus [18]
Syzygium guineense	Root and stem bark Leaf	Stomach aches and infertility [19] Diarrhea, intenstinal parasites [19]
Syzygium nervosum	Leaf and flower bud Leaf and bark Leaf	Abdominal pain, sores, acne [20] Scabies, skin diseases [20] Pimples, breast inflammation [20]
Syzygium jambos		Syphilis, wounds, leprosy [21]
Syzygium densiflorum	Leaf and ripened fruit	Diabetes [22]
Syzygium anisatum	Leaf	Labour pain and antibiotic [23]

Syzygium cordatum	Leaf, root and bark and fruit	Respiratory problems, tuberculosis, STDs, fever and malaria [24]
Syzygium grande		Diabetic-related complications [25]
Syzygium australe		Fungal skin infection [26]
Syzygium formosum	Leaf	Allergy or skin rash [27]

CHAPTER 3

SECONDARY METABOLITE PROFILING

3.1: - Phytochemical Constituents

3.1.1: - Flavonoids

A significant class of naturally occurring polyphenolic chemicals with antidiabetic, anti-inflammatory, antioxidant, and anti-allergic properties are called flavonoids; other flavonoid compounds demonstrate possible antiviral effects [28, 29,30]

The primary flavonoid present in *Syzygium* species is anthocyanin, which gives fruits and leaves their red, purple, or blue coloration. In addition to giving a plant its color, anthocyanins function as antioxidants, shielding it from oxidative stress brought on by illnesses and UV rays. The leaves of *S. aqueum* contained 87 distinct compounds that were high in flavonoids some of them are myrigalone-G pentoside, cryptostrobin, myricetin rhamnoside, myrigalone-B and quercetin galloyl-pentoside. [31,32] Few flavonoid components were identified in *S. cumini* in various plant parts, seed extract (rutin and quercetin), leaf extract (caffeic and ellagic acid), flower extract (dihydromyricetin and kaemferol) and bark extract (kaemferol and quercetin).[33] *S. malaccense* contains flavonoids like myricitrin and quercetin. [34]

3.1.2: - Phenols

Phenol is an aromatic hydrocarbon with -OH group having anti-inflammatory, antimicrobial and antioxidant properties. *S. alternifolium* has a high phenol content; GC-MS research revealed about 40 distinct types of chemicals, among those seven are phenols such as 2-furanmethanol, methylpropylcarbinol, 1- butanol, propol in methanol extract of bark, leaves and fruit. [35] Phenolic compounds are crucial to the bioactive profile of the *Syzygium* genus, contributing significantly to its medicinal properties.

3.1.3: - Tannins

Tannins are a class of polyphenolic compounds which exhibits antinutritional, astringent, antidiabetic, cardioprotective effects. Very few tannin compounds were

found in S. cumini in different plant components, as corilagin in seed extract and nilocetin in leaf extract. [36]

3.1.4: - Terpenoids

Terpenoids, also called isoprenoids, are a wide and diverse class of organic compounds that exist naturally. They are made up of five-carbon isoprene units organized in different structural configurations. These exhibits antimicrobial, anti-inflammatory, analgesic, neuroprotective, cardioprotective effects. There were nineteen chemicals in the chloroform extract of *S. corticosum* leaves. Of these, seven molecules were classified as triterpenoids. The two most prominent triterpenoid compounds were melaleucic acid and ursolic acid, which were isolated via chromatographic separation. [37]

3.1.5: - Alkaloids

Alkaloids are nitrogen containing compounds that occur naturally and have profound physiological effects on humans. They are one of the secondary metabolites produced by plants and they exhibit pharmacological activities such as antibacterial, antihyperglycemic, antimalarial. The alkaloid jambolsine, which is found in *S. cumini* seeds, is said to have antidiabetic properties. [38] Many alkaloids have been isolated from numerous *Syzygium* species, including *S. aromaticum, S. cumini*, and *S. polyanthum*. [39] The fruit pulp and seed of *S. cordatum* have alkaloids found in its methanol extract. [40]

3.1.6: - Glycosides

Glycosides are compounds formed by substituting a hydroxyl group in sugar molecule (glycone) to create a combination of simple sugar and another substance. The glycoside jambolin or antimellin found in *S. cumini* seeds shown antidiabetic properties by preventing the diastatic conversion of starch to sugar. [41]

3.2: - Phytochemical Compounds Screening [42]

3.2.1: - Collecting Plant Materials

Samples of various *Syzygium* species were gathered, and after being cleansed with tap water to get rid of dust, the fruit pulp was separated, the seeds were cleaned, and they were dried for one to two weeks at room temperature before being ground into powder using an electronic grinder.

3.2.2: - Plant Extract Preparation

Soxhlet extractor was used to permeate the powdered plant sample with organic solvents like ethanol, petroleum ether and methanol (70% w/v). After being taken, the extracts were stored for later research.

3.2.3: - Test for Alkaloids [Mayer's Test]

1.36 gm mercuric chloride was dissolved in 60 ml distilled water and 5 gm potassium iodide used in 10 ml distilled water. Both the solvents get mixed and diluted to 100 ml with distilled water. 1 ml acidic solution was added following up with few drops of reagent. White and pale precipitate formation confirms presence of alkaloids.

3.2.4: - Test for Tannins

Ferric chloride Test

Solution was made with 50 gm of sample in distilled water, few drops of neutral 5% ferric chloride solution was added to this. Dark green or black precipitate formation shows presence of tannins.

Lead Acetate Test

5 ml of plant extract solution was taken into test tube, some drops of 1% lead acetate solution was added to this. If bulky white precipitate form it shows tannins are present in that plant extract.

3.2.5: - Test for Saponins

Take 50 ml of plant extract solution in a test tube and add few drops of sodium bicarbonate to it. After giving the mixture a good shake, it was left undisturbed for two minutes. Saponins were visible in the form of a foam that resembled honeycomb.

3.2.6: - Test for Flavonoids

In a test tube, 0.5 ml of alcoholic extract of sample was taken, 5-10 drops of diluted hydrochloride acid were added to it and tiny bit of magnesium or zinc was also added after that mixture was boiled for few minutes. Flavonoids are indicated by their appearance as reddish-pink or turbid brown color.

3.2.7: - Test for Phenols

1 ml of alcoholic solution of plant extract was prepared, to this 2 ml distilled water was added. 10% aqueous solution of ferric chloride was added to this. Phenols are present when blue or deep green color develops.

3.2.8: - Test for Terpenoids

In a test tube, 1 mg of plant's extract was mixed with 2 ml of chloroform, to this 5-10 drops of conc. H2SO4 was added. The presence of terpenoids was detected by looking for a reddish-brown color.

3.2.9: - Test for Steroids [Salkowski's Test]

2 ml of $CHCl_3$ was diluted with 100 mg of dried plant's extract, H2SO4 was added slowly to form a lower layer. Reddish brown colored ring was formed between the interface that confirms presence of steroids.

3.2.10: - Test for Amino Acids

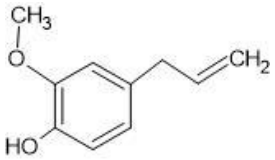
To 2 ml of plant's extract, 1-2 drops of ninhydrin reagent solution was added. Violet or purple color confirms the presence of amino acids.

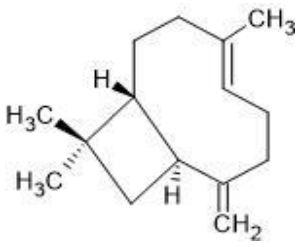
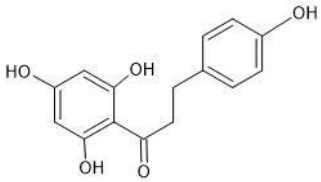
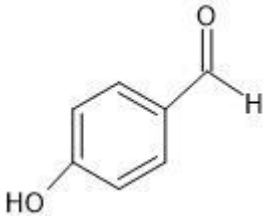
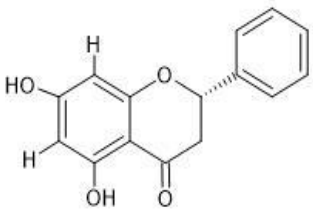
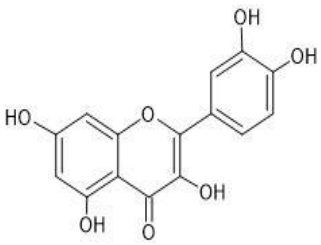
3.2.11: - Test for Anthraquinone Glycosides [Borntrager's Test]

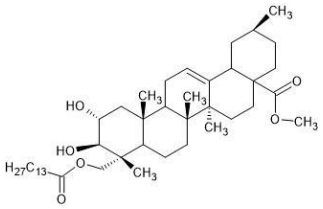
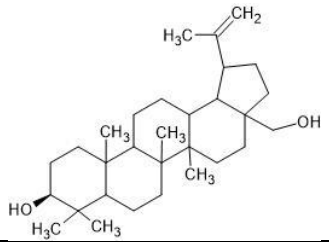
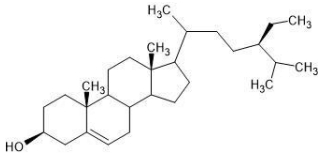
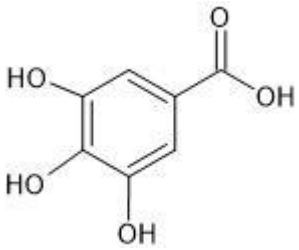
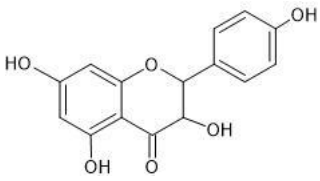
In a test tube, 5 ml of plant's extract was taken and 2 ml of diluted H_2SO_4 was added to this, mixture was allowed to boil for 5 minutes and then filtered. Equal amount of CHCl3 was added to the filtrate and mixed. After separating the organic layer, 10% ammonia solution was added. Appearance of brick pink color of ammonia's layer confirms presence of anthraquinone glycosides.

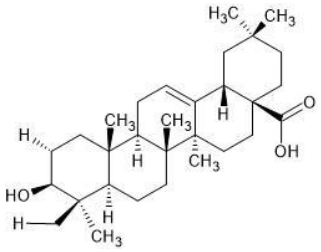
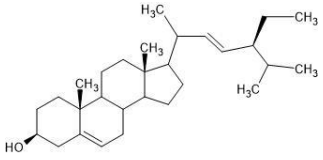
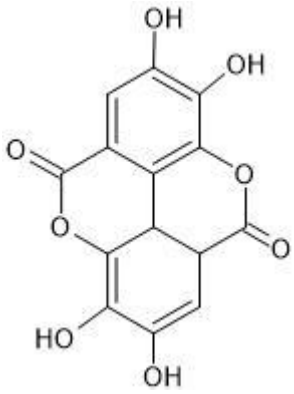
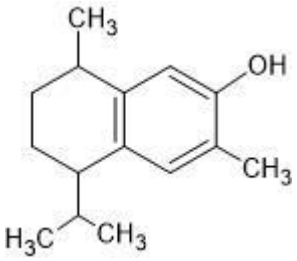
3.3: - Phytochemical Components of Different *Syzygium* Species

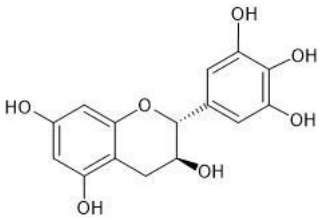
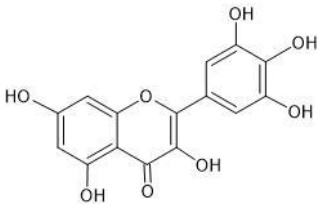
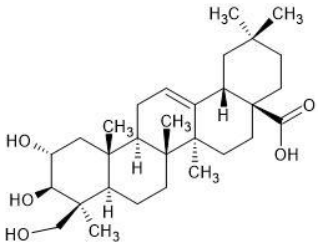
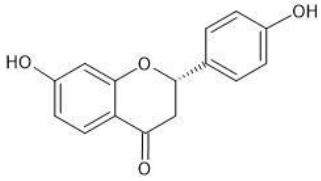
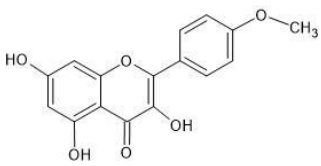
Table 3.3 List of Phytochemicals

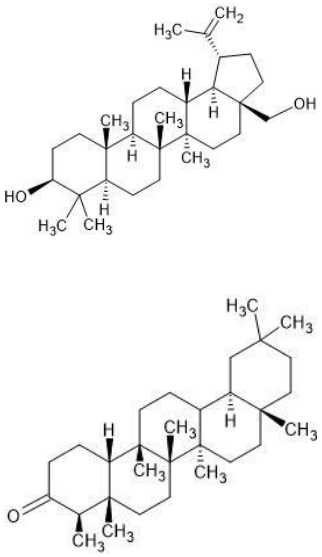
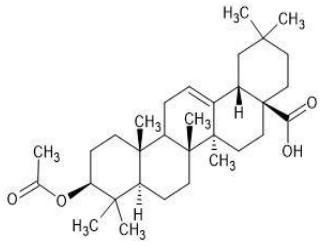
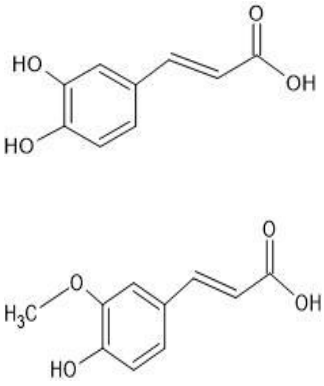
s.no.	Species Name	Type	Chemical Compound	Structure	Plant Part	Ref.
1.	*Syzygium aromaticum*	Phenols	Eugenol		Leaf	[43]

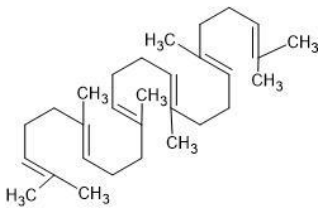
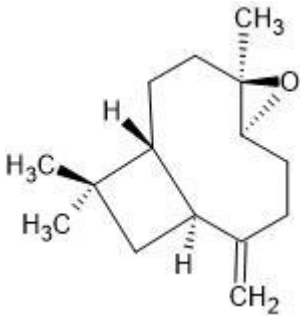
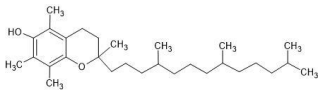
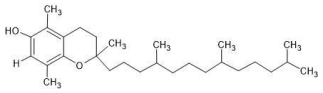
		Terpenoids	β-caryophyllene		Flower bud	[43]
2.	*Syzygium aqueum*	Flavonoids	Phloretin		Leaves	[44]
		Phenols	4-Hydroxybenzaldehyde		Leaves	[44]
3.	*Syzygium samarangense*	Flavonoids	Pinocembrin		Fruits and Leaves	[45]
			Quercetin		Fruits	

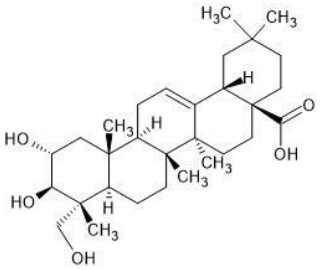
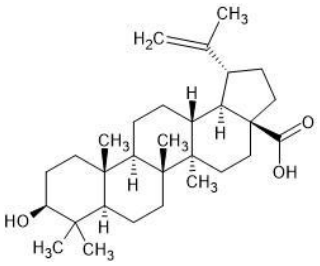
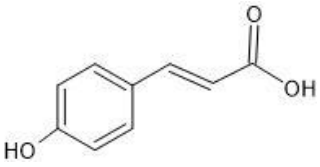
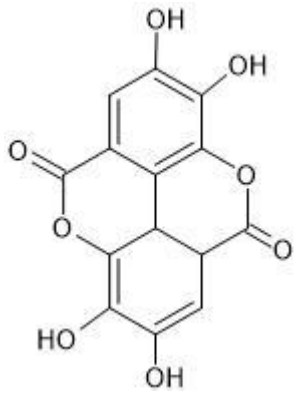
		Terpenoids	Lupeol Betulin	 	Leaves Leaves	[46, 47]
		Steroids	β-Sitosterol		Leaves	[48]
		Phenols	Gallic acid		Fruits	[49]
4.	*Syzygium Cumini*	Flavonoids	Kaempferol		Leaves	[50]

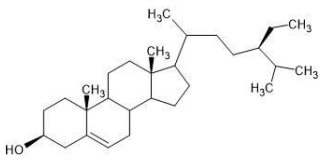
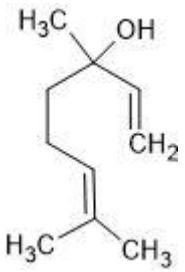
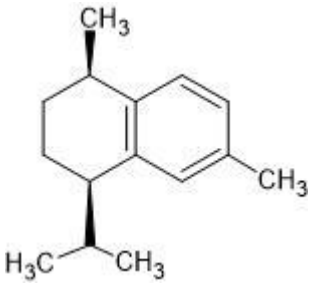
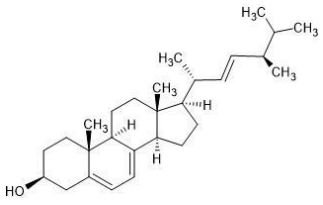
		Terpenoids	Oleanolic acid		Seeds	[51]
		Steroids	Stigmasterol		Leaves	[52]
		Tannins	Ellagic acid		Stem Bark	[53]
		Phenol	7-Hydroxycalamenene		Seeds	[54]

5.	*Syzygium Guineense*	Flavonoids	Gallocatechin Myricetin	 	Leaves Leaves	[55]
		Terpenoids	Arjunolic acid		Leaves and roots	[56]
6.	*Syzygium caryophyllatum*	Flavonoids	Liquiritogenin Kaempferide	 	Pulp Seeds	[57]

		Terpenoids	Betulin Friedelin		Pulp Seeds	[57]
		Saponins	Acetyl oleonolic acid		Pulp and Seeds	[57]
		Phenols	Caffeic acid Ferulic acid		Pulp Seeds	[57]

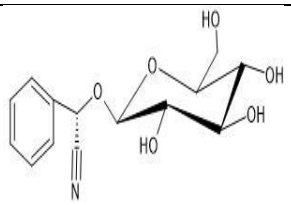
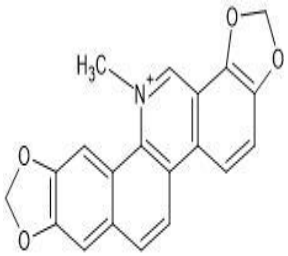
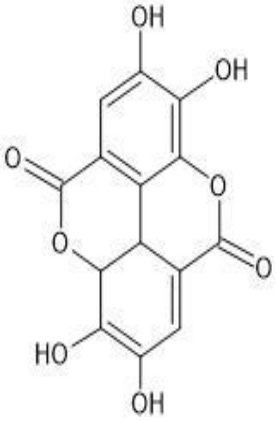
7.	*Syzygium Polyanthum*	Terpenoid	Squalene Caryophyllene oxide	 	Leaves Leaves	[58]
		Phenols	α-Tocopherol β-Tocopherol	 	Leaves Leaves	[58]

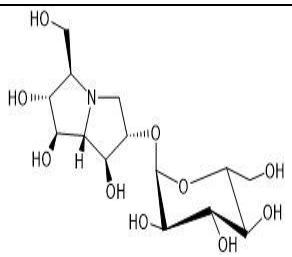
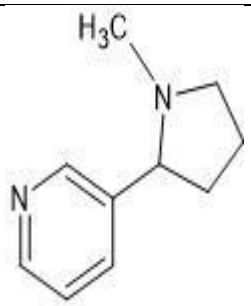
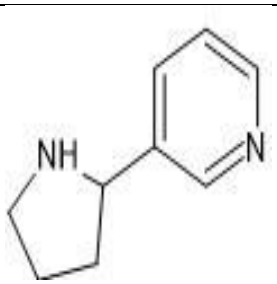
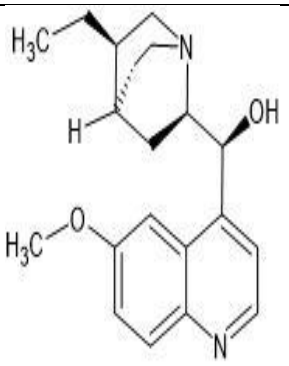
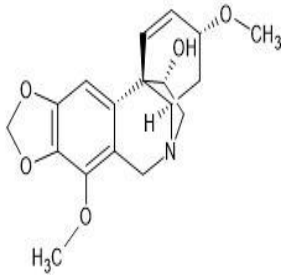
8.	*Syzygium Cordatum*	Terpenoids	Arjunolic acid		Bark, Wood	[59]
			Betulinic acid		Fruit	
		Phenols	p-coumaric acid		Bark, fruits	[59]
			Ellagic acid		Bark, wood	

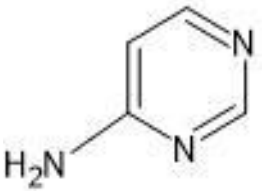
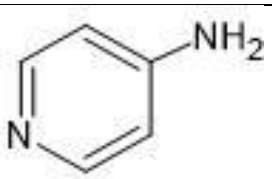
		Steroid	β-sitosterol		Bark, wood	[59]
9.	*Syzygium densiflorum*	Terpenoid	β-Linalool		Leaves	[60]
			Calamenene		Leaves	
		Steroid	α-ergosterol		Leaves	[60]

3.4: - Alkaloids in *Syzygium* genus

Table 3.4 A list of Alkaloids found in *Syzygium* genus

s.no.	Species Name	Alkaloid found	Structure	Plant Part	Pharmacological Activity
1.	*Syzygium Samarangense*	2R-prunasin [61]		Leaves	Anti-inflammatory
2.	*Syzygium Aromaticum*	Sanguinarine [62]	 [63]	Flower bud	Antimicrobial
3.	*Syzygium Cumini*	Jambosine [64]	 [65]	Seeds	Antidiabetic

4.	*Syzygium malaccense / Syzygium oleosum/ Syzygium paniculatum*	Casuarine 6-O-α-glucoside [66]	 [67]	Bark	Antiviral
5.	*Syzygium Caryophyllatum*	Nicotine [68]		Pulp	Antioxidant
6.	*Syzygium Caryophyllatum*	Nornicotine [68]		Pulp	Antioxidant
7.	*Syzygium Caryophyllatum*	Hydroquinidine [68]		Seeds	Antidiabetic
8.	*Syzygium Caryophyllatum*	Ambellin [68]		Seeds	Antidiabetic

9.	*Syzygium arnottianum*	4-Aminopyrimidine [69]		Leaf	Anti-virial
10.	*Syzygium calophyllifolium*	3-Piperidinamine [70]		Fruit	Anticancer

3.5: - Pharmacological Activities

3.5.1: - Antioxidant activities

Antioxidants are substances that remove free radicals, they increase the body's defense against oxidative damage, and lessen oxidative stress. Antioxidant activities are primarily due to the presence of bioactive compounds such as flavonoids, phenols, tannins and anthocyanins. Having a variety of foods high in phenolic and flavonoid components has antioxidant properties that may be beneficial to health. In vitro, *S. aqueum* leaf extract demonstrated potent antioxidant qualities and shielded human keratinocytes (HaCaT cells) from UVA toxicity. [71] *Syzygium Cumini* exhibits strong free radical scavenging activities, inhibits lipid peroxidation, and protects DNA from oxidative damage. *Syzygium aromaticum*(clove) is effective in scavenging free radicals, chelating metal ions, and inhibiting oxidative enzymes. It was found that methanol extract of *S. cordatum* have antioxidant activity and it proved to be more effective in scavenging DPPH free radicals.[72] *Syzygium samarangense* exhibits significant free radical scavenging ability and metal chelation capacity. Ethanol extract of *S. densiflorum* leaves at 200mg/kg concentration demonstrated considerable antioxidant activity by lowering the levels of TBARS and super oxide dismutase (SOD). Fruit ethanol extract demonstrated antioxidant action as well by lowering blood glucose levels. [73] *Syzygium jambos* exhibits free radical scavenging activity and inhibits oxidative stress. *Syzygium malacccense* strong antioxidant properties, effective in preventing lipid peroxidation and DNA damage. The dihydrofluorescein experiment showed that the essential oil and leaf aqueous extract of *S. grande* had a

greater capacity to scavenge hydrogen peroxide in rat peritoneal macrophages. [74] The S. guineense ethanol leaf extract showed antioxidant activity against ferric nitriloacetate-induced stress in the liver, kidney, heart, and brain tissues of Wistar rat homogenates through minimizing lipid peroxidation and restoring both enzymatic and nonenzymatic activities. Aqueous extract of fruit from *S. Paniculatum* shows antioxidant activity, shielded kidney and liver tissues from cytotoxicity and reduced OS marker levels in OS induced diabetic rat.

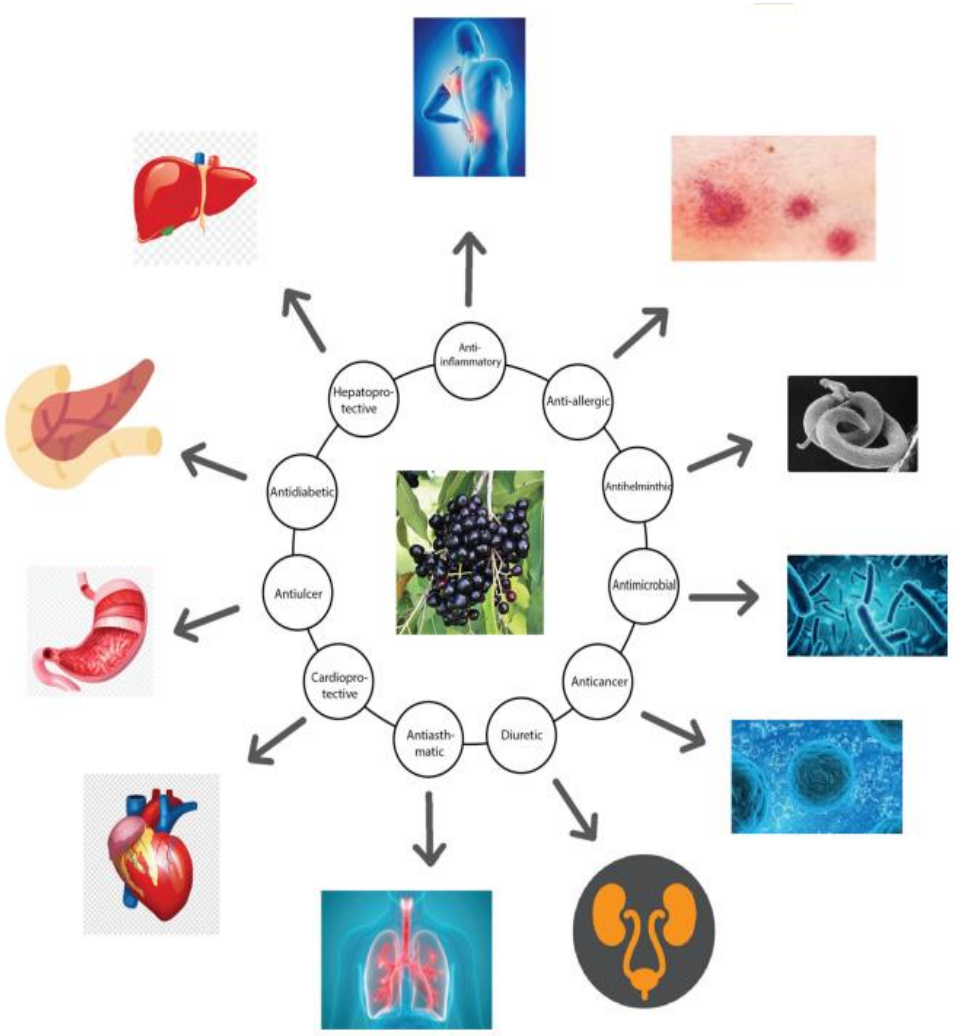


Figure 3.2 Pharmacological activities of genus syzygium

3.5.2: - Antibacterial activities

Antibacterial agents are compounds that are primarily used to either kill or inhibit pathogenic bacteria in order to save cells. Various species of the genus *Syzygium*

exhibit significant antibacterial activities due to the presence of diverse bioactive compounds. Gram-positive and gram-negative bacteria were significantly suppressed by *S. anisatum* methanol and aqueous leaf extract. Antibacterial activity showed by seed extract of S. aromaticum having 0.06 mg/ml of minimum bactericidal concentration (MBC) and 0.10 mg/ml of minimum inhibitory concentration (MIC). Pseudomonas aeruginosa, Staphylococcus aureus, and Escherichia coli all shown a considerable drop in optical density and colony-forming units (CFU) when time kill susceptibility at MBC value was observed. [75] *S. cumini* is effective against a range of bacteria such as Escherichia coli, Staphylococcus aureus, Bacillus subtilis and Pseudomonas aeruginosa. The microtiter plate dilution assay revealed that the bark extracts, both aqueous and dichloromethane–methanol, have antibacterial action by inhibiting the growth of many bacterial pathogens. The essential oils and phenolic compounds disrupt bacterial cell walls and inhibit bacterial enzymes. Aqueous extract of *S. cordatum* leaves showed strong antibacterial activity in a 96-well plate microdilution bioassay. *S. samarangense* shows significant activity against bacteria such as S. aureus, E. coli, and P. aeruginosa. The tannins and flavonoids interfere with bacterial cell wall synthesis and protein function. *S. malaccense* is effective against a variety of bacterial strains such as Bacillus cereus, Staphylococcus aureus and Escherichia coli. The phenolic compounds are thought to disrupt bacterial membranes and inhibit nucleic acid synthesis. An ethyl acetate extract of *S. densiflorum* leaves shown antibacterial efficacy against six bacterial species using disk diffusion method. [76] The antibacterial properties of *Syzygium* species can be used to treat and prevent bacterial infections, particularly in traditional medicine. Extracts from *Syzygium* species can be used as natural preservatives due to their ability to inhibit the growth of foodborne pathogens. Some *Syzygium* species, such as clove, are used in dental care products for their ability to inhibit oral bacteria and reduce tooth decay.

3.5.3: - Antifungal activity

The most potent antifungal component of *S. aromaticum* oil, sometimes known as clove oil, was eugenol. Clove oil shown high antifungal activity against Trichophyton mentagrophytes, Trichophyton rubrum, Microsporum gypseum, and Microsporum canis. *S. Cumini* exhibits effectiveness against a range of fungi including Candida albicans, Aspergillus niger, and Trichophyton mentagrophytes. The phenolic compounds and essential oils disrupt fungal cell walls and inhibit fungal enzyme activity. *S. samarangense* shows significant activity against fungi such as C. albicans and A. niger. Tannins and flavonoids interfere with fungal cell wall synthesis and inhibit spore germination. By employing the microtiter plate dilution assay, it was found that the *S. cordatum* bark's aqueous and dichloromethane-methanol extracts showed antifungal activity, creating an inhibitory impact against a number of bacterial pathogens. [77] *S. jambos* demonstrates activity against fungi such as C. albicans and A. niger. Essential oils and flavonoids damage fungal cell membranes and inhibit fungal proliferation. The antifungal properties of *Syzygium* species can be utilized in treating fungal infections, particularly in traditional medicine. Extracts from *Syzygium* species can be used as natural fungicides to protect crops from fungal pathogens.

3.5.4: - Anti-inflammatory activity

An anti-inflammatory medicine works by interfering with the central nervous system (CNS) to prevent pain signals from reaching the brain, hence lowering pain and inflammation. Many substances belonging to multiple classes that were extracted from various *Syzygium* species showed anti-inflammatory properties. The methanolic and ethyl acetate extracts of *Syzygium cumini* leaves have demonstrated notable anti-inflammatory activity in animal models. In particular, these extracts were effective in reducing paw edema induced by carrageenan in rats, indicating their potential for treating inflammation. The myeloperoxidase activity of human neutrophils was reduced by an aqueous extract of *S. aromaticum* flower buds, and mice were shielded against lung inflammation caused by LPS. Mice's paw swelling caused by carrageenan was successfully reduced by clove oil, implying that it may be used to treat inflammatory diseases. Clovinol, is a polyphenol-rich extract from clove buds, exhibited potent anti-inflammatory effects which includes inhibition of lipid

peroxidation and oxidative stress. *S. calophyllifolium* methanol bark extract at dose of 200 mg/kg has proved to be effective against formation of granulomas with an inhibition of 70.46%. This proved that bark extract is effective against migration of inflammatory cells to show anti-inflammatory activities and prevent abnormal permeability of blood capillaries. [78] The large number of phytochemicals found in *Syzygium* species including tannins, flavonoids, saponins and phenolic compound are mainly responsible for their anti-inflammatory properties. These bioactive substances function by lowering the synthesis of pro-inflammatory cytokines and changing several inflammatory pathways.

3.5.5: - Antidiabetic activity

Drugs comprising agents that lower or raise blood glucose levels to treat diabetes mellitus are referred to as antidiabetic drugs. A wide range of compounds from different classes that were isolated from many *Syzygium* species showed signs of anti-diabetic characteristics. It has been proven that *S. Cumini* extracts from the seeds, bark, and leaves show hypoglycemic properties. In diabetic animal models as well as in normal one, these plant's extract can reduce blood glucose levels. Mainly seed extract increases insulin secretion and improves glycogen production by liver. Phytochemicals such as flavonoids, saponins, tannins and alkaloids are mainly responsible for great antidiabetic properties of *S. cumini*. These phytochemicals increase insulin secretion, improve insulin sensitivity and guard pancreatic beta cells from oxidative damage. *S. aromaticum* clove shows antidiabetic potential and polyphenolic compounds in it can inhibit digestive enzymes that break down carbohydrates, that reduces blood glucose levels. Antidiabetic potential has been shown by leaf extract of *S. aqueum* which contain bioactive compounds such as myricetin-3-O-rhamnoside and 4-hydroxybenzaldehyde. These compounds enhanced glucose absorption and promoted adipogenesis. [79] Through its effect on glutathione levels in HepG2 cells and inhibition of P-glycoprotein efflux, the aqueous leaf extract of S. guineense exhibited antidiabetic activity. *S. polyanthum* aqueous leaf extract showed antidiabetic effect by reducing blood glucose levels in diabetic rats who were fed alloxan.

3.5.6: - Anticancer activity

Anticancer drugs are constituted of substances that have shown cytotoxic effect against many cancer cell lines. Extracts from *S. cumini* have showed effectiveness against various cancer cell lines, such as lung, cervical, and breast cancer. By causing death and disturbing cell cycles, the methanolic extract of the seeds has shown strong antiproliferative action against different cell lines. Nanoemulsions containing clove essential oil exhibited notable anticancer efficacy against MCF-7 breast cancer cells by reducing cell viability and suppressing VEGFR-2, a key player in tumor development. Broad-spectrum anticancer properties of this oil have also been proven against various cell lines, including liver and colon cancer cells. Extracts from the stem bark and leaves of *S. aqueum* have shown significant anticancer properties against cervical (HeLa) and breast (MCF-7) cancer cells. By inducing necrosis and messing with biological processes necessary for cancer cell survival, these extracts prevent the continued growth of cancer cells. The MTT experiment demonstrated that the ethyl acetate extract of *S. caryophyllatum* leaves exhibited the highest level of cell inhibition on the viability of Hep2 cell lines at higher dosages. *S. paniculatum* fruit extract showed anticancer effect by reducing the lifespan of ASPC-1 and MiaPaCa-2 pancreatic cancer cells. [80]

3.5.7: - Antidiarrheal activity

Fiber-forming compounds known as antidiarrheal agents are used to treat or lessen the symptoms of diarrhea. Mice treated with an aqueous extract of *S. cordatum* leaves had smaller feces, fewer episodes of diarrhea, and delayed their first episode of castor oil-induced diarrhea. Compounds that are isolated from S. myrtifolium leaves ethanol extract showed antidiarrheal potentiality for therapeutic effects. [81] The active compounds in *Syzygium* species often work by reducing the motility of the intestines, thus slowing down the passage of stool and reducing diarrhea.

3.5.8: - Heptaprotective activity

A substance's capacity to shield the liver from harm is referred to as antihepatotoxicity or hepatoprotective action. Known for its rich phytochemical content, *Syzygium cumini* exhibits significant hepatoprotective effects. By lowering oxidative stress and raising liver enzyme levels, extracts from its seeds can guard against liver damage caused by carbon tetrachloride (CCl4) and other hepatotoxins. Phenolic chemicals found in *S. jambos* have been reported to have hepatoprotective properties. These substances have antioxidant qualities and can consume free radicals to reduce liver damage. *S. samarangense* methanol leaf extract showed hepatoprotective activity by reducing liver injury using CCl4-inducedrats. [82] It has been found that clove oil, which is mostly made up of eugenol, has hepatoprotective properties. It functions by boosting liver's antioxidant defense system and lowering inflammation.

CHAPTER 4

CONCLUSION

In this review, we began with an overview of the complex genus *Syzygium* with a summary of its many species and their locations across the world. We next reviewed these species' diverse traditional uses, highlighting their importance in a range of cultural and medical practices. After a thorough analysis of *Syzygium* species' secondary metabolites, a variety of bioactive compounds were found, including tannins, flavonoids, phenols and alkaloids, which enhanced the plants' potential for pharmaceutical use. Different pharmacological activities, including those that are hepatoprotective, anti-inflammatory, antidiabetic, anticancer, and antioxidant, are displayed by these metabolites. Several research support the pharmacological activity of *Syzygium* species, demonstrating their effectiveness in treating a number of diseases. Through a variety of tests and structural identification, these secondary metabolites have been identified and analyzed, resulting to a more complete understanding of their mechanisms of action.

The alkaloids found in *Syzygium* species were the focus of particular investigation, as their important role in the pharmacological actions seen were emphasised. Along with other bioactive substances, these alkaloids support various *Syzygium* species hepatoprotective, anti-inflammatory, antidiabetic, anticancer, and antioxidant properties. This summary promotes more research on *Syzygium* species and their use towards enhancing medical practices and formulating natural remedies.

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