



Received on 04 August 2026; received in revised form, 25 August 2026; accepted, 27 August 2026; published 01 September 2026

A COMPREHENSIVE REVIEW ON SYZYGIVM AQUEUM: PHYTOCHEMISTRY, PHARMACOLOGICAL ACTIVITIES, TRADITIONAL USES AND THERAPEUTIC POTENTIAL

Poonam C. Rahangdale ^{* 1} and Harish Sharma ²

Department of Pharmacy ¹, Anjaneya University, Raipur - 492001, Chhattisgarh, India.

Department of Pharmacology ², Gondia College of Pharmacy Chulod, Tahula - 441601, Maharashtra, India.

Keywords:

Syzygium aqueum, Water apple, Myrtaceae, Phytochemistry, Antioxidant, Antidiabetic, Medicinal plant

Correspondence to Author:

Poonam C. Rahangdale

Department of Pharmacy,
Anjaneya University, Raipur -
492001, Chhattisgarh, India.

E-mail: poonamrahangdale1998@gmail.com

ABSTRACT: *Syzygium aqueum*, belonging to the family Myrtaceae, is an important medicinal and edible plant widely distributed in Southeast Asia, India, Sri Lanka, Australia, and the Pacific Islands. Commonly known as water apple, bell fruit, or watery rose apple, the plant has been traditionally used for treating fever, diabetes, gastrointestinal disorders, inflammation, skin diseases, and infections. Different parts of the plant, including fruits, leaves, bark, roots, and seeds, possess numerous bioactive compounds such as flavonoids, phenolic acids, tannins, terpenoids, anthocyanins, alkaloids, saponins, and essential oils. Recent scientific investigations have demonstrated its antioxidant, antidiabetic, antimicrobial, anti-inflammatory, hepatoprotective, anticancer, cardioprotective, nephroprotective, antihyperlipidemic, wound healing, and immunomodulatory activities. This review summarizes the taxonomy, botanical description, phytochemical composition, pharmacological activities, nutritional value, traditional medicinal uses, toxicity, and future prospects of *S. aqueum*. The review emphasizes the plant's potential as a promising source of natural therapeutic agents for pharmaceutical and nutraceutical applications.

INTRODUCTION: The family Myrtaceae includes over 5500 species covering between 130 and 150 genera. *Syzygium* is considered the largest genus of the flowering plants within the family. The genus includes 1100–1200 species that possess high diversity and are cultivated for many purposes. The species of this genus are distributed in the tropical and subtropical regions of the world. *Syzygium aqueum* (Burm. f. Alston f.), a synonym of *Eugenia aquea* Burm. f., is one of the most common species within the genus *Syzygium*.

It is native to the Pacific regions, viz., Malaysia and Indonesia, especially on Java Island, and extends to the tropics, Africa, and Southern Asia, specifically India and Thailand. The common names of *S. aqueum* are water apple and jambo apple that are related to its succulent fruit. It has numerous exceptional organoleptic features like its agreeable aroma of roses, in addition to being glossy, colorful, and with a sweet low-acidity taste ¹.

The plant has been widely employed in folk medicine and has been mentioned to have a plethora of biological activities. The fruit is used to treat liver diseases and the fresh leaves have been consumed to relieve childbirth pain and used as well in their dried powdered form to treat mouth ulcers. Preparations of the roots have been



employed to alleviate itching and reduce swelling, while a decoction of its bark is utilized for thrush.

Humans have been used medicinal plants from a very long time to treat various diseases. Currently, various medicinal plants have been scientifically reported to be able to help humans in overcoming various health problems. Medicinal components from plants plays an important role in the treatment of various health diseases. They were the sole source of active constituents capable of curing the

various disease and helps in maintaining the physiological condition².

Syzygium aqueum is widely cultivated because of its edible fruits and medicinal importance. Traditionally, various parts of the plant have been employed in treating fever, diabetes mellitus, dysentery, stomach disorders, skin infections, and inflammatory conditions. Modern pharmacological research has validated many of these traditional claims².

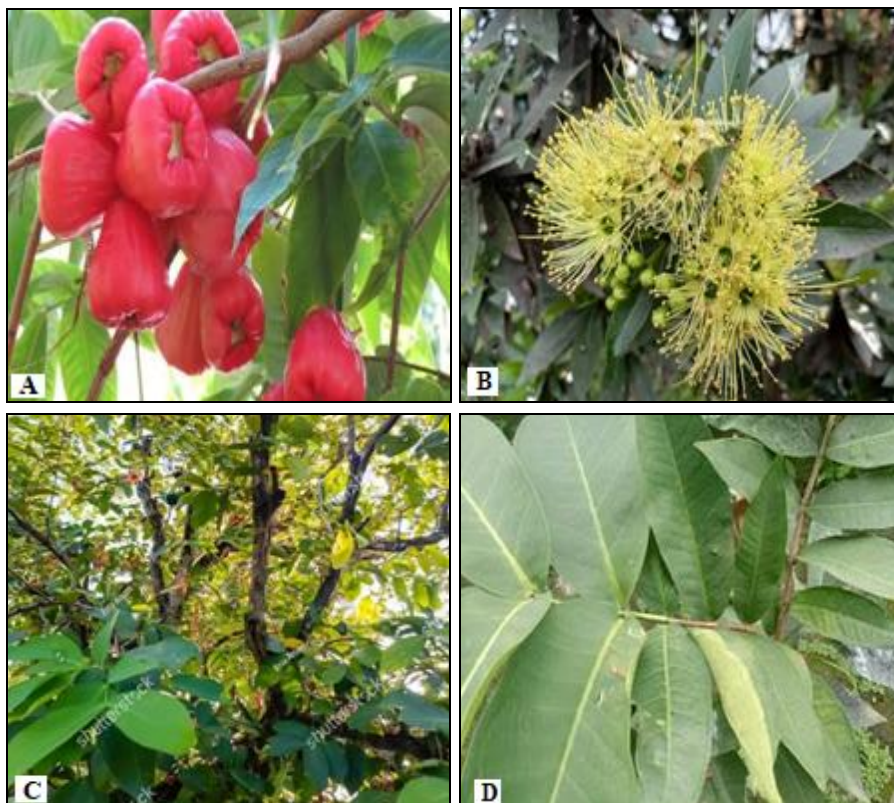


FIG. 1: (A) *S. AQUEUM* FRUIT (B) *S. AQUEUM* FLOWER (C) *S. AQUEUM* TREE (D) *S. AQUEUM* LEAVES³

TABLE 1: TAXONOMICAL CLASSIFICATION⁴

Kingdom	Plantae
Clade	Eudicots, Rosids
Order	Myrtales
Family	Myrtaceae
Species	<i>Syzygium</i>
Genus	<i>S. aqueum</i>
Genus	<i>S. aqueum</i>

Geographical Distribution: The species has its origin in tropical Asia to north Queensland. It is commonly cultivated in India, Southeast Asia and in the Pacific Islands. In the Philippines, *S. aqueum* thrives abundantly in the provinces of Mindanao, Basilan, Dinagat, and Samar, appearing almost as if it were growing wild. It is occasionally grown in Trinidad and Hawaii. *S. aqueum* particularly

distributed in Sri Lanka, Pakistan and Malaysia. In India, it is most likely to occur in moist deciduous forests up to an altitude of 1500 m. It generally grows in the warmer parts like Andhra Pradesh, Assam, Karnataka, Kerala, Orissa, Maharashtra, West Bengal, Punjab, Rajasthan and Tamil Nadu. It also grown in southern and south-eastern Asia including Philippines, Myanmar, and Afghanistan⁴.

Morphology:

- Evergreen tree, 3–10 m tall
- Leaves: Opposite, lanceolate, aromatic

- Flowers: White to yellowish, with numerous stamens
- Fruits: Bell-shaped, watery, crisp, and mildly sweet ⁵

Phytochemical Composition of *S. aqueum*: *S. aqueum* is rich in polyphenols, flavonoids, tannins, steroids, and volatile oils which confers its different biological activities. It is also an ample source of iron, calcium, vitamins, and antioxidants. Different studies have investigated and reported the biological activities of different parts of *S. aqueum*. These include antidiabetic cosmeceutical, antioxidant, anti-inflammatory, hepatoprotective, lipolytic, and anticellulite activities, as well as anticancer activity. Polyphenols are the most

abundant compounds found in different parts of *S. aqueum*, which provide nutritional advantages and contribute to preventing chronic diseases ⁶. The chemical composition of the plant and its involvement in human health will be discussed in this study. *S. aqueum* is still not well exploited as a medicinal plant which leaves room for research and could significantly contribute to the identification of novel drug leads. In this regard, this review is aimed at recapitulating the research established on the phytochemistry, pharmaceutical, toxicology, and food applications of *S. aqueum*, focusing on the role of its secondary metabolites in alleviating inflammation-related disorders. Further, this review highlights the importance of *S. aqueum* and provides a baseline for future research studies ⁷.

TABLE 2: DIFFERENT PHYTOCHEMICAL CONSTITUENTS PRESENT IN *S. AQUEUM* ⁸

Part of the plant	Phyto Constituents
Fruit	Alkaloids, glycosides, formic acid, tartaric acid flavonoids, phenolic content and steroids, and epigallocatechin gallate. myricetin-3-O-rhamnoside and europetin-3-O-rhamnoside
Bark	Tannin, Riedelin, beta-amyrin acetate, betulinic acid and lupeol
Leaf	Phenolic compounds, Flavonoids myricetin and quercetin3-O-βD-xylopyranosyl (1→2) α L rhamnopyranosides, Ursolic acid and myricitrin. Hydroxycoumarins, Stilbenes, p-Coumaric acid, myricetin rhamnosides, quercetin glucosides

A total of 42 volatile constituents were identified in water apple fruit, the largest number and proportion (41.4%) were terpenoids, among which gamma – terpinene was dominant

TABLE 3: SELECTED COMPOUNDS IDENTIFIED FROM *S. AQUEUM* EXTRACTS ⁹

Classes	Phytochemicals
Phenolic acids	4-Hydroxybenzoic acid 4-Oglucoside Methoxyphenyl acetic acid, Dihydro-p-coumaric acid, 5-Caffeoylquinic acid, 4-Caffeoylquinic acid, Chlorogenic acid, Gallic acid, p-Coumaric acid, Ferulic acid ¹⁹
Proanthocyanidins	(-)-Epigallocatechin, (-)-Epigallocatechin 3-gallate Epicatechin 3-O-gallate Prodelphinidin B-2,3,3 " -di-Ogallate, Samarangenin A, Samarangenin B
Stilbenes	Resveratrol , Resveratrol 5-O-glucoside
Flavonoids	Oleuropein- aglycone, 3,4-DHPEA-EA, 6-Gingerol, 2,4-Di-tertbutylphenol ¹⁸
Hydroxycoumarins	Myricetin-3-O-rhamnoside, Chrysoeriol 7-O-glucoside Quercetin 3-O-galactoside Quercetin 3-O-glucoside, Quercetin 4'-O-glucoside., Sakuranetin Europetin 3-O-rhamnoside.
Volatile compounds	Umbelliferone, Coumarin, 4-Hydroxycoumarin, Scopoletin, 3,4-Dihydroxyphenylglycol
Fatty acids and steroids	Eucalyptol α-Pinene L-Verbenone Borneol, α-Terpineol, Camphene Cis-Geraniol, Camphor, β-Linalool, α-Caryophyllene, 0 β-Caryophyllene
	Butyrospermol-3-β-palmitate, β-Sitosterone, Butyrospermol ¹⁹

Isolated Compounds:
Leaves and Fruits:

Flavonoids: Methanol extract of *S. aqueum* leaves contained a number of 87 different compounds rich in flavonoids, for example, myricetin rhamnoside, myrigalone G pentoside, quercetin galloylpentoside, cryptostrobin, in which myrigalone- B and myrigalone- G were the major flavonoid compounds. Six flavonoids (e.g., 4-hydroxybenzaldehyde, myricetin- 3- Orhamnoside,

europetin- 3- O- rhamnoside, phloretin, myrigalone- G, and myrigalone- B) were isolated from the ethanol leaf extracts of *S. aqueum*. Among them, myricetin- 3- Orhamnoside and europetin- 3- O- rhamnoside showed antihyperglycemic activity ¹⁰.

Phenols: Methanol extract of *S. aqueum* leaves contained a few phenolic compounds (e.g. caffeic acid).

Tannins: Methanol extract of *S. aqueum* leaves contained few number of tannin compounds (e.g. galloylquinic acid).

Proanthocyanins: Methanol extract of *S. aqueum* leaves contained 87 different compounds which were determined through high- resolution LC-ESIMS/MS analysis; among them, major proanthocyanins were samarangenin A; (epi)-gallocatechin gallate; (epi)- catechin- (epi)-gallocatechin.

Essential Oils: Essential oils can be utilized as a prime source of antioxidants in traditional remedies and cosmetics. The fruits and leaves of *S. aqueum* contain a considerable amount of essential oils. Terpenoids and γ -terpinene are the main predominant components present in the fruit volatile oils while the leaves contain α - and β -caryophyllene, β -selinene, caryophyllene oxide, cuminylaldehyde, cinnamaldehyde, β -elemene, and eudesm-7(11)-en-4-ol. However, the flavor profile of water apple juices and ciders showed different volatile compounds. 1-Butanol, 3-methyl- acetate, 4-hexen-1-ol, (E)-, ethene, fluoro-, and 3-methoxy benzenamine were predominant in the ciders, while hexanal, 4-hexen-1-ol, (E)-, caryophyllene, and 3-hexen-1-ol, (Z)- were the most predominant compounds in the juices ¹¹.

Qualitative Phytochemical Analysis:

Alkaloid:

Mayers Test: Add a few drops of Mayer's reagent (potassium mercuric iodide) to a sample of the extract. The formation of a cream-colored precipitate indicates the presence of alkaloids.

Hager's Test: Add a few drops of Hager's reagent (saturated picric acid) to another sample of the extract. A bright yellow precipitate suggests the presence of alkaloids.

Wagner's Test: Along the side of the test tube, add a few drops of Wagner's reagent (iodine in potassium iodide) to the extract. The appearance of a reddish-brown precipitate confirms the presence of alkaloids.

Dragendorff's Test: Add 1 ml of Dragendorff's reagent (potassium bismuth iodide solution) to 1 ml of the extract. An orange-red precipitate indicates the presence of alkaloids.

Glycoside:

Borntragers Test: Take 2 ml of extract, add dilute sulfuric acid, and boil and filter the solution. Cool the filtrate and add an equal volume of chloroform, shake well. Separate the chloroform layer and shake it with dilute ammonia. Ammonia layer turns a rose-pink or red color, which show presence of glycosides.

Keller-Kiliani Test (for Cardiacglycosides): Mix 2 ml of a plant extract with 1 ml of glacial acetic acid. Add a few drops of 5% iron (III) chloride solution. Carefully add 1 ml of concentrated sulfuric acid to the side of the test tube, allow it to form a layer below the acetic acid mixture.

Fehling's Test (for Reducing Sugars after Hydrolysis): Heat 1 ml of the plant extract with a small amount of dilute acid to hydrolyze the glycosides. After hydrolysis, neutralize the solution. Add equal amounts of Fehling's solution A and Fehling's solution B. Heat the mixture in a water bath. The formation of a brick-red precipitate indicates the presence of reducing sugars.

Legal's Test: To the plant extract, add 1 ml of pyridine and a few drops of sodium nitroprusside solution. Add sodium hydroxide solution to make the mixture alkaline. The appearance of a pink-to-red color indicates the presence of glycosides.

Saponins:

Test for Saponins: With 20 ml of distilled water, the extract was dissolved and agitated for 15 minutes. The presence of saponins was demonstrated by the creation of a 1 cm layer of foam over time.

Flavonoids:

With Sodium Hydroxide: 1 ml sodium hydroxide solution was added to the extract. Anthocyanins are found in blue to violet colors, Flavanones are found in yellow to orange colors and flavones are found in yellow.

Concentrated Sulphuric Acid: Concentrated sulphuric acid was added to the extract. The presence of anthocyanins is indicated by a yellow orange, while the presence of flavones is indicated by an orange-to-red tint.

Shinoda Test: Extract was dissolved in ethanol and magnesium turnings were added to perform Shinoda's test concentration of hydrochloric acid was added to this combination. The presence of flavonoids is indicated by a change in hue from magenta to purple.

Tannins:

Test for Tannins (Ferric Chloride Test): To every 2 ml of the extracts, 2 ml of water was added. Two (2) drops of 5% ferric chloride (FeCl_3) solution was added. The positive test was inferred by the appearance of blue, black, or green colour.

Phenol:

Phenol Test (Phenol Test): A gram of each extract was spotted on a filter paper followed by the addition of phosphomolybdic acid reagent (single drop). The spotted extract on the filter paper was exposed to ammonia vapours. A Positive result was observed following the appearance of blue colour on the spot.

Steroid:

Test for steroids (Liebermann-Burchardt Test): One (1) ml of each of the extract and that of chloroform was mixed and 2 ml of acetic anhydride was added. Two (2) drops of concentrated sulphuric acid were added again and the presence of dark green coloration indicates a positive result

Pharmacological Activities and Health Benefits:

Anticancer Activity: *S. aqueum* leaves underwent methanol extraction to assess cytotoxicity via the sulforhodamine B (SRB) assay.

The study evaluated its effects on human breast cancer cells (MDA-MB-231) in comparison to doxorubicin, a standard cytotoxic drug. The extract demonstrated lower toxicity towards the cancer cell line, with an IC_{50} value exceeding $100 \mu\text{g/mL}$ ²⁰.

Antiproliferative Property: The antiproliferative properties of *Syzygium* fruit, namely water apple (*S. aqueum*) against two types of cancer-origin cells, namely MCF-7 (hormone dependent breast cancer cell line) and MDA-MB-231 (non-hormone dependent breast cancer cell line) were investigated ¹².

Anti-inflammatory Activity: Anti-inflammatory is an action of a substance, which affects the CNS

to block the pain signalling to the brain and helps to reduce inflammation and pain.

The polyphenol- enriched leaf extract of *S. aqueum* exhibited promising anti-inflammatory activities where it inhibited LOX, COX- 1, and COX- 2 with a higher COX- 2 selectivity than that of standards indomethacin and diclofenac and reduced the extent of lysis of erythrocytes upon incubation with hypotonic buffer solution,

Antianging Activity: The ability of *S. aqueum* extracts to act as whitening agents by preventing melanin production was assessed by the inhibition of tyrosinase. As a result, the IC_{50} of ethanol ($71 \mu\text{g/mL}$) and propylene glycol ($57 \mu\text{g/mL}$) leaf extracts were comparable to that of kojic acid, positive control used as a skin whitening agent ($\text{IC}_{50} = 52 \mu\text{g/mL}$). The plant may also possess UVB blocking ability ¹⁶. In another study, the methanol extract of the leaves exhibited shielding properties against oxidative stress induced by UVA radiation. In general, UVA significantly increased DCF fluorescence intensity in keratinocytes (HaCaT cells), compared to the no irradiated cells ¹³.

Cosmeceutical Activity: *S. aqueum* leaf extracts may be used as a skin treatment ingredient because it is not only an antioxidant but has tyrosinase inhibition activity and may also possess UVB blocking ability.

Prevent Constipation: The dietary fibres present in Rose Apple aid in promoting regular bowel movements and alleviating constipation, thereby supporting overall digestive health. Additionally, these fibres contribute to maintaining a healthy weight and reducing the risk of heart disease and diabetes.

Prevent Muscle Cramping: Rose Apple possess adequate amount of potassium. It enhances the strength of muscles and reduces the muscle cramps which is due to the low level of potassium ^{16, 17}.

Fights Free Radical Damage: Rose Apple is renowned for its high Vitamin C content, which serves to counteract the damage caused by free radicals, pollutants, and toxins implicated in health conditions like heart disease, cancer, and arthritis. Free radicals arise in the body due to exposure to

radiation, tobacco, smoke, and the metabolic breakdown of food. Vitamin C supports the production and function of white blood cells, acting as an antioxidant to mitigate oxidative damage and promote optimal functioning. Additionally, it is believed to bolster the immune system, aiding in the defense against colds¹⁴.

Reduced Risk of Stroke: The abundance of Vitamin C in Rose Apples contributes to reducing the risk of stroke and various health conditions, including inflammation, oxidative damage, cardiac issues, atherosclerosis, high blood pressure, and endothelial dysfunction. By countering the development of plaque in the body, Vitamin C plays a crucial role in minimizing the likelihood of strokes and heart attacks.

Boost Good HDL Cholesterol: Rose Apple serves as a natural source of niacin, a nutrient known to regulate cholesterol levels. Niacin supplementation is associated with increased HDL cholesterol levels and decreased levels of triglycerides and LDL cholesterol.

Prevent Diabetes: Research indicates that the consumption of Rose Apple leads to a reduction in blood glucose levels by enhancing the activities of key carbohydrate metabolic enzymes, including glucose-6-phosphate dehydrogenase, hexokinase, and glucose-6-phosphatase¹⁵.

Hepatoprotective Activity: A single dose of the methanol extract of the plant reduced the elevated levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol (TC), total bilirubin (TB), and triglycerides (TG) in acutely CCl₄ -intoxicated rats. In addition, the extract noticeably restored superoxide dismutase (SOD) and liver glutathione (GSH) to the normal control levels in liver tissue homogenates and stabilized the damaging histopathologic changes in the liver after CCl₄ injection¹⁹. The obtained activities were attributed to the presence of several polyphenolic compounds, including myricetin rhamnosides, quercetin glucosides, and epigallocatechin gallate. Triterpene acids that show strong protective effects against liver injury¹³.

Traditional Uses of *S. aqueum*: *S. aqueum* has been used traditionally for several medicinal purposes. Leaves, bark, and fruits possessed many

medicinal uses for digestive conditions, liver detox, headaches, fever treatments, skin conditions, and cancer prevention. In Malaysia, powdered dried leaves are utilized to cure a cracked tongue and a root preparation is applied to relieve itching and reduce swelling. An infusion of the leaves is used in the treatment of stomach aches and dysentery. The leaves have been utilized to relieve childbirth pains. The decoction of the bark can alleviate thrush that is caused by *Candida albicans* and affecting the oral cavity and other parts of the body. The efficacy of a plant as traditional medicine is related to the bioactive compounds contained in the plant extract such as phenolic acids, flavonoids, tannins, lignans, and stilbenes^{18, 19}.

CONCLUSION: *Syzygium aqueum* is a valuable medicinal and nutritional plant with a wide range of traditional and scientifically validated pharmacological activities. Leaves of *S. aqueum* with either pink or red fruits contained secondary metabolites, namely flavonoids, phenolics, and triterpenoids, while their stem barks contained not only flavonoids, phenolics, and triterpenoids but also saponins and alkaloids. Leaves and stem bark extracts of these plants with either pink or red fruits exhibited antioxidant activities and contributes to potent antioxidant, antidiabetic, antimicrobial, anti-inflammatory, hepatoprotective, cardioprotective, nephroprotective, and anticancer properties. Although preclinical evidence is promising, further standardization, toxicological studies, and well-designed clinical trials are necessary to support its therapeutic use. With continued research, *S. aqueum* has significant potential as a source of novel phytopharmaceuticals, functional foods, and nutraceutical products.

ACKNOWLEDGEMENT: Nil

CONFLICT OF INTEREST: Nil

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How to cite this article:

Rahangdale PC and Sharma H: A comprehensive review on *Syzygium aqueum*: phytochemistry, pharmacological activities, traditional uses and therapeutic potential. Int J Pharmacognosy 2026; 13(9): 943-49. doi link: [http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.13\(9\).943-49](http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.13(9).943-49).

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