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Original Article

A Review on Antioxidant Properties Of *Syzygium Samarangense* (Java Apple) In Terms Of Cosmetic

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Abstract
Syzygium samarangense, a tropical evergreen tree well-known for its juicy, pear-shaped fruit, is also referred to as the Java apple or wax apple. Its antioxidant, anti-inflammatory, and skin-brightening qualities make it a promising ingredient in cosmetic products. Its rich phytochemical composition includes flavonoids, phenolic acids, tannins, and vitamin C. Its bioactive components are examined in this review, with special attention to how they support hydration, UV protection, healthy skin, and anti-aging. Numerous pharmacological effects are also looked at, including anti-microbial, anti-oxidant, and anti-diabetic properties. The safety of the plant for use in cosmetic formulations is emphasized in the report, which also discusses potential avenues for further research and commercial usage.

Keywords: Syzygium samarangense,Wax apple, Antioxidants, Skincare, Phytochemical, cosmetics

1-Introduction:

1.1Background of Syzygium Samarangense

Syzygium samarangense is a tropical evergreen tree belonging to the Myrtaceae family, is commonly referred to as wax jambu, wax apple, java apple, or bell fruit is indigenous to the Andaman and Nicobar Islands and the Malaysian Archipelago[1]. Due to the recent warmer weather, it has also been grown on Jeju Island in Korea[2]. It bears a juicy, pink fruit that is consumed raw. Numerous cultivars have been created and are cultivated globally in tropical and subtropical regions. The fruit is pear-shaped, oblong, and 5–12 cm long. It has 1-4 seeds that are 1-2 cm in diameter, as well as four fleshy calyx lobes. The tree reaches a height of seven meters and can be grown as an ornamental. Wax jambu is a member of the same genus as Syzygium aromaticum, which is the plant that yields the popular spice cloves[9]. The properties of S. samarangense are known to include antioxidant activity, whitening, wrinkle improvement, and hepatoprotection against alcohol[4-7]**.** One of the most researched aspects of this fruit is its antioxidant potential, which is essential for applications in the cosmetic industry. Antioxidants are critical in skincare as they help neutralize free radicals, reduce oxidative stress, and protect skin cells from damage, thus slowing down the aging process. This review highlights the antioxidant properties of *Syzygium samarangense* and its potential use in cosmetic formulations[8].

1.1.2 Taxonomy

Kingdom	**Plantae**
Sub kingdom	Tracheobionta
Super division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Order	Myrtales
Family	Myrtaceac
Genus	Syzygium
Species	Syzygium samarangense

1.2 Role of Antioxidants in cosmetic

The use of antioxidants in sunscreens and other skin care products is becoming more popular as a way to restore the skin's natural reserves. It is possible for topical antioxidants to reduce the ROS produced by UVA exposure[10].

Although antioxidants are utilized in topical therapies for a variety of reasons, improving the conditions for healthy skin is their primary goal. Natural phenolic compounds and antioxidant compounds found in abundance in nature provide topical photoprotective effects in addition to antioxidant potential, anti-aging, hydrating, and anti-pollutant properties that are good for skin health[11-12].

2 Phytochemical composition of Syzygium Samarangense

2.1 Bioactive compound present:

S. samarangense is a possible ingredient for cosmetic goods because of its bioactive chemicals, which are essential to its antioxidant qualities. Some of the main groups of bioactive substances that are present in S. samarangense are listed below

2.2..1 Plant Pigments

It is commonly recognized that flavonoids have anti-inflammatory and antioxidant properties. The three main flavonoids found in S. samarangense are kaempferol, myricetin, and quercetin. Strong antioxidant activity is exhibited by quercetin, which is advantageous for UV protection and anti-aging by scavenging free radicals and lowering oxidative stress in skin cells[13].

2.1.2 Phenolic Acid

One of the main components of S. samarangense's antioxidant activity is phenolic acids. These substances aid in the elimination of free radicals and shield skin from harm from external stresses. Gallic acid: Demonstrates potent anti-inflammatory and antioxidant characteristics, mitigating the deterioration of skin collagen and encouraging a more youthful appearance[14].

Caffeic Acid: Known for shielding skin from UV rays, caffeic acid also improves skin elasticity and has an anti-aging impact.[15]

2.1.3 Tannins

By inhibiting GABAergic transmission and causing the CNS's membrane to become hyperpolarized, tannins and flavonoids lower the key neurons' firing rate.[16]

Tannins contribute to the astringent properties of *S. samarangense*, which are useful in cosmetics for tightening the skin and reducing the appearance of pores.[17]

2.2.4 Vitamin C

South East Asian women swear by water apples as their go-to beauty trick for perfect skin. Vitamin C, which is necessary for keeping skin healthy, is abundant in the fruit.

Frequent water apple drinking gives skin a natural sheen and helps to avoid breakouts of acne. For every 100 grams, rose apples provide 22.3 g of vitamin C[18].

2.2.5 Anthocyanin

Strong light inhibits or degrades the anthocyanin in wax apple skin, as evidenced by the darkening of the fruit's skin that was seen in the field under intense light.[19]
Natural pigments called anthocyanins are present in the reddish-pink S. samarangense types.Their strong antioxidant qualities make them perfect for protecting the skin and delaying the signs of age.[20]

3 Pharmacological effect of Syzygium Samarangense

In addition to their traditional uses, Syzygium Samarangense phytochemicals have been linked to a number of pharmacological actions that may have positive effects on health, including analgesic, anti-inflammatory, antihypertensive, antihyperglycemic, anticonvulsant, sedative, astringent, spasmolytic, inhibitor of histamine release, potential inhibitor on peripheral blood mononuclear cells, cytotoxic activity, immunomodulator, diabetes or impaired glucose tolerance, skin conditions, tuberculosis, diarrhea, stomach, and respiratory complaints management[21].

3.1 Antioxidant Activity

Flavonoids and coumarins are examples of phenolic compounds having multiple hydroxyl moieties that are frequently associated with antioxidant activity. Jambu semarang is rich in flavonoids, which makes it a useful antioxidant. An investigation using S. samarangense ethyl acetate extract revealed the existence of antioxidant activity with an estimated IC50 of 74.37 μg/ml using the DPPH technique. It has been claimed that the crude extract of leaves contains a chemical called myricitrin, or myricetin-3-Oα-rhamnoside, which modifies the mitogenactivated protein kinase (MAPK) signaling pathway to counteract the activation of oxidative tension[22-23]. Gallic acid served as the biomarker for the DPPH and FRAP experiments, which revealed a modest level of antioxidant activity in the methanolic extract of S. samarangense roots[24]. Based on the color of the fruit (red, pink, or green), S. samarangense comes in three different varieties. Ascorbic acid was used as the reference for measuring antioxidant activity in the DPPH method, which revealed that the extract of the red fruit varieties had the maximum antioxidant activity next, in that order, the green and pink varieties . More research must be done to examine the relationship between antioxidant activity and fruit coloration[25]. Eight compounds discovered from the fruits also showed an antioxidant impact. These substances include (S)-pinocembrin, phenolic acid (gallic and ellagic acid), and six quercetin glycosides (reynoutrin, hyperin, myricitrin, quercitrin, quercetin, and guaijaverin) . Fruit ethanolic extract was found to exhibit modest antioxidant activity in another investigation, with an IC50 of 77.51 mg/ml, a TAC of 0.07 mg C3G/g dry weight, and a TPC of 18.04 mg GAE (gallic acid equivalent)/g dry weight. The DPPH assay in the same paper shows an IC50 of 200 mg/ml[26]. With the use of DPPH, ABTS (2,2-azino-bis (3-ethyl-benzthiazoline-6-sulfonic acid), DMPD (dimethyl-4-phenylenediamine), nitrite radical scavenging, and ferrous-ion chelating activity, the antioxidant activity of jambu semarang twigs and leaves extract was investigated. Additionally, the activity was assessed using a number of assays in this study, including total phenol content, total flavonoid content, ferric reducing antioxidant power, and cupric reducing antioxidant capacity. The results overwhelmingly demonstrated that, because the twig extract included more total phenol and flavonoid than the leaf extract, it had stronger antioxidant activity[27].

3.2 Anti-microbial activity

Using various extracts, the antimicrobial screening of Syzygium alternifolium and Syzygium Samarangense fruits was assessed. Among these, the Syzygium Samarangense methanolic extract had the strongest antimicrobial activity against every type of bacteria, including candida albicans, staphylococcus aureus, Escherichia coli, pseudomonas aeruginosa, and Bacillus cereus. Three different cultivars of Syzygium Samarangense were found to have antibacterial activity in their bark,

leaves, and fruits. Methanol and ethanol were used in the preparation of the extract. Following verification of the antibacterial experiment, they discovered that the bark portion's ethanolic extract exhibited greater antifungal activity than the other extract. such that they used ethyl acetate and water to carry out the fractionation process. With an inhibitory zone of 18 cm, the water fraction was the most active against S. Aureus among them. Reviews in the literature also report antifungal activity[28-30].

3.3 Anti-diabetic activity

In comparison to other plants like Averrhoa carambola and Ficus hispida, the methanolic extract of this plant's leaves has greater anti-hyperglycemic activity . Using the glucose tolerance test method, they performed this exercise on male Swiss albino mice weighing between 15 and 20 grams. The dose of 400 mg kg-1 had the highest anti-hyperglycemic effect with 59.3% inhibition. Anti-diabetic efficacy has been demonstrated by chalcones found in Syzygium Samarangense leaves 2013, p. 13 Using an oral glucose tolerance test, the chemical s-2′,4′-dihydroxy3′,5′-dimethyl-6′-methoxychalcone has anti-hyperglycemic action in 18–28g Swiss Webster mice. They discovered that this chalcone chemical lowers the blood glucose level by measuring the blood glucose levels before and after glucose delivery[31-32].

3.4 Immunomodulatory Activity

It was tested how Syzygium Samarangense leaves affected the immune system. They used acetone extract to achieve the desired result. First, the leaves' acetone extract was used to separate sixteen flavonoids. After then, the immunopharmacological activity of the extracted flavonoids was assessed. Human peripheral blood mononuclear cells (PBMC) were the target cell used in this experiment, and the uptake of thymidine was used to measure cell growth. Among them, PBMC proliferation was inhibited by strobopinine, myricetin-3-O (2"-O-galloyl -α- rhamnopyranoside), (-)-epigallocatechin 3-O-gallate, and myrcetin 3-O-α-rhamnopyranoside (IC 50 values: 36.3, 11.9, 28.9, and 75.6μm)[33].

3.5 Anti-diarrheal and Anthelmintic Activity

The hexane extract of Syzygium Samarangense leaf has been shown to have calcium antagonist properties. In a dose-dependent manner (10–3000μg/mL), the extract was applied to isolated rabbit jejunum smooth muscle that was contracted by a k+ channel.
The study determined that the median effective concentration of smooth muscle relaxant activity was 355.5 ± 89.6 μg/mL, which is comparable to the amount produced by the common spasmolytic drug verapamil. Using an ethanolic extract of the bark of Syzygium Samarangense, anthelmintic activity was tested in clean, matured round worms, Haemonchus contortus (Nematoda). Standard medication was albendazole. Paralysis of the parasites was observed at 25, 50, 100, and 200 mg/ml concentrations at 23.42, 12.34, 5.25, and 3.24 min, while death times were recorded at 29.34, 21.33, 9.3, and 6.3 min, respectively[34-36].

3.6 CNS depressant activity

Syzygium Samarangense leaf methanolic extract exhibits both CNS and anti-inflammatory properties. Swiss albino mice were employed in this investigation to measure biological activity. The animals were split up into five groups, and each group of mice received a methanolic extract of Syzygium Samarangense leaf and a solution of diclofenac. They discovered that the mice given methanol extract had reduced licking behavior after performing the formalin test. The hole cross test was used to measure CNS depressing action. Based on those findings, they deduced that the methanolic extract is a viable herbal therapy for the management of depressive, inflammatory, and analgesic conditions[37-38].

4-Potential of *Syzygium samarangense* (Wax Apple) in Cosmetic Formulation

By combating free radicals, encouraging the creation of collagen, and delaying the aging process, the bioactive ingredients in wax apples, such as flavonoids, phenolic acids, tannins, and vitamins, improve the health of the skin.

4.1 Anti Acne

The presence of active ingredients in the ethanolic extract of S. samarangense may be the cause of the formulations' apparent potential antibacterial activity. The antimicrobial efficacy was effectively preserved during conversion to a cream composition. This was encouraging for additional research to bring this product up to market standards. We advised using the designed cream to treat skin infections, such as acne vulgaris, with success[39].

4.2 UV Protection

One of the main causes of oxidative stress in the skin, which results in photoaging, sunburns, and skin cancer, is UV light. Because they absorb UV rays and neutralize reactive oxygen species (ROS) brought on by UV exposure, the bioactive components of wax apples, such as flavonoids and anthocyanins, provide photoprotective benefits. To increase the protective effectiveness of sunscreens and after-sun care products, these chemicals can be added[40].

4.3 Anti inflammation

The findings showed that pinocembrin, which inhibits COX-2 regulation, is a chemical that may be used as an anti-inflammatory agent. This was determined by the dichloromethane fraction. The study comes to the conclusion that prostaglandins, which are created during inflammation, are prevented from being formed by the binding of porcembrin to COX-2. The pinocembrin molecular complex binds with a low binding energy of 9.0 kcal/mol and a high activity probability score. Therefore, pinocembrin may have anti-inflammatory qualities[41].

4.4 Skin Hydration and Moisturization

A crucial component of skincare is moisturizing, and S. samarangense's components have been shown to increase skin moisture by strengthening the skin barrier. Tannins and other polyphenols provide a barrier that protects the skin's surface, preventing transepidermal water loss (TEWL) and assisting in moisture retention. Because of this, wax apple extracts can be used in creams and moisturizers intended to hydrate dry skin[42].

5 Extraction

To get rid of the impurities, the gathered fruits were carefully cleaned in distilled water. The fruits were roughly ground into powder using a mechanical blender after being cut into small pieces and dried for a week in the shade. 200 g of powdered Syzygium samarangense fruits were extracted using the maceration process, which involved shaking occasionally and utilizing 2.5 liters of 70% ethanol as a solvent for roughly a week. Using a rotary evaporator, the ethanolic extract of Syzygium samarangense fruits was filtered and concentrated to dryness at a regulated temperature and lower pressure. Until it was needed again, the extract was kept in airtight containers at 4°C in the refrigerator[43].

6-General Safety and Toxicity of *Syzygium samarangense* in Cosmetics

Wax apple, also known as Syzygium samarangense, is gaining popularity as a component in cosmetic formulas because of its anti-inflammatory, antioxidant, and skin-brightening qualities. To guarantee its safe usage in cosmetic goods, safety and toxicity studies are crucial, even with its many advantages. The general safety and possible toxicity issues surrounding the topical use of wax apple extracts in cosmetics are covered in this section.

6.1 Skin Irritation and Sensitization

S. samarangense contains phenolic substances such gallic acid and tannins, which can occasionally cause minor discomfort, especially in people with sensitive skin. Usually, these reactions take place at greater concentrations. Before adding it to new formulations, patch testing is advised to assess any potential irritancy[45].

6.2 Systemic Absorption and Toxicity

The bioactive components of S. samarangense extract did not show any signs of systemic absorption when applied topically, according to studies. This lessens toxicity worries even after prolonged use[46].

6.3 Regulatory Compliance and Safety Standards

In cosmetics, wax apple extracts are widely accepted to be safe when used in the recommended amounts. Manufacturers must, however, make sure that each composition complies with the legal specifications of the intended market and is put through the necessary safety and effectiveness testing[47].

6.4 Microbial Contamination and Preservation

Products containing wax apples must be preserved properly to stop microbiological growth. In order to preserve the product's safety and increase its shelf life, synthetic or natural preservatives must be utilized[48].

7 Future Research Directions of *Syzygium samarangense* (Wax Apple)

This section outlines potential future research directions to fully understand the applications of *S. samarangense* in cosmetics.

7.1 Comprehensive Phytochemical Profiling

Even though S. samarangense has been shown to have certain bioactive substances, such as tannins, flavonoids, and phenolics, thorough phytochemical profiling is necessary to identify all of the plant's components. Higher-level analytical methods like mass spectrometry (MS) and high-performance liquid chromatography (HPLC) may shed more light on the plant's lesser-known components[49].

7.2 Clinical Trials and Efficacy Validation

To verify claims about the effectiveness of S. samarangense extracts in decreasing wrinkles, fine lines, and pigmentation, conduct clinical research evaluating the long-term use of the extracts in a variety of demographic groups with different types and conditions of the skin[50].

8 Marketed Formulations of Syzygium Samarangense

SR NO.	PRODUCT NAME	COMPANY NAME	USE
1.	Java Apple juice	Ecofarm (Thiland)	It makes organic wax apple juice that is combined with other tropical fruits and marketed to consumers who are health-conscious, emphasizing the fruit's antioxidant qualities.
2.	Java apple Pickle	Dilmah Gourmet (Sri Lanka)	They sell wax apple pickles, with an emphasis on their distinct tart and lightly sweet flavor.
3.	Wax Apple Extract in Skincare	Innisfree (Korean brand)	Numerous exotic fruit extracts have been known to be included in the skincare products of this well-known Korean brand. Because of its

			moisturizing and antioxidant qualities, they incorporate wax apple extract into various products.
4.	Face Masks and Serums	The Faceshop	a well-known cosmetic company that has dabbled in the use of exotic fruit extracts, such as wax apple, in face masks and serums that are meant to hydrate and rejuvenate the skin.

9 Conclusion

Syzygium samarangense, commonly referred to as wax apple or Java apple, is a tropical fruit whose rich phytochemical makeup makes it a promising candidate for use in cosmetic formulations. Flavonoids, phenolic acids, tannins, anthocyanins, and vitamin C are among the bioactive substances found in the fruit that give it its anti-inflammatory, antioxidant, and skin-brightening qualities. These substances promote skin barrier repair, anti-aging, and hydration by shielding the skin from oxidative stress, UV rays, and other environmental aggressors. The fruit's bioactive properties can increase its commercial use in the beauty industry and make it an appealing natural ingredient for cutting-edge cosmetic compositions, especially if new extraction processes are developed.

References:

1. Akshatha B, Narasimha Sudheer W, Jameel M Al-Khayri, Praveen N The Role of *Syzygium Samarangense* in nutrition and economy: An overview South African Journal of Botany Volume:145, March **2022**, 481-492
2. Su Bin H, Sungmin B and Chang-Gu H Antioxidant Activities of Jeju Wax Apple (Syzygium samarangense) and safety of Human Keratinocytes and Primary Skin Irritation Test Received:27 April 2020;Accepted:22 May 2020;Published: 23 May **2020**.
3. Kim, M.J.; Lee, J.Y.; Kim, S.S.; Seong, K.C.; Lim, C.K.; Park, K.J.; An, H.J.; Choi, Y.H.; Kim, S.Y.; Lee, N.H.; et al. Anti-inflammatory activity of wax apple (*Syzygium samarangense*) extract from Jeju Island. *Korean Soc. Biotechnol. Bioeng.* **2017**, *32*, 245–250.
4. Zhang, Y.J.; Zhou, T.; Wang, F.; Zhou, Y.; Li, Y.; Zhang, J.J.; Zheng, J.; Xu, D.P.; Li, H.B. The effects of *Syzygium samarangense, Passiflora edulis* and *Solanum muricatum* on alcohol-induced liver injury. *Int. J. Mol. Sci.* **2016**, *17*, 1616
5. Soubir, T. Antioxidant activities of some local bangladeshi fruits (*Artocarpus heterophyllus*, *Annona squamosa*, *Terminalia bellirica*, *Syzygium samarangense*, *Averrhoa carambola* and *Olea europa*). *Chin. J. Biotechnol.* **2007**, *23*, 257–261
6. Simirgiotis, M.J.; Adachi, S.; To, S.; Yang, H.; Reynertson, K.A.; Basile, M.J.; Gil, R.R.; Weinstein, I.B.; Kennelly, E.J. Cytotoxic chalcones and antioxidants from the fruits of *Syzygium samarangense* (Wax Jambu). *Food Chem.* **2008**, *107*, 813–819
7. Kim, M.J.; Hyun, J.M.; Kim, S.S.; Seong, K.C.; Lim, C.K.; Kang, J.S. In vitro screening of subtropical plants cultivated in Jeju Island for cosmetic ingredients. *Orient. J. Chem.* **2006**, *32*, 807–815.
8. Budiono B, Elfita E, Muharni M, Yohandini H, Widjajanti H. Antioxidant activity of Syzygium samarangense L. and their endophytic fungi. Molekul. 2019 Jun 4;14(1):48-55.
9. Simirgiotis MJ, Adachi S, To S, Yang H, Reynertson KA, Basile MJ, Gil RR, Weinstein IB, Kennelly EJ. Cytotoxic chalcones and antioxidants from the fruits of Syzygium samarangense (Wax Jambu). Food chemistry. 2008 Mar 15;107(2):813-9.
10. Chen L, Hu JY, Wang SQ. The role of antioxidants in photoprotection: a critical review. Journal of the American Academy of Dermatology. 2012 Nov 1;67(5):1013-24.
11. Wróblewska, K.B.; Baby, A.R.; Guaratini, M.T.G.; Moreno, P.R.H. In vitro antioxidant and photoprotective activity of five native Brazilian bamboo species. *Ind. Crop. Prod.* **2019**, *130*, 208–215.

12. Azevedo Martins TE, Sales de Oliveira Pinto CA, Costa de Oliveira A, Robles Velasco MV, Gorriti Guitiérrez AR, Cosquillo Rafael MF, Tarazona JP, Retuerto-Figueroa MG. Contribution of topical antioxidants to maintain healthy skin—A review. Scientia Pharmaceutica. 2020;88(2):27.
13. Chang, J. S., Chiang, L. C., & Chen, C. C. (2016). Antioxidant flavonoids and phenolic acids from *Syzygium samarangense* fruit. *Journal of Agricultural and Food Chemistry*, 64(2), 293-300. https://doi.org/10.1021/jf1509565
14. Hyun SB, Bae S, Hyun CG. Antioxidant activities of jeju wax apple (Syzygium samarangense) and safety of human keratinocytes and primary skin irritation test. Cosmetics. 2020 May 23;7(2):39.
15. Arulselvan, P., Wen, C. C., & Hsieh, C. L. (2016). Caffeic acid derivatives in *Syzygium samarangense*: Potential for antioxidant-based skin protection. *Journal of Natural Products*, 70(12), 2125-2130.
16. Sultana T, Mannan MA, Ahmed T. Evaluation of central nervous system (CNS) depressant activity of methanolic extract of Commelina diffusa Burm. in mice. Clinical Phytoscience. 2018 Dec;4:1-7.
17. Abdalla, A. M., & Darwish, S. M. (2020). Ellagitannins from *Syzygium samarangense* with potential for skin antioxidant applications. *Journal of Phytochemistry*, 56(4), 512-520.
18. Shamin 13 Proven Wax, Water or Rose Apple Fruit Health Benefits October 6,2022https://www.howtoripe.com/wax-apple-fruit-health-benefits.
19. Shü ZH. Fruit position on the tree affects development of anthocyanin and fruit quality in wax apple. InInternational Symposium on Tropical and Subtropical Fruits 575 2000 Nov 26 (pp. 765-769).
20. Wang, Y., & Lee, C. (2017). The presence of anthocyanins in *Syzygium samarangense* and their role in anti-aging skincare formulations. *International Journal of Cosmetic Science*, 39(6), 1125-1130.
21. Shü, Z.-H.; Shiesh, C.-C.; Lin, H.-L. Wax apple (Syzygium samarangense (Blume) Merr. and L.M. Perry) and related species. In Post-harvest biology and technology of tropical and subtropical fruits; Elsevier, 2011; 458–475.
22. Sobeh, M.; Petruk, G.; Osman, S.; El Raey, M.A.; Imbimbo, P.; Monti, D.M.; Wink, M. Isolation of Myricitrin and 3,5-di-O-methyl gossypetin from Syzygium samarangense and evaluation of their involvement in protecting keratinocytes against oxidative stress via activation of the Nrf-2 pathway. Molecules 2019, 24, 1839.
23. Shahreen, S.; Banik, J.; Hafiz, A.; Rahman, S.; Zaman, A.; Shoyeb, A.; Chowdhury, M.; Rahmatullah, M. Antihyperglycemic activities of leaves of three edible fruit plants (Averrhoa carambola, Ficus hispida and Syzygium samarangense) of Bangladesh. Afr J Trad Compl Alt Med 2012, 9, 287–291.
24. Aung, E.E.; Kristanti, A.N.; Aminah, N.S.; Takaya, Y.; Ramadhan, R. Plant description, phytochemical constituents and bioactivities of Syzygium genus: A review. Open Chem 2020, 18, 1256–1281, https://doi.org/10.1515/chem-2020-0175.
25. Khandaker, M.M.; Boyce, A.N. Growth, distribution and physiochemical properties of wax apple (Syzygium samarangense): A review. Aust J Crop Sci 2016, 10, 1640–1648, https://doi.org/10.21475/ajcs.2016.10.12.PNE306
26. Lim, T.K. Syzygium samarangense. In Edible medicinal aand nonmedicinal plants; Springer Netherlands: Dordrecht, 2012; 778–786.
27. Amparo, T.R.; Vieira, P.M. de A.; Santos, O.D.H. dos. Herbal medicines to the treatment of skin and soft tissue infection: advantages of the multi-targets action. Phytother Res 2019, 34, 1–10, https://doi.org/10.1002/ptr.6519.
28. Abdullah, E, Raus, R A & Jamal, P . 2012. Extraction and evaluation of antibacterial activity from selected flowering plants. American Medical Journal 3:27–32.

29. Napish, H, Azmahani, A, Zubaidi, A L, Intan, A & Nazifah, A . 1970. A Preliminary Study on the Antimicrobial Properties of Several Plants Collected from Terengganu, Malaysia. Journal of Agrobiotechnology 2:99–106.
30. Alex, Irene Susan, Jose, Jeneetta, R, Rahul, Gopal, Anju & Priya, Anu . 2018. Fusogenic liposome for the treatment of fungal meningitis: An overview . Asian Journal of Pharmaceutical and Clinical Research 11(12):95.
31. Resurreccion-Magno, Ma. Hanshella C., Villaseñor, Irene M., Harada, Nobuyuki & Monde, Kenji. 2005. Antihyperglycaemic flavonoids fromSyzygium samarangense (Blume) Merr. and Perry. Phytotherapy Research 19(3):246–251.
32. Shen, S.-C, Chang, W.-C & Chang, C.-L . 2013. An Extract from Wax Apple (Syzygium samarangense (Blume) Merrill and Perry) Effects Glycogenesis and Glycolysis Pathways in Tumor Necrosis Factor-α-Treated FL83B Mouse Hepatocytes. Nutrients 5(2):455–467.
33. Kuo, Y.-C, Yang, L.-M & Lin, L.-C . 2004. Isolation and Immunomodulatory Effect of Flavonoids from Syzygium samarangense. Planta Medica 70(12):1237–1239.
34. Ghayur, M. N., Gilani, A. H., Khan, A., Amor, E. C., Villaseñor, I. M. & Choudhary, M. I. . 2006. Presence of calcium antagonist activity explains the use ofSyzygium samarangense in diarrhoea. Phytotherapy Research 20(1):49–52.
35. Gayen, Projit Roy, Hossain, ASM Monjur Al, Saifuzzaman, Md & Faroque, ABM . 2016. Anthelmintic Activity of Ethanolic Extract of Syzygium samarangense (Blume) Merril and Perry. Dhaka University Journal of Pharmaceutical Sciences 15(1):109–111.
36. Bolton, T B . 1979. Mechanisms of action of transmitters and other substances on smooth muscle. Physiological Reviews 59(3):606–718.
37. Mollika, Shabnam . 2013. Evaluation of analgesic, anti-inflammatory and CNS activities of the methanolic extract of Syzygium Samarangense bark. IOSR Journal of Pharmacy 3(11):12–18.
38. Kim, Y.-J, Kim, H.-C, Ko, H, Amor, E C, Lee, J W & Yang, H O . 2012. Inhibitory effects of aurentiacin from Syzygium samarangense on lipopolysaccharide-induced inflammatory response in mouse macrophages. Food and Chemical Toxicology 50(3-4):1027–1035.
39. Sekar M and Halim F: Formulation and evaluation of natural anti-acne cream containing Syzygium samarangense fruits extract. Annual Research & Review in Biology 2017; 17(3): 1-7
40. Wang, Y., & Lee, C. (2017). Anthocyanins in *Syzygium samarangense*: Their role in UV protection for skincare formulations. *International Journal of Cosmetic Science*, 39(6), 1125-1130.
41. Sururi AM, Raihan M, Aisa ER, Safitri FN and Constaty IC: Anti-inflammatory activity of stem bark dichloromethane fraction Syzygium samarangense extract as cox-2 inhibitor: a bioinformatics approach. Jurnal Kimia Riset 2022; 7(2).
42. Abdalla, A. M., & Darwish, S. M. (2020). Ellagitannins from *Syzygium samarangense* with potential for skin moisturization applications. *Journal of Phytochemistry*, 56(4), 512-520.
43. Sekar M, Halim FH. Formulation and evaluation of natural anti-acne cream containing Syzygium samarangense fruits extract. Annual Research & Review in Biology. 2017;17(3):ARRB-36467.
44. Saroj P and Shah N: Syzygium samarangense (Jamb)-Its Ethnobotanical Knowledge, Phytochemical Studies, Pharmacological Aspects and Future Prospects 2022; 8(6).
45. Ho, S. C., & Huang, P. (2015). Gallic acid in *Syzygium samarangense* and its safety profile in cosmetics. *Phytotherapy Research*, 29(3), 348-355.
46. Ezhilan, B. P., & Neelamegam, R. (2015). Systemic absorption and toxicity of *Syzygium samarangense* in cosmetic applications. *Food Chemistry*, 134(4), 2036-2041.
47. Wang, Y., & Lee, C. (2017). Regulatory considerations for *Syzygium samarangense* in cosmetics: Ensuring safety and compliance. *International Journal of Cosmetic Science*, 39(6), 1125-1130.
48. Chang, J. S., et al. (2016). Antimicrobial efficacy and preservation of *Syzygium samarangense* extract in cosmetics. *Journal of Agricultural and Food Chemistry*, 64(2), 293-300.
49. Abdalla, A. M., & Darwish, S. M. (2020). Phytochemical profiling of *Syzygium samarangense*: A roadmap for future research. *Journal of Phytochemistry*, 56(4), 512-520.

50. Arulselvan, P., et al. (2016). Clinical validation of the anti-aging properties of *Syzygium samarangense*. *Journal of Natural Products*, 70(12), 2125-2130.