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Wax Apple (*Syzygium samarangense* (Blume) Merr. & L.M. Perry): A Comprehensive Review in Phytochemical and Physiological Perspectives

Arnia Sari Mukaromah[1]
[1]Departement of Biology, Faculty of Science and Technology,
Universitas Islam Negeri Walisongo Semarang
E-mail: arnia_sm@walisongo.ac.id

Abstract

Wax apple (*Syzygium samarangense* (Blume) Merr. & L.M. Perry) is a tropical non-climacteric fruit and belongs to *Myrtaceae*. It has high diversity in cultivars, metabolite content, and its biological activities. In this comprehensive review, research findings had revealed that various metabolites found in the wax apple have biological activities. The said biological activities such as: antioxidant, immunomodulatory, antibacterial, anticancer, anti-glycation, anti-inflammation, anti-hypertriglyceridemic, anti-hyperglycemic, relaxant, and spasmolytic activities. Other potential use for the metabolites also includes the treatments for neurodegenerative abnormality, analgesic, and central nervous system (CNS) depression agent. Furthermore, wax apple physiological and phytochemical characteristics can be enhanced by girdling technique, hydrogen peroxide treatment, plant growth regulators treatment, and fruit bagging treatment. Meanwhile, postharvest technology of wax apple fruit utilizes nitric oxide treatment, oxalic acid treatment, cold treatment, and *Aloe vera* gel coating. Wax apple has also been evolved as an ointment, anti-acne cream, and nata de guava. However, environmental stress becomes a challenge in the wax apple plantation. Therefore, the development of molecular biology, chemistry, and postharvest technology will solve those challenges. This review concludes that wax apple (*S. samarangense*) is a tropical fruit that promises to support the nutritional values and human health.

Keywords: Wax apple, Metabolite, Biological activities, Fruit quality enhancement

Abstrak

Wax apple (*Syzygium samarangense* (Blume) Merr. & L.M. Perry) adalah buah tropis non klimakterik dan termasuk dalam keluarga *Myrtaceae*. Buah ini memiliki keanekaragaman kultivar yang tinggi, kandungan metabolit dan aktivitas biologisnya. Dalam tinjauan komprehensif ini, penelitian menemukan berbagai metabolit dalam *wax apple* memiliki aktivitas biologis seperti antioksidan, imunomodulator, antibakteri, antikanker, anti-glikasi dan anti-inflamasi, anti-hipertrigliseridemia, anti-hiperglikemik, relaksasi, spasmolitik, pengobatan kelainan neurodegeneratif, dan agen depresi analgesik sistem saraf pusat (SSP). Selain itu, karakteristik fisiologis dan fitokimia *wax apple* dapat ditingkatkan melalui *girdling technique*, perlakuan hidrogen peroksida, penggunaan zat pengatur pertumbuhan tanaman, dan perlakuan pembungkusan buah. Sementara itu, teknologi pasca panen buah *wax apple* menggunakan perlakuan nitrat oksida, perlakuan asam oksalat, perlakuan suhu dingin, dan pelapis gel lidah buaya. *Wax apple* juga telah dikembangkan sebagai salep, krim anti-jerawat, dan nata de jambu. Namun, cekaman lingkungan akan menjadi tantangan di perkebunan *wax apple*. Oleh karena itu, perkembangan di bidang biologi molekuler, kimia dan teknologi pasca panen akan menyelesaikan tantangan tersebut. Kajian ini menyimpulkan bahwa *wax apple* (*S. samarangense* adalah buah tropis yang menjanjikan untuk mendukung nilai-nilai gizi dan kesehatan manusia.

Kata kunci: *Wax apple*, Metabolit, Aktivitas biologis, Peningkatan kualitas buah

Introduction

Syzygium samarangense (Blume) Merr. & L.M. Perry, a tropical non-climacteric fruit that belongs to *Myrtaceae,* can be found in South Asia, Southeast Asia, Taiwan, and other tropical countries. *S. samarangense* has various local names such as wax apple; java apple; water apple; *djamboe semarang*, *jambu semarang, samarang rose apple* (Indonesia); *makopa* (Philipppines); *chomp u kao* or *chomp u kio*, etc. (Morton, 1987; Shü, Shiesh, & Lin, 2011; Widodo, 2015). It is commonly cultivated in the low land, and it's flowering and fruit production influenced by

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light. Wax apple fruit has high diversity in cultivars and recommended as an export product with high economic values. Wax apple fruit can be generally utilized as fresh fruit, juice, jelly, and medicine. However, wax apple leaves are commonly used as medicine and food cover. Indonesian wax apple fruit has four subspecies and 73 cultivars. Meanwhile, other countries have other various popular wax apple cultivars. Wax apple fruit cultivars have various color, taste, fruit texture, and shape (Widodo, 2015). The various physiological, phytochemical, and biological activities of wax apple cultivars have been known. The aims of this review are to investigate the diversity of wax apple cultivars, identify the phytochemical and biological activities of wax apple cultivars, explore the technology for phytochemical and physiological characteristics enhancement, show the environmental challenges and its cultivars adaptation, postharvest technology, explore the wax apple product development and predict the future perspectives.

Syzygium samarangense (Blume) Merr. & L.M. Perry Morphology

Wax apple plants include small or medium-sized trees that have a height of 4-15 m and 5-40 cm in diameter. It shows a straight or irregular winding stem with many branches. The stem is brownish gray with a rough and peeling bark or not. The cylindrical or slightly flaky branch is located under the nodes, reddish-brown in color, and 2-4 mm in diameter. In general, leaf strands are stretched, extending to the lancet—the length and width of the leaves in the range of 6-30 cm and 4-15 cm. Wax apple flower is consisting of 3,9,15 or more flowers, which can be found at the tip, armpits of leaves, twigs, and old branches. The length of the flower stalk is around 3-5 mm with a width of 8-10 mm, and the flower calyx is semicircular, yellowish-green, or white. The corolla is rounded, white with a length of 8-12 mm. Stamens number around 200-500 with a length of 3-4 cm. Meanwhile, the pistils are one mm in diameter with a length of 4 cm. The fruit is bell-shaped, has a pseudostipe or is not equipped with a pseudostipe as seen in a rounded, obovate-shaped wax apple. Furthermore, Indonesian wax apple grown in Papua has a vertical and concave flat shape on the base. Moreover, the presence of *Syzygium aqueum* has usually confused with *S. samarangense* in the field (Widodo, 2015). Therefore, Widodo (2015) had been developed determination keys to differ *S. samarangense* cultivars and *Syzygium aqueum*.

Syzygium samarangense (Blume) Merr. & L.M. Perry Cultivars

In Indonesia, *Syzygium samarangense* can be found at Sumatra, Java and Papua. However, *S. samarangense* 'Citra' and *S. samarangense* 'Delima' have been the most cultivated cultivars especially in the Central Java province (Widodo, 2015). Furthermore, the wax apple tree has been cultivated with minor economic status in Malaysia (Milow, Malek, Edo, & Ong, 2014). There are popular wax apple fruit cultivars such as 'Masam Manis Pink', 'Giant Green', and 'Jambu Madu Red'. These cultivars reveal differences in the physiological responses such as stomatal conductance, net photosynthesis, chlorophyll content, carotenoid content, and leaf area. According to (Idris, Ismail, Mat, & Khandaker, 2018; Mohammad Moneruzzaman Khandaker, Alebidi, Hossain, Mat, & Boyce, 2015), 'Jambu Merah Red' and 'Masam Manis Pink' cultivars show the highest physiological characters than other cultivars. Therefore, wax apple fruit 'Jambu Merah Red' and 'Masam Manis Pink' recommended cultivating in Malaysia and South Asian countries (Idris et al., 2018; Mohammad Moneruzzaman Khandaker et al., 2015; Moneruzzaman, Al-Saif, et al., 2011). The number of wax apple cultivars can be shown in Table 1. and Table 2.

Table 1. Indonesian Wax Apple *Syzygium samarangense* (Blume) Merr. & L.M. Perry Subspecies and Cultivars (Widodo, 2015)

No.	Subspecies Type	Specific Characteristics	Cultivar type
1.	*Syzygium samarangense* subsp. *album* Widodo *subsp. nov.*	White fruit until ripening condition	- *Syzygium samarangense* 'Kaget Putih' - *Syzygium samarangense* 'Mutiara' - *Syzygium samarangense* 'Madura Putih' - *Syzygium samarangense* 'Tamansari Putih' Widodo *cult. nov* - *Syzygium samarangense* 'Bancarkembar Putih' - *Syzygium samarangense* 'Berlian Putih' *cult. nov.* - *Syzygium samarangense* 'Fateta IPB' - *Syzygium samarangense* 'Lilin Putih'

Table 1. *Continued*

No.	Subspecies Type	Specific Characteristics	Cultivar type
			- *Syzygium samarangense* 'Sokaraja Putih' Widodo *cult.nov* - *Syzygium samarangense* 'Karangsalam Putih' - *Syzygium samarangense* 'Dot Putih' *cult. nov.* - *Syzygium samarangense* 'Camplong Putih' - *Syzygium samarangense* 'Klampok Putih' Widodo *cult. nov* - *Syzygium samarangense* 'Asli Sumatra'
2.	*Syzygium samarangense* subsp. *viride* Widodo *subsp. nov.*	Green fruit, sometimes appear other colors such as white, yellowish or pink in the fruit tip. Green color fruit appears until the ripening stage.	- *Syzygium samarangense* 'Pudding Hijau' Widodo *cult. nov.* - *Syzygium samarangense* 'BT3 Hijau' - *Syzygium samarangense* 'Camplong Hijau' - *Syzygium samarangense* 'Hijau Kecil' - *Syzygium samarangense* 'Demak Hijau Mini' *cult. nov* - *Syzygium samarangense* 'Demak Hijau' - *Syzygium samarangense* 'Kaget Hijau' - *Syzygium samarangense* 'Dot Hijau' Widodo *cult. nov* - *Syzygium samarangense* 'Wosi Hijau' Widodo *cult. nov.* - *Syzygium samarangense* 'IPB Hijau' - *Syzygium samarangense* 'Kancing Hijau' - *Syzygium samarangense* 'Apel' - *Syzygium samarangense* 'Kutasari' - *Syzygium samarangense* 'Nusakambangan' - *Syzygium samarangense* 'Cincalo Hijau' - *Syzygium samarangense* 'Cincalo Hijau Semarang'
3.	*Syzygium samarangense* subsp. *roseum* Widiawati *subsp. nov.*	Pink color – reddish fruit	- *Syzygium samarangense* 'Madu Panjang' - *Syzygium samarangense* 'Cincalo Merah Mekarsari' - *Syzygium samarangense* 'Yogya Pink' - *Syzygium samarangense* 'Kebocoran Pink' - *Syzygium samarangense* 'Cincalo Pink' - *Syzygium samarangense* 'Kaget Oranye' - *Syzygium samarangense* 'Klampok Sukaluyu' - *Syzygium samarangense* 'Klampok Karangsalam' - *Syzygium samarangense* 'Padang Pink' - *Syzygium samarangense* 'Lilin Pink' - *Syzygium samarangense* 'Tangkweh' - *Syzygium samarangense* 'Bell Apple' - *Syzygium samarangense* 'Reremi Yapis' Widodo *cult. nov.* - *Syzygium samarangense* 'Cincalo Merah' - *Syzygium samarangense* 'Banjarsari Kulon' - *Syzygium samarangense* 'Camplong Kuning' - *Syzygium samarangense* 'Kancing Kuning' - *Syzygium samarangense* 'Lilin Merah' - *Syzygium samarangense* 'Kalibamban' - *Syzygium samarangense* 'Manokwari Pink' - *Syzygium samarangense* 'Lilin Pink' - *Syzygium samarangense* 'Mutiara Merah'

Table 1. *Continued*

No.	Subspecies Type	Specific Characteristics	Cultivar type
4.	*Syzygium samarangense* subsp. *rubrum* Widodo *subsp. nov.*	Red – dark red fruit	- *Syzygium samarangense* 'Kaget Merah' - *Syzygium samarangense* 'Irung Petruk' - *Syzygium samarangense* 'Silado' - *Syzygium samarangense* 'Pink Rose Apple' - *Syzygium samarangense* 'Purwokerto' - *Syzygium samarangense* 'King Rose Apple' - *Syzygium samarangense* 'Arcawinangun' - *Syzygium samarangense* 'Kecil Sumpyuh' - *Syzygium samarangense* 'Baturraden Maroon' - *Syzygium samarangense* 'Cincalo Maroon' - *Syzygium samarangense* 'Cokelat' - *Syzygium samarangense* 'Lilin Maroon' - *Syzygium samarangense* 'Citra' - *Syzygium samarangense* 'Merah Delima' - *Syzygium samarangense* 'Dot Merah' *cult. nov.* - *Syzygium samarangense* 'Unsoed' - *Syzygium samarangense* 'Cindaga' - *Syzygium samarangense* 'Sanggeng' - *Syzygium samarangense* 'Rowokele Manis' - *Syzygium samarangense* 'Demak Merah Mini' - *Syzygium samarangense* 'Samaraqua'

Table 2. Other popular wax apples (*Syzygium samarangense* (Blume) Merr. & L.M. Perry) cultivars

No.	Region	Cultivar type	References
1.	Malaysia	- *Syzygium samarangense* 'Masam Manis Pink' - *Syzygium samarangense* 'Jambu Madu Red' - *Syzygium samarangense* 'Giant Green'	(Idris et al., 2018) (Mohammad Moneruzzaman Khandaker et al., 2015) (Moneruzzaman, Al-Saif, et al., 2011)
2.	Thailand	- *Syzygium samarangense* 'Thongsamsee' - *Syzygium samarangense* 'Taaptimjaan' - *Syzygium samarangense* 'Thabthimchan'	(Muchjajib, Muchjajib, & Jumee, 2016) (Mothina & Yapwattanaphun, 2017) (Supapvanich, Mitrsang, Srinorkham, Boonyaritthongchai, & Wongs-Aree, 2016)
3.	Taiwan	- *Syzygium samarangense* 'Taiwan Pink'	(Reynertson, Yang, Jiang, Basile, & Kennelly, 2008)

Molecular Systematics Analysis of Wax Apple Cultivars

In Malaysia, wax apple cultivars ('Masam Manis Pink'; 'Jambu Madu Red'; Giant Green) differ in the morphological and physiological characteristics. It may be influenced by genetic diversity (Mohammad Moneruzzaman Khandaker, Alebidi, & Al-saif, 2012). The genome size of diploid *S. samarangense* is 0,56 pg (2C DNA) equivalent with 548,33 Mbp length (Matra et al., 2019). Meanwhile, chloroplast genome sequences can be developed as some molecular markers for phylogenetic and population genetic analysis of wax apple. The chloroplast genome of *S. samaragense* MH371141 is 159,109 bp and consists of 113 genes. The chloroplast genome consists of a single large copy (88,533 bp), a small single copy (18,882 bp), and an inverted repeat region (25,847 bp) (Liu, Ni, Zheng, Shi, & Niu, 2018). Random Amplified Polymorphic DNA (RAPD), and Inter Simple Sequence Repeat (ISSR) have been utilized in *Syzygium* phylogeny analysis. However, its techniques are not able to reveal phylogenetic relation between *Syzygium* species. Therefore, plant DNA barcoding is better used to observe phylogenetic analysis (Cheong & Ranghoo-Sanmukhiya, 2013). Furthermore, the twenty new primers can be analyzed for the microsatellite loci of wax apple. It is utilized to genetic diversity determination, cultivar identification, lineage analysis, and linkage mapping in wax apple species (Lai et al., 2015). Besides, Simple Sequence Repeats (SRR) specified for *Syzygium* species contribute to getting comprehensive information about the relationship between species, taxonomy, structure and genetic diversity, genetic mapping, breeding, and conservation program(Nogueira, Ferreira, & da Silva Ferreira, 2016). Comprehensive molecular systematic analysis of wax apple cultivars has not been reported yet. Therefore, the development of a molecular marker for DNA barcoding analysis and DNA fingerprinting is very recommended to identify, explore, and determine was apple cultivars diversity.

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Metabolite Content and Biological Activities

Wax apple tree has diverse metabolite content, which spreads in whole plants with interest biological activities. The details of metabolite content and biological activities have been shown in Table 3.

Table 3. Metabolite Content and Biological Activities of Wax Apple (*Syzygium samarangense* (Blume) Merr. & L.M. Perry)

Wax apple part	The type of extract/fraction	Metabolite content	Biological Activities	References
Leaves	Methanol	- Phenolic compound (100,48 ± 0,21 GAE, mg/g of each extract), flavonoid (111,40 ± 0,23 QAE, mg/g of each extract), proanthocyanidin (9,26 ± 0,45 CAE, mg/g of each extract), and flavonols (46,40 ± 0,7 QAE, mg/g of each extract). - Taxiphyllin *6'-O*-gallate **(1)**, actinidioinoside *6'-O*-gallate **(2)**, myricetrin 2"-*O*-sulfate **(3)**, lupeol **(4)**, demethoxymatteucinol **(5)**, cryptostrobin **(6)**, betulinic acid **(7)**, *β*-sitosterol glucoside **(8)**, 2*R*-prunasin **(9)**, myrciaphenone A **(10)**, 1-feruloyl-*β*-D-glucopyranoside **(11)**, (3*S*,5*S*,6*R*,7*E*,9*S*)-3,5,6,9-tetrahydroxymegastigman-7-ene **(12)**, guaijaverin **(13)**, myricetin 4'-methyl ether 3-*O*-α-L-rhamnopyranoside **(14)** myricetrin **(15)**, gallic acid **(16)**, and actinidioionoside **(17)**. - Myricetin-3-*O*-α-rhamnoside **(18)**, 7,8,3',4'-tetrahydroxy-3,5-dimethoxyflavone (3,5-di-*O*-methyl gossypetin) **(19)**.	- The methanol extract of *S. samarangense* leaves (MSSL) and bark (MSSB) function as analgesic, anti-inflammatory, central nervous system (CNS) depression agent, anti-diarrheal activity (Majumder, Nur-E-Hasnat, Ashraf-Uz-Zaman, & Alam, 2014), and anti-hyperglycemic activity (Shahreen et al., 2012). - The MSSL reveals higher antioxidant activity than a various solvent-soluble fraction of *S. samarangense* leaves (Majumder, Alam, Chowdhury, Bajpai, & Shukla, 2017). - Compounds **1**, **3**, and **13-16** have significant antioxidant activity (Mamdouh Nabil Samy, Sugimoto, Matsunami, Otsuka, & Kamel, 2014). - Potential candidate for antioxidant and liver-protecting medicine (Sobeh et al., 2018). - Compound **18**, and **19** have an antioxidant and anti-inflammatory effect. - 3,5-di-*O*-methyl gossypetin **(19)** shows the antioxidant activity by nuclear transcription factor-2 (Nrf-2) pathway and stimulating antioxidant protein such as HO-1 and Mn-SOD-3 (Sobeh et al., 2019).	(Majumder et al., 2014); (Shahreen et al., 2012); (Majumder et al., 2017); (Mamdouh Nabil Samy et al., 2014) (Sobeh et al., 2018)

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Table 3. *Continued*

Wax apple part	The type of extract/fraction	Metabolite content	Biological Activities	References
Leaves	Ethanol	- Flavonol glycosides such as mearnsitrin **(1)** and 2'-*C*-methyl-5'-*O*-galloylmyricetin-3-*O*-α-L-rhamnopyranoside **(2)**. - Nine acylphloroglucinol derivates **(3-11)**. - Castalagin (0.12%) **(12)** and vescalagin (0.29%) **(13)**.	- *S. samarangense* leaves reveal antibacterial activity toward *Bacillus cereus* and *Salmonella enterica* with minimum inhibition concentration at 78 µg/mL (Choironi & Fareza, 2018). - Nine acylphloroglucinol derivates have cytotoxic activity against HepG2 and MDA-MB-231 tumor cell lines (Yang et al., 2018). - Castalagin and vescalagin have been suggested as powerful poly(ADP-ribose) polymerase 1 (PARP1) inhibitors and DNA topoisomerase II. Therefore, its compounds promise as a cancer chemotherapy agent (Kamada et al., 2018).	(Choironi & Fareza, 2018) (Nair, Krishnan, Ravikrishna, & Madhusudanan, 1999); (Yang et al., 2018); (Kamada et al., 2018)
Leaves	Ethyl acetate fraction (ESSL)	- Phenolic compound (148,57 ± 0,22 GAE, mg/g of each extract), flavonoid (207,40 ± 0,12 QAE, mg/g of each extract), proanthocyanidin (16,87 ± 0,58 CAE, mg/g of each extract), and flavonols (57,80 ± 0,05 QAE, mg/g of each extract).	- Ethyl acetate fraction (ESSL) show higher antioxidant activity than other fractions and may use in the free radical interceded disease treatment.	(Majumder et al., 2017)
Leaves	Acetone	- Acetone extract of wax apple leaves contains sixteen various flavonoid compounds.	- There are four flavonoid compounds having immunomodulatory activity such as (-)-strobopinin, myricetin 3-*O*-(2"-*O*-galloyl)-α-rhamnopyranoside, (-)-epigallocatechin 3-*O*-gallate, and myricetin 3-*O*-α-rhamnopyranoside. These compounds prevent interleukin-2 (IL-2) and interferon-γ (IFN-γ) production in peripheral blood mononuclear cells (PBMC).	(Kuo, Yang, & Lin, 2004)

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Table 3. *Continued*

Wax apple part	The type of extract/fraction	Metabolite content	Biological Activities	References
Leaves	Dichloromethane	- Triterpenes and sterol such as cycloartenyl stearate **(1)**, lupenyl stearate **(2)**, sitosteryl stearate **(3)**, and 24-methylenecycloartanyl stearate **(4)**. - 2',4'-dihydroxy-6'methoxy-3'-methylchalcone **(5)**, 2',4'-dihydroxy-6'methoxy-3',5'-dimethylchalcone **(6)**, 2'hydroxy-4',6'-dimethoxy-3'methyl chalcone **(7)**, squalene **(8)**, botulin **(9)**, lupeol **(10)**, sitosterol **(11)** and triterpenes and sterol mixtures.	- The compound mixture shows analgesic activity and anti-inflammatory activity at 6,25 mg/kg body weight and 12,5 mg/kg body weight, respectively. Furthermore, the compound mixture reveals negligible toxicity toward zebrafish embryonic tissues (Raga et al., 2011). - The triterpenes and sterol mixtures exhibit low to moderate antifungal and antibacterial activity (Ragasa, Franco Jr, Raga, & Shen, 2014).	(Raga et al., 2011); (Ragasa et al., 2014).
Leaves	Hexane	- 2'-hydroxy-4',6'-dimethoxy-3'-methylchalcone **(1)**, 2',4'-dihydroxy-6'-methoxy-3',5'-dimethylchalcone **(2)**, 2',4'-dihydroxy-6'-methoxy-3'methylchalcone **(3)** and 7-hydroxy-5-methoxy-6,8-dimethylchalchone **(4)**. - *α*-carotene and *β*-carotene mixture **(*5*)**, lupeol **(6)**, botulin **(7)**, *epi*-betulinic acid **(8)**, and 7-hydroxy-5-methoxy-6,8-dimethylflavanone **(9)**, *β*-sitosterol **(10)** and *β*-D-sitosterylglucoside **(11)**.	- Compound **1-4** show relaxant activity; Compound **2** shows spasmolytic activity and neurodegenerative abnormality treatment (Amor, Villaseñor, Nawaz, Hussain, & Choudhary, 2005; Ghayur et al., 2006). - It can be developed as to blockade calcium influx in diarrhea (Ghayur et al., 2006). - Aurentiacin (2'-hydroxy-4',6'-dimethoxy-3'-methylchalcone) reveals anti-inflammatory activity by preventing nuclear factor-kB (NF-kB) activation in mouse macrophages (Kim et al., 2012).	(Ghayur et al., 2006); (Amor, Evangeline C, Villasenor, Yasin, & Choudhary, 2004; Amor, Villaseñor, Ghayur, Gilani, & Choudhary, 2005) (Kim et al., 2012).
Leaves	Essential oils	- α-pinene (24,2%) **(1)**, limonene (7,0%) **(2)**, β-pinene (11,7%) **(3)** and *p*-cymene (7,4%) **(4)**.	-	(Farag et al., 2018)
Bark		-	- The bark extract of 'Green' cultivar reveals the highest antioxidant activity than 'Masam Manis Pink' and 'Jambu Madu Red'.	(M. M. Khandaker, Sarwar, Mat, & Boyce, 2015)

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Table 3. *Continued*

Wax apple part	The type of extract/fraction	Metabolite content	Biological Activities	References
Fruit		- Wax apple fruit dried powder (DP) contains moisture (16%), crude fat (3.85%), crude protein (2.32%), ash (2.32%), crude fiber (5.19%), available carbohydrate (75.04%), total dietary fiber (8.86%), total phenolics (872.69 mg GAE/100g DP), total flavonoid (148.21 mg QE/100g DP) and total anthocyanin content (11.66 mg CGW/100g DP). - Wax apple fruit contain moisture (80%), total phenolic compound (1.07 mg GAE/g FW), ascorbic acid (1.6 µg AA/g FW), Lutein (0.07 µg/g FW), β-cryptoxanthin (0.02 µg/g FW) and α-tocopherol (0.08 µg/g FW), and γ-tocopherol (0.18 µg/g FW). - Ellagitannin vescalagin / vescalagin - *S. samarangense* var. Taiwan pink fruit contains cyanidin 3-glucoside, quercitrin, ellagic acid, and myricetin (Reynertson et al., 2008). - Wax apple fruit 'Masam Manis Pink' and 'Jambu Madu Red' cultivars contain the highest sources of anthocyanin, carotene, and vitamin C.	- Wax apple fruit dried powder reveal antidiabetic activity toward streptozotocin (STZ) diabetic rats through oxidative stress and pro-inflammatory cytokine inhibition, and anti-apoptotic protein activation. Wax apple treatment reveals lowered fasting blood glucose (FBG) and enhanced body weight of diabetic rats. Furthermore, improvement of pancreatic β-cell function is marked by enhanced HOMA-B and insulin level in the pancreas and serum of diabetic rats. Pancreatic apoptosis and dysfunction of the diabetic rats are prevented by caspace-3 and Bax protein down-regulated expression and Bcl-2 and Bcl-xl protein upregulated expression. In addition, oxidative stress and pro-inflammatory cytokine inhibition are developed by inducing CAT and SOD activities, and diminishing nitrotyrosine and TNF-α level (Khamchan, Paseephol, & Hanchang, 2018). - Vescalagin of wax apple fruit can be developed as therapeutic value as anti-hypertriglyceridemic and anti-hyperglycemic effects. Vescalagin at 30 mg/kg administrated to high-fructose diet (HFD)-induced diabetic rats can decrease fasting blood glucose, C-peptide, fructosamine, triglyceride, and fatty acid content. Meanwhile, high-density lipoprotein content enhances as 14.4% in the HFD rats (Shen & Chang, 2013). - Wax apple fruit contained ellagitannin vescalagin (VES) is potential as antiglycation and anti-inflammation in Methylglyoxal (MG)-induced carbohydrate metabolic disorder rats. VES induces insulin secretion of β-cells in the MG-rats and down-regulates pro-inflammation factors implicated in MG metabolism. Therefore, VES of wax apple fruit can be used as supplements to prevent diabetes mellitus and its complications (W.-C. Chang, Shen, & Wu, 2013).	Isabelle *et al*. (2010); (Shen & Chang, 2013); (Shen, Chang, & Chang, 2012); (Shen, Chang, & Chang, 2013); (Zhang, Zhou, et al., 2016); (Zhang, Wang, et al., 2016); (Reynertson et al., 2008); (Khamchan et al., 2018) (M. M. Khandaker et al., 2015).

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Table 3. *Continued*

Wax apple part	The type of extract/fraction	Metabolite content	Biological Activities	References
Fruit			- A fraction from wax apple fruit (FWFE) may decrease insulin resistance by preventing intracellular c-Jun N-terminal kinase (JNK) inflammatory signaling cascades, ameliorating the Phosphatidylinositol-3-kinase-protein B (PI3K-Akt/PKB) insulin signaling pathway, and the enhancing glucose uptake in tumor necrosis factor-alpha TNF-α-treated FL83B mouse hepatocytes. Therefore, FWFE may develop as anti-diabetic drugs, health food, and dietary supplements (Shen et al., 2012). - Wax apple fruit extract (WAE) can enhance glycolysis, gluconeogenesis, and glycogen storage in the insulin-resistant FL83B mouse hepatocytes (Shen et al., 2013). - Wax apple fruit can protect the liver from alcohol injury. Therefore, wax apple fruit can be recommended as functional food or drug to treat alcohol disorder (Zhang, Wang, et al., 2016; Zhang, Zhou, et al., 2016). - 'Jambu Madu Red' cultivar shows the best antimicrobial activity than other cultivars (M. M. Khandaker et al., 2015). - Fruit extract of 'Green' cultivar reveals the highest antioxidant activity than other cultivars (M. M. Khandaker et al., 2015).	

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Table 3. *Continued*

Wax apple part	The type of extract/fraction	Metabolite content	Biological Activities	References
Fruit pulp	Methanol	Reynoutrin **(1)**, -hyperin **(2)**, myricitrin **(3)**, quercitrin **(4)**, (*S*)-pinocembrin **(5)**, quercetin **(6)**, guaijaverin **(7)**.	Four compounds have cytotoxic effect toward SW-480 human colons cancer cell line such as 2',4'-dihydroxy 3',5'-dimethyl-6'methoxychalcone, stercurensin, cardamonin, and (*S*)-pinocembrin. Other compounds show antioxidant activity .	(Simirgiotis et al., 2008)
Seed	Methanol	2',4'-dihydroxy 3',5'-dimethyl-6'methoxychalcone **(1)**, stercurensin **(2)**, cardamonin **(3)**, gallic acid **(4)** and ellagic acid **(5)**.		

Environmental Stress and Adaptation

In the flooding condition, wax apple trees appear physiological tolerance mechanisms such as aerenchyma adaptation, induce alcohol dehydrogenase (ADH) enzyme activity, and lowered the respiration rate and vegetative growth. The aerenchyma supply oxygen in the root, inducing ATP production, and adequate to convert 1-aminocyclopropane-1carboxilic acid (ACC) to ethylene. The wax apple will sustain 40 days in flooding conditions (Lin & Lin, 1992). Furthermore, pest and disease are big challenges influencing phytochemical and physiological characteristics of wax apple. According to the research, *Lasiodiplodia theobromae, Pestalotiopsis samarangensis, Fusarium solani, Oligonychus litchi* Lo&Ho, and *Anselmella malacia* is commonly found in the wax apple plantation.

Lasiodiplodia theobromae, a group of fungi, inflicting black spot disease on wax apple fruit can be controlled by *Brevibacillus brevis* FJAT-0809-GLX strain in the in vitro experiment (Che, Liu, Ruan, Tang, & Huang, 2015). *Pestalotiopsis samarangensis*, a new fungal species, has caused fruit rot on wax apple fruit in Thailand. Several symptoms appear on the surface of the wax apple fruit, such as circular, black, and slightly concave spots. Its fungi induce soft decaying of fruit flesh throughout storage. Black conidia induce concentric band on the surface of the wound and surrounding by white mycelium. The spot symptoms can merge become irregular form lesions found into the pulp. Therefore, careful postharvest handling and storage should be applied to prevent the spreading of the disease (Maharachchikumbura, Guo, Chukeatirote, McKenzie, & Hyde, 2013). *Fusarium solani* causes twig blight disease in a healthy wax apple fruit tree (Wang, Chen, Lin, Tsou, & Ko, 2010). In addition, *Oligonychus litchi* Lo&Ho, one of major litchi spider mite, founded on wax apple fruit has developmental stages and hatching eggs influenced by temperature. According to Chen et al. (2016), 95% litchi spider eggs hatch at 20, 25, and 30°C. For while, the whole developmental stages of litchi spider mite at high temperatures (32°C) are faster than lower temperatures (16°C) (W. H. Chen, Li, & Chang, 2016). *Anselmella malacia*, a new pest wasp is found in wax apple fruit. *Anselmella* larvae evolve as seed-eater and reduce fruit quality(Xiao, Xu, Huang, & Zhao, 2006).

Physiological and Phytochemical Fruit Enhancement

Physiological and phytochemical fruit characteristics

Eight developmental stages of wax apple fruit classified into young fruits (appropriate to 3 Day After Full Bloom (DAFB) and 13 DAFB, successively), small bell (23 DAFB), big bell (28 DAFB), breaker (34 DAFB), small red (38 DAFB), big red (45 DAFB), and mature (59 DAFB). During wax apple fruit development, water content enhances to 92% in the breaker stage (34 DAFB) and declines to 88 % in the harvest period (59 DAFB). It is concomitant to the increasing of wax apple fruit dry weight. The size diameter of wax apple fruit increase throughout eight developmental stages. Wax apple fruit diameter size and length increase throughout eight developmental stages. Furthermore, biochemistry characteristics such as total soluble solid content (TSSC), titratable acidity (TA), and anthocyanin reveal a specific pattern based on the developmental stages. At the beginning of the wax apple fruit breaker stage, TSSC shows low concentration and significantly enhances

corresponding to the declining of TA and water content. Anthocyanin as a color pigment in the wax apple fruit skin appears at the onset of the breaker stages (34 DAFB), especially around the proximal end, it is gradually advanced to the distal end. Calcium concentration enhances until the breaker stages and declines in the further developmental stages. The proximal end of wax apple fruit contains higher calcium concentration than the distal end. It is influenced by the damaging of xylem function. Therefore, the breaker stage is an important developmental stages marked by the onset of skin fruit coloration. Also, reducing the potential risk of corky calyx end disorder (calcium deficiency problem) can be solved by calcium spray application to the young developing of wax apple fruit (S.-J. Chen, Yeh, Lin, & Li, 2019). Furthermore, soluble solids (SSs) and anthocyanins concentration influenced by sucrose in the cultured medium. Wax apple fruit aged four to eight weeks after anthesis has higher anthocyanin concentration induced by sucrose (Y. J. Chang, Chung, Tseng, Chu, & Shü, 2003).

The amount of light determines the quality and quantity of wax apple fruit. Different canopy positions will receive different portions of the light. Chlorophyll and stomatal conductance of outer canopy leaves show the highest value than other positions. Outer canopy position of wax apple fruit var. Jambu Madu induce the better quality and quantity of wax apple fruit such as fruit number, fruit size, fruit weight, chlorophyll content, total soluble solid content, and peel color percentage (Mohammad Moneruzzaman Khandaker, Amran, & Ismail, 2017).

Temperature also influences wax apple fruit quality, such as anthocyanin content, total soluble solids (TSS), soluble sugar (SS), starch, total phenolic compound (TPC), the free amino acid (FA) and soluble protein (SP). During in vitro research, temperature between 20° and 25°C and day/night temperature between 25/20 °C and 25/15 °C shows the best condition inducing the best quality of wax apple fruit (Pan & Shü, 2007).

Girdling technique

Enhancing the quality of wax apple fruit quality in the field condition is achieved by the girdling technique. Its technique take place by strip bark removal from the trunk or major branch of fruit tree, thereby photo-assimilate translocation is blocked. Application of girdling technique before flowering increases inflorescence development, yield, and quality of wax apple fruit in the field condition. The C-shaped girdling enhances the inflorescence progress, chlorophyll fluorescence, fruit storage, the number of wax apple fruit, fit weight, dry matter, chlorophyll content, total sugar, total phenol, and anthocyanin content. Meanwhile, the V-shaped girdling influence total flavonoid and antioxidant activity of wax apple fruits. The C and V-shaped girdling is the promising girdling techniques to improve fruit retention, yield, and quality of wax apple fruit in the field condition (Mohammad Moneruzzaman Khandaker, Hossain, Osman, & Boyce, 2011). These findings are supported by (Mohammad Moneruzzaman Khandaker, Osman, Hossain, & Boyce, 2012) showed that the C-shaped girdling technique shows enhancing fruit growth production, and inducing the best final fruit length and diameter. Furthermore, it increases yield, juice percentage, dry leaf matter, biomass, and TSS content. Therefore, C-shape girdling application two weeks before flowering is the best-girdling treatment to improve fruit growth, yield, and quality of wax apple fruit in the field condition (Mohammad Moneruzzaman Khandaker, Osman, et al., 2012).

Hydrogen peroxide treatment

Hydrogen peroxide treatment reduces the loss of exhaustive chilling-induced wax apple fruit abscission (Lai, Mao, Yo, Hsu, & Lin, 2001). Hydrogen peroxide spraying treatment result in enhancing fruit growth, yield, and quality of wax apple fruit in the field condition. The optimum H_2O_2 spraying treatment concentrations are 5 and 20 mM. Once a week, this H_2O_2 treatment is sprayed in the leaves, flower, and small fruit of the selected uniform branches throughout the wax apple var. Jambu Madu fruit development (Mohammad Moneruzzaman Khandaker, Boyce, & Osman, 2012). Furthermore, combination H_2O_2 treatment and methyl eugenol or methyl eugenol treatment play an important role in reducing fruit fly infestation in wax apple fruit under field conditions (Mohammad Moneruzzaman Khandaker, Ismail, Hafiza, Mat, & Ngah, 2018). Moreover, utilizing H_2O_2 treatment should consider environmental safety and health care procedures (Lai et al., 2001).

Plant growth regulators treatment

Plant growth regulators (GA_3, NAA, 2,4-D) treatment on the wax apple var. Jambu Madu fruit tree will enhance physiological and phytochemical fruit characteristics. Once a week, PGRs are applied on the leaves, flower, and small fruit of the selected uniform branches from bud development until fruit ripening. Gibberellic acid (GA_3), Naphthalene acetic acid (NAA), and 2,4-dichlorophenoxyaceticacid (2,4-D) treatment reveal diminishing titratable acidity and increasing total sugar and carbohydrate content. Furthermore, the influence of 50 mg/L GA_3, 10

mg/L NAA, and 5 mg/L 2,4-D treatment are increasing phenol, flavonoid and vitamin C content, affecting chlorophyll, anthocyanin and carotene content, and enhancing antioxidant activity level. Moreover, sensory assessments of fruit treated with GA_3 or auxin reveal the highest score than other treatments (Moneruzzaman Khandaker, Nasrulhaq Boyce, Osman, & Sharif Hossain, 2012)(Moneruzzaman, Hossain, Normaniza, & Boyce, 2011).

Fruit bagging treatment

Fruit bagging treatment prevents fruit flies, birds, and rats attack. Although white plastic is suitable to produce the better quality and quantity of wax apple 'Thabthimchan' cultivar, it cannot prevent wax apple fruit from birds. Therefore, red and yellow plastic bags recommended as a white plastic replacement because those color bags will produce similar quality and quantity of wax apple fruit Thabthimchan' cultivar covered by the white plastic bag. The mean weight of 'Thabthimchan' fruit is 142,62 g (red bag) and 140,70 (yellow bag). Meanwhile, the total soluble content of 'Thabthimchan' fruit is 9,73°Brix (red bag) and 9,55°Brix (yellow bag) (Mothina & Yapwattanaphun, 2017). On the wax apple 'Thongsamsee' fruit, fruit bagging is applied at the stamen abscission stage. It will reduce fruit flies and fruit drop(Muchjajib et al., 2016)

S. samarangense 'Thongsamsee' fruit can be influenced by either GA and NAA application or fruit wrapping. GA treatment at 2500 mg L^{-1} enhance fruit size, fruit yield, and fruit quality. The fruit color will enhance throughout the GA application at 2500 – 5000 mg L^{-1}. Meanwhile, NAA treatment at 5000 mg L^{-1} enhances fruit size, yield, and fruit quality but the fruit shape is dissimilar with the origin cultivar. The better PGRs application time is at the stamen abscission stage and immediately bagged with a plastic bag, vented, and lined with newspaper for air circulation(Muchjajib et al., 2016).

Post-harvest Technology

Nitric oxide treatment

Cottony softening appeared in wax apple fruit can be prevented using nitric oxide treatment by several mechanisms such as arrangements of cell wall degradation, oxidation-reduction, carbohydrate metabolism, and signal transduction pathway of plant hormone. Therefore, NO potentially is utilized in the post-harvest technology of wax apple fruit (F. Chen, Hao, Yin, Wu, & Jiang, 2017). According to Hao *et al*., 2016, nitric oxide (NO) is an appropriate post-harvest treatment to delay the wax apple fruit softening and senescence. During storage, NO treatment maintains fruit assertiveness, reducing weight loss, and delay cottony softening. NO treatment (10 µL/L) can regulate the expression of the related genes and enzyme activity in the lignin biosynthesis (Hao, Chen, Wu, & Gao, 2016).

Storage treatment and challenges

Oxalic acid treatment is the best treatment to maintain fresh-cut wax apple fruit quality because it can preserve antioxidant activity, total phenolic content, and storage of fruit assertiveness (Izzah, Awang, Ding, Hafiza, & Satar, 2015). Decreasing whiteness index and enhancing the browning index of fresh-cut wax apple flesh is useful in fruit quality determination of fresh-cut wax apple fruit. Cold treatment at 4 ± 2°C prevents the flesh color changing and maintains the peel color and nutritional value of fresh-cut wax apple fruit throughout storage (Supapvanich, Pimsaga, & Srisujan, 2011). Furthermore, *Aloe vera* gel coating can preserve and delay the browning process of fresh-cut wax apple fruit cv. Taaptimjaan during storage (Supapvanich et al., 2016). Salicylic acid pre-harvest treatment at 0.5 mM concentration can maintain the physiochemical quality of wax apple fruit throughout short-term storage. Antioxidant, total phenols and total flavonoid contents increase during salicylic acid pre-harvest treatment (Supapvanich, Mitsang, & Youryon, 2017). During wax apple fruit storage at room temperature (23°C ± 1°C) with 88% relative humidity, it might be appeared spoilage microorganisms either bacteria or fungi. According to Esua *et al*., 2017, *Klebsiella pneumoniae* and *Penicillium purpurogenum* are the most common spoilage microorganisms in the wax apple fruit throughout storage. Those microorganisms have various effect on phenolic compounds and vitamin C of wax apple fruit. Therefore, it is essential to prevent contamination in the post-harvest technology (Esua, Chin, Yusof, & Sukor, 2017).

Wax Apple Product Development

An ointment containing wax apple fruit ethanolic extract enhances wound healing process of the skin burn in Rattus Wistar. Flavonoid and Saponin may play an important role to increase macrophage activation to produce growth factors and cytokine. Therefore, it will produce collagen and wound quickly closed (Insani et al., 2017). Furthermore, the ethanolic extract of wax apple fruit has been developed as anti-acne cream. According to the research, anti-acne cream containing wax apple fruit extract exhibits antibacterial activity toward

Staphylococcus aureus, Salmonella enterica, and Escherichia coli using the disc diffusion method. In addition, anti-acne cream should be tested in other bacteria causing skin acne (Sekar & Halim, 2017). Meanwhile, in Indonesia, wax apple fruit becomes the substrate in nata food production. Nata-de guava exhibits the good rendemen, thicknesses, water content, color, taste, and texture when added by 5% sprout extract (*Phaseolus vulgaris*) and 5% sucrose. Sprout extract and sucrose may play an important role as a nitrogen source and carbon source for *Acetobacter xylinum* growth (Setiani, Pramono, & Darmawan, 2019).

Future Perspectives

The development of molecular biology, chemistry, and post-harvest technology can support research expansion of wax apple fruit. Wax apple fruit cultivars can be identified with DNA barcoding or DNA fingerprinting. It will facilitate plant breeding and agricultural sectors. Furthermore, the metabolomics approach can be used to determine the excellent characteristics of each wax apple cultivars. Physiological and phytochemical treatment can be spread to the farmer in the wax apple tree plantation so that it will enhance the yield and fruit production. Therefore, every challenge is expected to solve based on the research implementation.

Conclusion

Wax apple (*Syzygium samarangense* (Blume) Merr. & L.M. Perry) has high diversity in cultivars and can cultivate in the tropical region. It contains various metabolites that have biological activities such as antioxidant activity, immunomodulatory activity, antibacterial activity, anticancer activity, anti-glycation and anti-inflammation activity, anti-hypertriglyceridemic, anti-hyperglycemic, relaxant activity, spasmolytic activity and neurodegenerative abnormality treatment, analgesic, and central nervous system (CNS) depression agent. Furthermore, the enhancement of wax apple physiological and phytochemical characteristics can be developed by girdling technique, hydrogen peroxide treatment, plant growth regulators treatment, and fruit bagging treatment. Meanwhile, post-harvest technology of wax apple fruit uses nitric oxide treatment, oxalic acid treatment, cold treatment, and *Aloe vera* gel coating. Wax apple has been developed as an ointment, anti-acne cream, and nata de guava. However, environmental stress will be a challenge in the wax apple plantation. Therefore, the development of molecular biology, chemistry, and post-harvest technology will solve those challenges.

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