Chemical Content and Pharmacology of Pomelo Orange (*Citrus Maxima*) Fruit Peel: A Review

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Abstract. Pomelo (*Citrus maxima*) is one of the citrus species that is widely consumed. Consumption of pomelo oranges produces fruit peels that tend to be underutilized, so it may produce some waste. Most of the reported research has been extensively studied for its phytochemical and pharmacological properties. The objective of this review article is to provide a comprehensive overview of the chemical compounds and pharmacological activity of the pomelo peel as an introduction to further research related to structure determination and activity testing. Several phytochemicals have been reported from *Citrus maxima* fruit peel including flavonoids, coumarins, phenylpropanoids, phenolics, steroids, and essential oils. These phytochemicals also exhibit some pharmacological activities, including antioxidant, antimicrobial, anti-inflammation, insecticidal, anti-alzheimer, and antidiabetic. Further research is needed to explore the fruit peel extract's activities and compounds in more detail for drug design, herbal products, and or functional foods. Proposed development based on pharmacological activities such as external remedies, internal remedies, dietary supplements, and pesticides.

1 Introduction

Pomelo also known as *Citrus maxima* is a common consumable fruit widely distributed and cultivated in China to Southeastern Asia. As the largest producer, China has an average of 1.4 million hectares of pomelo planting area. From 2017 to 2021, the pomelo production in China was 4.67, 5.05, 5.08, 5.12, and 5.16 million tons, respectively. Pomelo consumption in China in 2021 and the first half of 2022 was 4.96 and 1.86 million tons, respectively [1]. However, the consumption of pomelo fruit results by-product of pomelo peel approximately 30–50% (w/w) of the fruit [2]. This leads to a large amount of pomelo peel waste that may increase year to year.

The peel of pomelo often overlooked and discarded, may hold significant potential. The compounds within pomelo peel may have benefits that are not fully explored. Therefore, it is essential to conduct in-depth research to uncover the various components and compounds present in pomelo peel, as well as their potential uses that can contribute positively to various fields [3,4]. Pomelo peel waste has the potential to be utilized to manufacture value-added products [1,2,5].

Various studies have reported chemical constituents from peels of the *C. maxima* fruit, and extracts or pure compounds have also been analyzed for various biological activities. This

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article focuses on compiling several chemical contents and activities contained in pomelo peel into this review article. The results obtained are analyzed to predict the future prospects. Additionally, it highlights the utilization of valuable compounds from waste to provide sustainable solutions while using waste to generate economic benefits. The sources used were obtained using Google Scholar, Publish or Perish, and ScienceDirect. The objective of this review article is to provide a comprehensive overview of the chemical compounds and pharmacological activity of the pomelo peel as an introduction to further research related to structure determination and activity testing. These results are hoped to engage the scientific community in further studies and provide innovative solutions for managing and utilizing waste of *C. maxima* peel waste in the pharmaceutical, nutraceutical, and cosmetic industries.

2 Taxonomy and Morphology

Pomelo (*Citrus maxima*, previously known as *Citrus grandis*) is a perennial fruit plant that belongs to the Rutaceae family [6]. The naming of this fruit varies in each region, as listed in Table 1. The taxonomy of pomelo is as follows:

Kingdom : Plantae
Division : Tracheophyta
Class : Magnoliopsida
Order : Sapindales
Family : Rutaceae
Genus : Citrus
Spesies : Citrus maxima (Burman) Merrill [7]

Table 1. Citrus maxima local names [8]

Language	Common Name
English	Pomelo, Pummelo, Shaddock
Indonesia	Jeruk bali, jeruk besar
France	Pamplemousse, Shadek
Germany	Adamsapfel, Pampelmuse
Spanish	Pampelmusa
Dutch	Pompelmoes
Portuguese	Jamboa
China	Zhu Luan
Tamil	Gadarangai

The pomelo plant is a species of tropical fruit plant originating from Southeast Asia, which yields fruit twice a year. Commercially, this plant is grown in Malaysia, Thailand, Vietnam, Indonesia, India, and even China. The pomelo plant thrives in tropical lowlands up to an altitude of 400 meters, with an average temperature of 25–32°C and rainfall ranging from 1,500–2,500 mm, accompanied by a dry period of 3–4 months. Its fruit is large and round, with a diameter of 10-30 cm, consisting of thick skin (flavedo as the outer skin and albedo as the inner skin), which makes up 30% of its weight, and its flesh is pink or white with a sweet, bland, or sweet-tart taste [3,6–9]. The picture of pomelo is shown in Figure 1.

In traditional Chinese medicine, pomelo is used to treat flu, fatigue, wounds, coughs, phlegm, nausea, and congestion [10–12]. The fruit's peel can be used to repel mosquitoes and flies from food [13]. The essential oil obtained from pomelo fruit can be used in the industry for lotions, shampoos, disinfectants, and insecticides. Its essential oil can also be used to address fatigue, reduced strength, low stamina, inflammation, burns, acne, or skin disorders. [14].

(a) (b) (c)

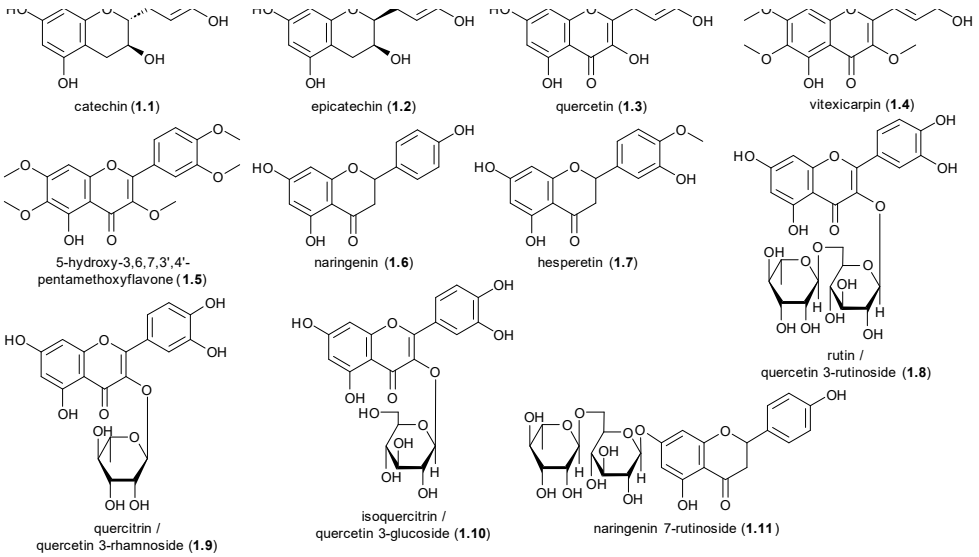
Figure 1. (a) Pomelo tree [8], (b) Pomelo flesh [7], (c) Pomelo peel

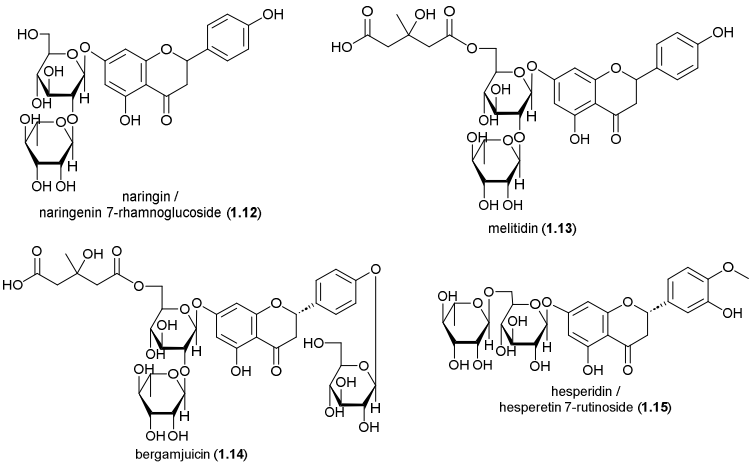
3 Chemical Constituents

The pomelo peel contains a variety of chemical compounds, with the focus of this discussion centered on its secondary metabolite content. The compounds found in the peel of pomelo consist of flavonoids, coumarins, phenylpropanoids, phenolics, steroids, and essential oils.

3.1 Flavonoids

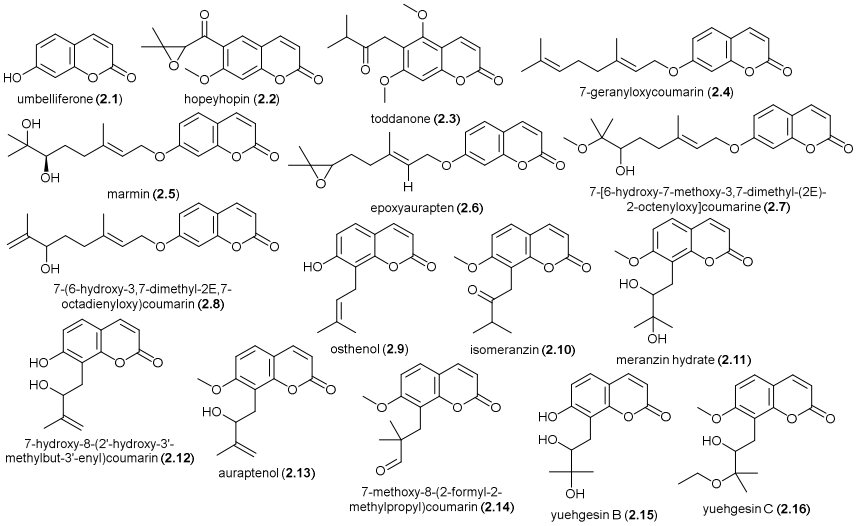
Several studies have conducted the extraction and identification of flavonoid compounds from the peel of pomelo. The techniques used to obtain extracts involve extraction with solvents such as ethanol, methanol, or water. The isolation of pure compounds is carried out using column chromatography (conventional, LC or HPLC). Compounds that have been identified include flavanol groups such as catechin (**1.1**) and epicatechin (**1.2**). Flavonol groups such as quercetin (**1.3**), vitexicarpin (**1.4**), and 5-hydroxy-3,6,7,3',4'-pentamethoxyflavone (**1.5**) have also been identified. Flavanon groups such as naringenin (**1.6**) and hesperetin (**1.7**). These flavonoids also have some glycoside derivatives, that are made from the main structure. These glycosides come from plant metabolites which generally produce sugar, so it is possible for presence of the sugar. Quercetin (**1.3**) glycoside derivatives are rutin (**1.8**), quercitrin (**1.9**), isoquercitrin (**1.10**). Naringenin (**1.6**) glycoside derivatives are naringenin 7-rutinoside (**1.11**), naringin (**1.12**), melitidin (**1.13**), bergamjuicin (**1.14**). Hesperetin (**1.7**) glycoside derivative is hesperidin (**1.15**) [4,10,15–20].

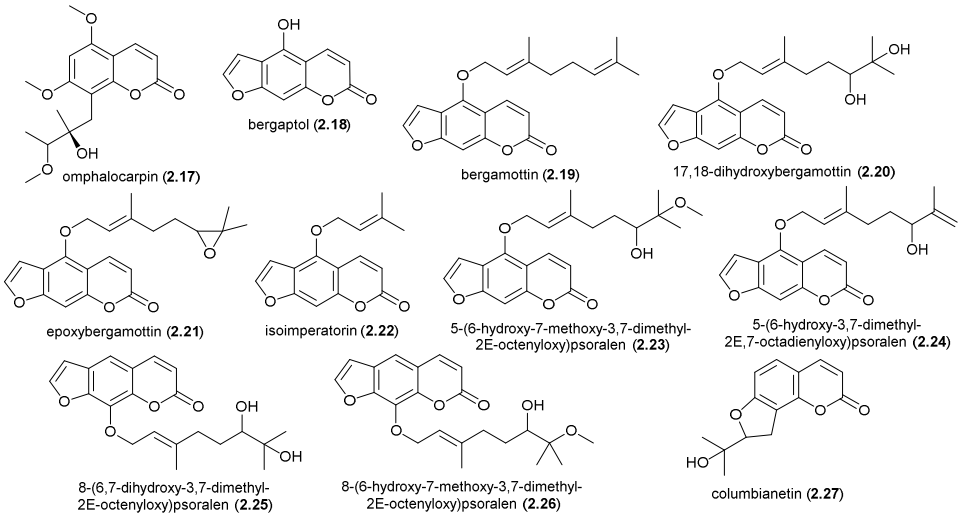




3.2 Coumarins

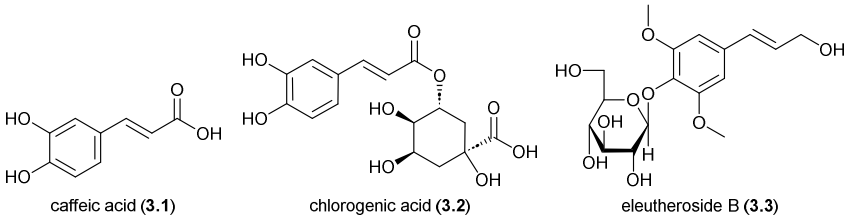
Coumarins compound has also been identified from several other studies in pomelo peel. The technique used to obtain the compound is using solvent extraction. Most of the coumarin compounds could be obtained in the ethyl acetate fraction. The isolation of pure compounds is carried out using column chromatography (conventional, LC or HPLC). Some of the coumarin compounds obtained from the peel extract of pomelo include umbelliferone (**2.1**), hopeyhopin (**2.2**), toddanone (**2.3**), 7-geranyloxycoumarin (**2.4**), marmin (**2.5**), epoxyaurapten (**2.6**), 7-(6-hydroxy-7-methoxy-3,7-dimethyl-(2*E*)-2-octenyloxy)coumarine (**2.7**), 7-(6-hydroxy-3,7-dimethyl-2*E*,7-octadienyloxy)coumarin (**2.8**), osthenol (**2.9**), isomeranzin (**2.10**), meranzin hydrate (**2.11**), 7-hydroxy-8-(2'-hydroxy-3'-methylbut-3'-enyl)coumarin (**2.12**), auraptenol (**2.13**), 7-methoxy-8-(2-formyl-2-methylpropyl)coumarin (**2.14**), yuehgesin B (**2.15**), yuehgesin C (**2.16**), omphalocarpin (**2.17**), bergaptol (**2.18**), bergamottin (**2.19**), 17,18-dihydroxybergamottin (**2.20**), epoxybergamottin (**2.21**), isoimperatorin (**2.22**), 5-(6-hydroxy-7-methoxy-3,8-dimethyl-2*E*-2-octenyloxy)psoralen (**2.23**), 5-(6-hydroxy-3,7-dimethyl-2*E*,7-octadienyloxy)psoralen (**2.24**), 8-(6,7-dihydroxy-3,7-dimethyl-2*E*-octenyloxy)psoralen (**2.25**), 8-(6-hydroxy-7-methoxy-3,7-dimethyl-2*E*-octenyloxy)psoralen (**2.26**), and columbianetin (**2.27**) [10,21–24].





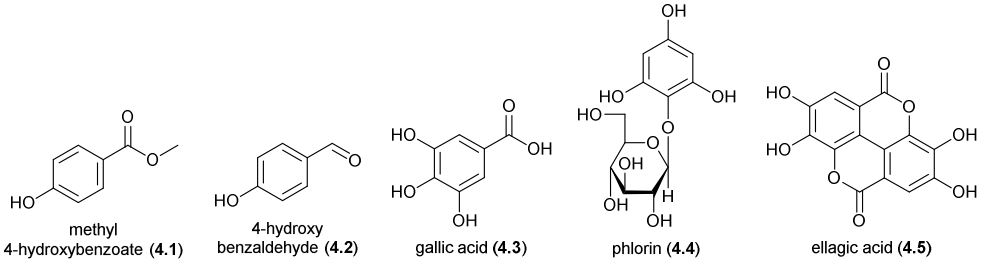
3.3 Phenylpropanoids

Phenylpropanoid compounds are more specific than phenolic compounds, but they are discussed separately due to their distinctive structural characteristics. Phenylpropanoid compounds found in the peel of pomelo include caffeic acid (**3.1**), chlorogenic acid (**3.2**), and eleutheroside B (**3.3**) [10,15,25]



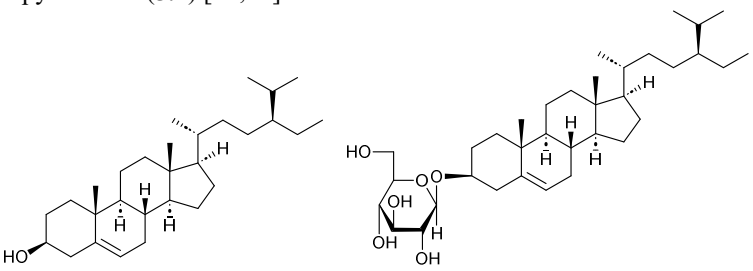
3.4 Phenolics

Phenolic compounds are compounds consisting of benzene rings with hydroxyl groups. The compounds consisted in this group re hydroxy benzene compounds which cannot be included in flavonoids, coumarins, and phenylpropanoids. The phenolic compound group mentioned here, in its basic structure, includes more complex structures of phenolic compounds in the phenylpropanoid, coumarin, and flavonoid groups as mentioned before. Phenolic compounds found in the peel of pomelo include methyl 4-hydroxybenzoate (**4.1**), 4-hydroxy-benzaldehyde (**4.2**), gallic acid (**4.3**), phlorin (**4.4**), and ellagic acid (**4.5**) [10,15,25]



3.5 Steroids

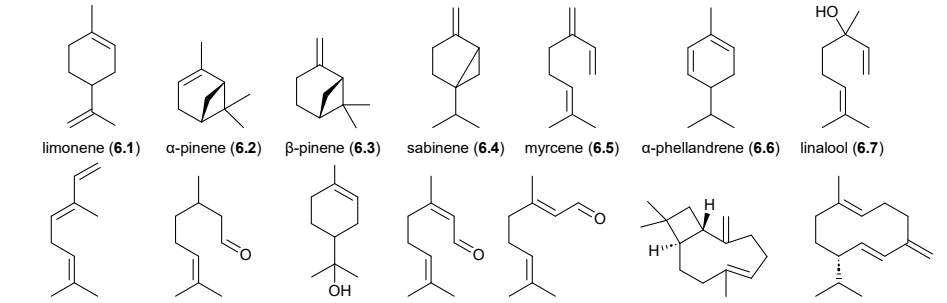
The steroid compounds found in the peel of pomelo are *β*-sitosterol (**5.1**) and *β*-sitosterol-3-O-*β*-D-glucopyranoside (**5.2**) [10,26]



β-sitosterol (**5.1**) β-sitosterol-3-O-β-D-glucopyranoside (**5.2**)

3.6 Essential Oils

Essential oil, also referred to as volatile components, is a substance that possesses the distinctive aroma of the tissue from which it is obtained. Most of the essential oil content in the peel of pomelo belongs to the terpenoid group (monoterpenoids and sesquiterpenoids). There are numerous components present in its essential oil, but the most dominant component is limonene (**6.1**). Other components are minor constituents often obtained from the essential oil, including α-pinene (**6.2**), β-pinene (**6.3**), sabinene (**6.4**), myrcene (**6.5**), α-phellandrene (**6.6**), linalool (**6.7**), trans-β-ocimene (**6.8**), citronellal (**6.9**), α-terpineol (**6.10**), neral (**6.11**), geranial (**6.12**), β-caryophyllene (**6.13**), and germacrene D (**6.14**) [14,27–29].



limonene (**6.1**) α-pinene (**6.2**) β-pinene (**6.3**) sabinene (**6.4**) myrcene (**6.5**) α-phellandrene (**6.6**) linalool (**6.7**)

trans-b-ocimene (**6.8**) citronellal (**6.9**) α-terpineol (**6.10**) neral (**6.11**) geranial (**6.12**) β-caryophyllene (**6.13**) germacrene D (**6.14**)

4 Pharmacological Activities

Several studies have been conducted on the pharmacological effects of *C. maxima* extracts and isolated compounds. Pharmacological studies have confirmed their efficacy as traditional medicine. In this review, we have gathered available information and described the pharmacological properties, including antioxidant, antimicrobial, anti-inflammatory, insecticidal, anti-Alzheimer's, and anti-diabetic activities. Below are some studies that have investigated different activities of pomelo peel.

4.1 Antioxidant activity

Antioxidant activity is an activity that can reduce or inhibit the oxidation reaction of a molecule by a reactive species or free radical. *In vitro* antioxidant activity test was conducted on methanol extracts of pomelo peel using the DPPH radical reagent. The results showed

IC_{50} values of 0.1251 and 0.1376 mg/mL for the flavedo and albedo, respectively [30]. The essential oil contains high of limonene (**6.1**) was tested for its antioxidant activity using the DPPH radical reagent, and it exhibited an IC_{50} value of 70.12 mg/mL [31]. *In vivo* antioxidant activity test was done using aqueous-ethanolic pomelo peel extract containing flavonoids against lipid peroxidation in the fish tissue. The result showed a reduction in peroxide value as evidence of positive activity inhibition of lipid peroxidation in fish tissue [32].

4.2 Antimicrobial activity

Antimicrobial activity is the activity of a substance that can inhibit, kill, or prevent the growth of microorganisms such as bacteria or fungi. Ethanol extracts of pomelo peel (flavedo) and the essential oil of pomelo peel have shown activity against bacteria including *Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, Staphylococcus aureus, Chromobacterium violaceum,* and *Vibrio anguillarum* [33]. The essential oil of pomelo peel exhibited antibacterial activity against *Escherichia coli, Pseudomonas aeruginosa, Bacillus subtilis, Staphylococcus aureus, Bacillus licheniformis*, and *Bacillus altitudinis* [29]. Antifungal activity has been observed in the essential oil of pomelo peel against fungi such as *Mucor hiemalis, Penicillium expansum,* and *Fusarium proliferatum* [34].

4.3 Anti-Inflammatory Activity

Anti-inflammatory activity is related to substances that work by reducing inflammation in the body. Anti-inflammatories help to alleviate symptoms of inflammation such as redness, swelling, and pain. The testing of anti-inflammatory activities is using the RAW 264.7 cells stimulated by lipopolysaccharide, the essential oil from *C. maxima* peel, which inhibited the expression of inflammatory mediators and pro-inflammatory cytokines. After testing the activity of each compound in the essential oil, it was found that α-terpineol (**6.10**) significantly contributed to the anti-inflammatory activity [35]. The ethyl acetate fraction of methanol extracts from *C. maxima* peel, containing coumarins, was tested for anti-inflammatory activity by inhibiting ear edema induced by xylene and paw edema induced by carrageenan in rats, as well as the production of inflammatory cytokines (interleukin 1β, prostaglandin 2, and tumor-necrosis factor α) in lipopolysaccharide (LPS)-induced RAW 264.7 cells. Test results showed that compounds 7-geranyloxycoumarin (**2.4**), marmin (**2.5**), isomeranzin (**2.10**), and meranzin hydrate (**2.11**) inhibited xylene and carrageenan-induced swelling. Compounds 7-geranyloxycoumarin (**2.4**), 7-(6-hydroxy-3,7-dimethyl-2*E*,7-octadienyloxy)coumarin (**2.8**), toddanone (**2.3**), 5-(6-hydroxy-3,7-dimethyl-2*E*,7-octadienyloxy)psoralen (**2.24**), and 8-(6-hydroxy-7-methoxy-3,7-dimethyl-2*E*-octenyloxy) psoralen (**2.26**) exhibited significant inhibition of inflammatory factor secretion in LPS-induced macrophages, with their activity being comparable to dexamethasone [21].

4.4 Insecticidal Activity

Insecticidal activity is the activity of a substance that is designed to control insects. Insecticides can be used in pesticides or other products to prevent or reduce damage caused by insects. The presence of limonene (**6.1**) and α-pinene (**6.2**) in the essential oil of pomelo peel shows potential as larvicides, which is shown by significant larvicidal activity against *Culex tritaeniorhynchus* and *Aedes aegypti*; however, *Armigeres subalbatus* showed greater resistance [26]. Another test was done on each growth stage of *Aedes aegypti* mosquitoes, from eggs to larvae to adults, using essential oil from *C. maxima* peel. Ovicidal activity did not show significant activity at 72 hours, larvicidal activity showed activity (LC_{50} = 61.71

ppm at 72 hours), and adulticidal activity showed activity (LC_{50} = 174.96 ppm). Therefore, the essential oil of pomelo peel has the potential to control the developmental stages of *Aedes aegypti* [36]. The essential oil from *C. maxima* peel exhibited activity against *Thrips flavus* Schrank (LC_{50} = 0.44 g/L) under laboratory conditions after 7 days of treatment [37].

4.5 Anti-Alzheimer Activity

Anti-Alzheimer's activity aims to prevent or reduce the risk of Alzheimer's disease, a type of neurodegenerative disease that commonly affects cognitive function and memory. Ethanol extract of *C. maxima* peel was tested for anti-Alzheimer's activity by dividing rats into four groups, and changes in behavioral aspects were analyzed using the Morris maze and Y Maze methods. Rivastigmine was used as a standard. After the study, the entire brain was collected, and acetylcholinesterase levels were examined. The research results showed a decrease in brain acetylcholinesterase levels, which can be considered an effective treatment for Alzheimer's disease [12]. The ethyl acetate fraction of pomelo peel extract containing 17,18-dihydroxybergamottin (**2.20**) and 7-hydroxy-8-(2'-hydroxy-3'-methylbut-3'-enyl) coumarin (**2.12**) demonstrated neuronal protection against Aβ-mediated neurotoxicity at 50 μM [10].

4.6 Antidiabetic Activity

Antidiabetic activity involves reducing blood glucose levels in individuals with diabetes to manage the symptoms and risks of diabetes-related complications. An 80% ethanolic extract of pomelo peel was tested on rat subjects that were divided into five groups, each consisting of 8 rats. Two treatment groups were given oral doses of the extract (400 and 600 mg/kg) and were compared with two control groups and a standard plant used for wound healing. Diabetes was induced by a single intraperitoneal injection of streptozotocin (STZ) at a dose of 65 mg/kg of body weight. After induction, wounds were created on the rats, and the study continued for 3 weeks. The results showed a significant decrease in blood glucose levels, as well as a significant improvement in wound closure percentage and time in the treatment groups. There was also a significant increase in hydroxyproline and total protein content in the healed wound tissue of the treatment groups compared to the control groups, and this was comparable to the standard plant extract [19]. Additionally, an ethanol extract of pomelo albedo was tested to reduce blood glucose levels in rats induced with aloxan-induced hyperglycemia (from 350 mg/dL to 150 mg/dL). There was no significant difference in anti-hyperglycemic activity between the extract and the chemical drug (Glucophage) [38].

5 Conclusion and Future Prospects

The peel of pomelo fruit contains a variety of secondary metabolite compounds, including flavonoids, coumarins, phenylpropanoids, steroids, and essential oils. Several pharmacological activities have shown positive effects, including antioxidant, antimicrobial, anti-inflammatory, insecticidal, anti-alzheimer, and anti-diabetic activities. Knowing the compound content and pharmacological activities of pomelo peel opens possibilities for future development. Pomelo peel can be developed into external remedies, such as creams, to alleviate pain in wounds and prevent infections, supported by its antimicrobial and anti-inflammatory activities. Pomelo peel can also be developed as an internal remedy for diabetes patients or the elderly suffering from dementia. Another potential development is as a dietary supplement to enhance the body's immune system against diseases. The unique aroma of pomelo peel, disliked by insects, can be utilized as the main ingredient or an additive component in insecticide products.

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