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Antioxidant and Anti-Collagenase Activity of *Solanum betaceum* Cav. Fruit Ethanolic Extract

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Abstract

Background: The oxidative stress theory of aging has gained traction as a contributing factor to the aging process. Free radicals greatly contribute to skin damage and hasten ageing by interfering with defence and restorative systems. Natural compounds in plants that have the capacity to scavenge free radicals and have antiaging capabilities. *Solanum betaceum* or tamarillo fruit has been known has many bioactive compounds such as anthocyanins, phenolics, carotenoids, and flavonoids compounds. *S. betaceum* also contains vitamins and nutrients that are vital for human health have strong antioxidant and antiaging properties. **Objective:** This research aimed to determine the antioxidant and antiaging activities of *S. betaceum* fruit extract (SBFE). **Methods:** The extraction of *S. betaceum* fruit extract using 70% ethanol and maceration method. *S. betaceum* antioxidant activities are conducted by measuring 2,2-diphenyl 1-pichylhydazyl (DPPH) scavenging activity while antiaging activity was investigated by inhibitory activity of collagenase enzyme. **Results:** SBFE showed the highest percentage in DPPH scavenging activity was 80.70%, while the Median Inhibitory Concentration (IC_{50}) value was 101.13 µg/mL. The highest collagenase inhibitory activity of SBFE was 43.91% with IC_{50} value was 50.64 µg/mL. **Conclusion:** In summary, *Solanum betaceum* fruit extract has potential as natural antioxidants and antiaging.

Key words: Antioxidant, Antiaging, DPPH, Collagenase, *Solanum Betaceum*

Introduction

Reactive oxygen species (ROS) damage, often known as oxidative stress, is now widely acknowledged to contribute to aging. Variations in the susceptibility of diverse organisms, tissues, and cell types to oxidative stress can impact their rate of aging. According to the oxidative stress theory of aging, ROS which are mostly produced by normal mitochondrial metabolism cause cumulative damage that eventually leads to the functional decrease that characterizes aging (Jomova et al., 2023). Oxidative stress is the results of an imbalance the generation and neutralization of oxidants. Its leads to the against of various diseases and aging. The steady decrease of organ and tissue function is one of the hallmarks of aging (Hajam et al., 2022). The

aging process leads to a diminished capacity of tissues to operate efficiently, impacting all organs in the human body, including organs both internal and external, such the skin (Juliana et al., 2020).

Skin aging is characterized by gradual alterations in the skin combined with a cumulative extrinsic factor, primarily resulting from exposure to free radicals such as UV radiation and air pollution (Girsang et al., 2020a). Photoaging refers to the aging of the skin caused by environmental stressors such as UV radiation. The absorption of this radiation by the skin leads to heightened levels of ROS, thereby exacerbating the aging phenomenon. UV radiation induces the generation of ROS such as hydrogen peroxide (H_2O_2) and supresses the production of collagen procollagen (Ndlovu et al., 2013; Jusri et al., 2019). Free radical such as 2,2-diphenyl-1-picrylhydrazyl (DPPH), as an aging factor has the potential to harm biological constituents within the body, culminating in oxidative stress and apoptosis cell (Khare et al., 2015; Juliana et al., 2020). ROS have the capacity to trigger intricate molecular pathways, leading to the activation of enzymes like collagenase, elastase, and hyaluronidase, which are involved in the degradation of Extracellular Matrix (ECM) components (Mukherjee et al., 2011). Consequently, these processes contribute to observable alterations in the skin, including the formation of wrinkles and changes in thickness (Bravo et al., 2016). Additionally, the prevention of aging requires the suppression of ROS and those enzyme-activated substances.

Collagen as the predominant protein in the ECM and plays a pivotal role in preserving the skin's elasticity, robustness, and suppleness (Ndlovu et al., 2013). It is the primary component of hair, nails, and connective tissue (Widowati et al., 2016; 2018). That enzyme has play role in degradation of collagen matrix. Human collagenase comes in three varieties : Matrix Metalloprotease (MMP)-1, MMP-13, and MMP-8 (Geeta et al., 2019). Collagenase inhibitors are present in a large number of skincare or cosmetic products that are marketed for commercial use. Through the Mitogen-Activated Protein Kinase (MAP-kinase) pathway and ultraviolet (UV) radiation, indirectly ROS can promote the formation of MMPs (Gu et al., 2020). Collagenase inhibition is a key target for the drug and cosmetic industries (Marques et al., 2021). Though there exist numerous synthetic skincare products containing active ingredients targeting skin aging, they have the potential to provoke adverse reactions like allergies, irritations, and photoallergic responses. Hence, there's a pressing need to explore natural resources for safe and efficient skincare and cosmetic ingredients (Mukherjee et al., 2011).

Tamarillo fruit (*Solanum betaceum* Cav.) is a tropical fruit from the Solanaceae family that has low in calorie and fat content (Rohilla et al., 2021; Wang et al., 2019). *S. betaceum* commonly referred to as tree tomato, bears resemblance to the tomato in terms of the texture of its flesh, ovoid to ellipsoid-shaped, juicy that can grow alone or in clusters. Fruit colour is used to differentiate between different varieties, red, orange, yellow, and purple (Lister et al., 2005; Isla et al., 2022). *S. betaceum* contains anthocyanins, isoflavones, carotenoids, fiber, vitamins and has anti-dyslipidemic properties. Six additional compounds were identified in tamarillo, comprising ellagic acid, rutin, catechin, epicatechin, kaempferol-3-rutinoside, and isorhamnetin-3-rutinoside (Diep et al., 2020). Both the fruit and its peel from S. betaceum are utilized for their antimicrobial and anti-inflammatory properties, particularly in treating sore throats and inflamed gums. Additionally, they serve as a dietary aid in lowering cholesterol levels (Vasco et al., 2009). This plant also exhibits various health benefits, including anti-inflammatory, antioxidative, antiobesity, antinociceptive, allergenicity, and antiproliferative properties. Numerous phytochemicals found in tamarillo fruit possess notable pharmacological and nutritional properties, including non-starch polysaccharides (pectins), flavonoids, carotenoids that potential as antioxidant and antiaging (Osorio et al., 2012, Wang et al., 2019). Aging skin caused by extrinsic factor can precipitate skin diseases, so that the natural sources of free radical scavenger and collagenase inhibitors were needed. Hence, this study aimed to evaluate the antioxidant and antiaging activity of *S. betaceum* fruit extract through DPPH scavenging and collagenase inhibitory activities.

Materials and Methods

Extraction of *Solanum betaceum* Fruit

The fresh tamarillo (*Solanum betaceum*) fruit were obtained from Berastagi fruit market, Berastagi, North Sumatra, Indonesia. The *S. betaceum* plant was identified by a staff member of the herbarium from Bandung Institute of Technology, Indonesia. The fruit undergoes a drying

process before being finely ground into simplicia powder (100 g). The extraction was carried out using 1200 mL of 70% ethanol solvent using maceration technique. The filtrate was gathered at 24-hour intervals until the ethanol filtrate became devoid of color. Then the ethanol is evaporated until a paste of tamarillo fruit extract is obtained using evaporator 50 ^{0}C. The yield of extract in pasta was 22.38 g and stored at -20 ^{0}C for further assay (Widowati et al., 2018; Dewi et al., 2020).

DPPH Scavenging Activity Assay

The approach was based on an alcoholic DPPH reduction with the existence of a hydrogen-donating antioxidant regarding the non-radical formation of the DPPH-H reaction. In each well, 50 µL samples were dropped in a 96-well microplate. After which 200 µL of 2,2-Diphenyl-1-picrylhydrazile (DPPH) solution (0,077 mM in methanol) was applied to the well. Afterwards, the solution was incubated at room temperature for 30 minutes in the dark. The absorbance of the mixture was then read with a microplate reader (MultiskanTM GO) (Widowati et al., 2017; Siregar et al., 2019; Girsang et al., 2020b).

Scavenging % = (Ac – As) / Ac x 100

Ac: negative control absorbance (without sample)

As: sample absorbance

Collagenase Inhibitory Activity Assay

The inhibition activity of collagenase was measured based on modified method of Sigma-Aldrich, Widowati et al. (2016, 2017, 2018) and Geeta et al. (2019). The mixed solution was incubated at 37 °C for 20 minutes and included 10 µL of *Clostridium histolyticum* Collagenase (0.01 U/mL in cool aquadest), 60 µL of Tricine buffer (50 mM, pH 7.5, 10 mM CaCl2 and 400 mM NaCl), and 30 µL of sample (0-250 µg/mL in DMSO). 20 µL N-[3-(2-Furyl) acryloyl]-leu-gly-Pro-Ala was added to the sample during incubation. After incubation, the substrate (1 mm in the Tricine buffer) was added. The absorbance was measured at 335 nm in wavelength using a microplate reader.

% Collagenase inhibition = (Ac – As) / Ac x 100

Ac: negative control absorbance (without sample)

As: sample absorbance

The median inhibitory concentrations (IC_{50}) of collagenase assay were also calculated.

Results and Discussion

Effect of *S. betaceum* Fruit Extract on DPPH Scavenging Activity

DPPH serves as a reagent utilized to examine the free radical scavenging capabilities of compounds. During the DPPH test, the extract demonstrated the ability to convert the stable radical DPPH into yellow-colored diphenylpicrylhydrazine (DPPH-H) (Widowati et al., 2015). The DPPH scavenging activity of *S. betaceum* fruit extract can be seen in Figure 1 and the IC_{50} of sample can be seen in Table 1.

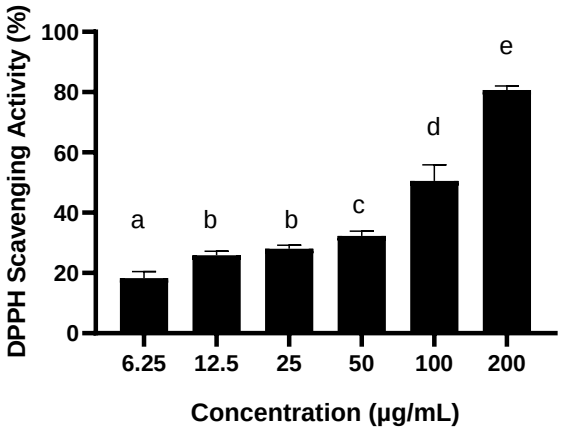

Figure 1. Effect various concentration of SBFE toward DPPH scavenging activity

*The data presented are mean values ± standard deviation from 3 replications. The different letter (a,b,c,d,e) showed significant difference based on Independent T-Test ($p<0.05$).

Table 1. Effect various concentration of SBFE toward DPPH scavenging activity

Concentration (µg/mL)	DPPH Scavenging Activity (%)
6.25	18.32 ± 2.17[a]
12.5	25.84 ± 1.33[b]
25	28.00 ± 1.20[b]
50	32.33 ± 1.53[c]
100	50.52 ± 5.38[d]
200	80.70 ± 1.32[e]

*Data was presented as mean values ± standard deviation. The different letter (a,b,c,d,e) showed significant difference based on Independent T-Test ($p<0.05$).

Table 2. The IC_{50} value of antioxidant and antiaging activities of SBFE

Assay	Equation	R^2	IC_{50} (µg/mL)
DPPH Scavenging	y = 0.3085x + 19.039	0.99	101.13 ± 0.67
Collagenase Inhibitory	y = 0.1170x + 43.996	0.99	50.64± 2.28

Based on Figure 1 and Table 1, SBFE showed the highest percentage with value of 80.70% at the highest concentration (200 µg/mL). In the lowest concentration SBFE showed the value of 18.32%. The IC_{50} value of DPPH scavenging activity of SBFE also can be seen in Table 2. SBFE has IC_{50} value of 101.13 ± 0.67 µg/mL. This result indicated that SBFE has antioxidant activity.

Effect of *S. betaceum* Fruit Extract on Collagenase Inhibitory Activity

A spectrophotometric technique was employed for collagenase activity assessment, aiming to identify potential inhibitors of collagenase (Widowati et al., 2016). The collagenase enzyme degradation of collagen in the skin. Collagenase activity inhibition postpones the formation of pre-collagen fibre and the wrinkle-forming process (Widowati et al., 2016; 2017). The collagenase inhibitory activity of *S. betaceum* fruit extract (SBFE) can be seen in Figure 2.

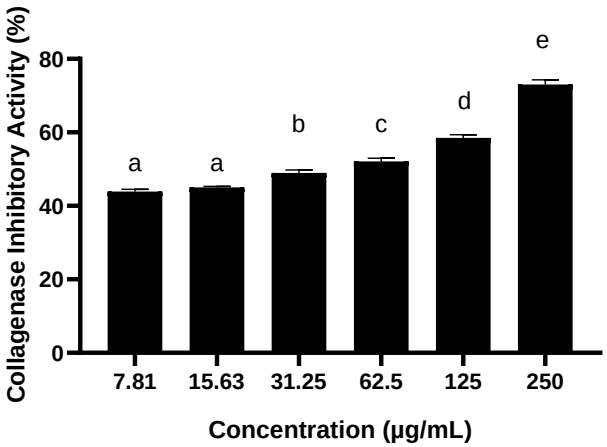

Figure 2. Effect various concentration of SBFE toward collagenase inhibitory activity

*The data presented are mean values ± standard deviation from 3 replications. The different letter (a,b,c,d,e) showed significant difference based on Tukey Post Hoc test ($p<0.05$).

Table 3. Effect various concentration of SBFE toward collagenase inhibitory activity

Concentration (µg/mL)	Collagenase Inhibitory Activity (%)
7.81	43.91 ± 0.58[a]
15.63	45.05 ± 0.28[a]
31.25	48.97 ± 0.79[b]
62.5	52.08 ± 0.87[c]

125	58.53 ± 0.86[d]
250	73.01 ± 1.28[e]

*Data was presented as mean values ± standard deviation. The different letter (a,b,c,d,e) showed significant difference based on Tukey Post Hoc test ($p<0.05$).

Based on Figure 2 and Table 3, the highest concentration of SBFE (1000 µg/mL) showed the highest collagenase inhibitory activity with value 73.01%, while in the lowest concentration showed percentage of 43.91. However, IC_{50} value of SBFE showed 50.64 ± 2.28 µg/mL (Table 2). The result indicated SBFE has antiaging activity.

Discussion

The aging phenomenon in living organisms is predominantly attributed to physiological processes, wherein factors such as free radicals play a significant role among various other contributors (Siregar et al., 2019). In the process of skin aging, collagenase enzymes exhibit heightened expression and activity, leading to the degradation of dermal extracellular matrix (ECM) components. This enzymatic activity contributes to the manifestation of aging-related clinical features such as skin dryness, wrinkles, and reduced elasticity (Orqueda et al., 2022). Natural compounds form indigenous plants are extensively potential as antioxidants and agents combating the aging process, such as *S. betaceum* or tamarillo fruit (Siregar et al., 2019; Asih et al., 2018). *S. betaceum*, commonly known as tamarillo, is a fruit rich in essential nutrients and vitamins crucial for human health that has antioxidant and antiaging activity (Asih et al., 2022).

The DPPH radical is commonly utilized to assess the initial radical scavenging capability of plant extracts (Deshpande et al., 2013). In this study, SBFE showed the highest percentage of 80.70% and has IC_{50} value of 101.13 µg/mL (Figure 1, Table 2). The effectiveness of a compound in biological or biochemical roles measured by its ability to inhibit the oxidation process by 50% (IC_{50}), is categorized into several groups: <50 µg/mL (very strong), 50-100 µg/mL (strong), 101-150 µg/mL (moderate), >150 µg/mL (weak) (Budaraga et al., 2016; Kuswanto et al., 2020). However, the IC_{50} value of DPPH scavenger activity of this study has moderate activity. Based another study, the flavonoid glycosides (kaempferol 3-O rutinoside, routine, 3-O rhamnoside) in *S. betaceum* n-butanol extract show strong antioxidant activity through DPPH scavenging activity with IC_{50} value 70.11 mg/L (Asih et al., 2018). Another study was reported that tamarillo has total flavonoid content was 7.42 mg QE/g extract, total polyphenol content was 66.62 mg GAE/g extract, and also has antioxidant activity (IC_{50}=47.94 ppm) (Silitonga et al., 2024). The tamarillos showed notable antioxidant capacity with high values, which were closely associated with their elevated total phenolic content. The presence of these bioactive compounds underscores the promising potential of tamarillo for expanded utilization in both the food and pharmaceutical sectors (Diep et al., 2020). *S. betaceum* fruits also contain significant amounts of other antioxidants such as vitamin C and carotenoids, which are likely to enhance its overall antioxidant capacity (Acosta-Quezada et al., 2015; Espin et al., 2016). In another study, rosmarinic acid and hydroxycinnamoyl acids which are majority phenolic compounds in *S. betaceum* fruit, have been shown to possess higher scavenging activity than ascorbic acid and tocopherol (Alamed et al., 2009).

Collagenase enzymes, which participate in the degradation of these components, have been directly associated with the process of skin aging (Mukherjee et al., 2011). In terms of ageing skin, utilizing a natural compound that hinders collagenase activity could potentially deter the aging process by preventing the depletion of skin elasticity (Geeta et al., 2019). In this study, SBFE showed the highest collagenase inhibitory activity with value 73.01%; IC_{50}=50.64 µg/mL (Figure 2, Table 2). *S. betaceum* has inhibition activity of collagenase, its delays the process of collagen degradation, thus delaying the onset of the wrinkling process (Bravo et al., 2016). *S. betaceum* extract active as antiaging due to elastase and tyrosinase inhibitory activity cause the source of bioactive phenolic. The utilization of waste from indigenous fruits *(S. betaceum)* is emerging as a highly promising alternative in the formulation of cosmetic products, offering potential applications in the development of hydrogels, creams, and lotions in the future use (Orqueda et al., 2022). Furthermore, the material from plant-derived extracts being both sustainable and cost-effective while maintaining efficiency, which is often associated with skincare cosmetic formulations (Isla et al., 2022).

Conclusion

This study shows that SBFE has the potential as antioxidant agent through against free radical of DPPH, and also has an antiaging properties through collagenase enzyme inhibitory activity based on in vitro studies. Further research could involve testing extracts from *S. betaceum* on based *ex vivo* and *in vivo* studies. Hence, this studies could yield valuable insights for formulating ingredients of anti-aging cosmetic products.

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Conflict of Interest

The authors declare that we have not conflict of interest in this study.

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