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Serum Gel Formulation of Mundu Fruit Extract (*Garcinia dulcis* Roxb. Kurz.) as Antioxidant and Anti-elastase

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ABSTRACT: UV radiation can generate Reactive oxygen species (ROS), thereby damaging neutrophils, leading to the uncontrolled release of elastase, and causing aging. This study aims to examine the antioxidants and anti-elastase activity of the *Garcinia dulcis* Roxb-Kurz (Mundu) fruit and in the serum gel extract preparation. Extraction of *Garcinia dulcis* was carried out using microwave-assisted extraction (MAE) using ethanol, and the antioxidants activity test was done using the ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) method. Preparation of serum gel uses three formulas (F1, F2, and F3) that contained extract ethanol of *Garcinia dulcis* with the concentrations 100x, 200x, and 300 x IC_{50} value, consecutively. The test results for the three formulas showed the IC_{50} of antioxidants were 88.61, 71.47, and 66.26 µg/ml. The anti-elastase activity of serum gel obtained 150.32, 134.47, and 111.48 µg/ml, respectively. This shows that the best activity is the F3 of serum gel, indicating that the higher the extract concentration in the formulation provides better activity in the serum gel preparation. In addition, evaluation of serum gel for three formulas were carried out, including pH, viscosity, and spreadability, and F3 was the best formula. In conclusion, the Mundu fruit extract has antioxidant and anti-elastase activity and, after being applied to serum gel preparations, still provides good antioxidant and anti-elastase activity results.

Keywords: ***Garcinia dulcis* Roxb-Kurz extract, antioxidants; anti-elastase; formula; gel.**

Introduction

Skin aging is a skin problem that concerns some people. Based on its structure, the skin is the outermost layer that functions to protect the organism, so it has the consequence of being exposed to UV rays. As a result, skin can experience change because of UVB and UVA and can cause DNA damage by generating free radicals or reactive oxygen [1]. The primary mechanism of damage to DNA due to reactive oxygen species (ROS) is the formation of oxidized nitrogen bases [1]. Biological factors caused by UV radiation include burn effects on the skin, decreased skin elasticity, pigmentation, and even premature aging [2]. ROS are created when the components of skin cells absorb UV radiation energy. Furthermore, damage to neutrophils brought on by excess reactive oxygen species might result in the uncontrollable release of elastase. This enzyme can damage tissues, including collagen and elastin [3].

Therefore, the role of antioxidants and anti-elastase is needed. Antioxidants prevent reactions caused by free radicals by inhibiting or deactivating oxidants and radicals [4]. Meanwhile, Elastase is a protease enzyme responsible for degrading elastin by hydrolyzing the protein components in connective tissue. Under oxidative stress conditions, ROS can trigger an excessive increase in elastase production, which contributes to the aging process [5]. Thus, to prevent skin aging, it is necessary to inhibit elastase [6]. The *Garcinia dulcis* Roxb. Kurz. plant is known to have secondary metabolites of biflavonoids and their derivatives, so they have antioxidant activity [7]. One of the prevention methods for premature aging can be done by applying an appropriate dosage form that contains antioxidant and anti-elastase properties. The intended dosage forms should be easy to apply and can be absorbed well to obtain maximum results. Serum gel that has antioxidants and anti-elastase provides some advantages, including absorbing quickly into the skin, thus providing comfort

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to the user, and it has a low viscosity, so it is easy to spread on the skin surface [8].

Previous research by Santosa *et al.* on the antioxidant activity of *Garcinia dulcis*, Blumea mollis, Siegesbeckia orientalis, and Salvia riparia found that the highest antioxidant activity was obtained from *Garcinia dulcis* with an IC_{50} value of 38.613 µg/ml [9]. In Ambarwati's 2024 study, antioxidant activity testing was conducted on the extract of G. *dulcis* fruit using the microwave-assisted extraction (MAE) method, which showed a phenolic content of 13.98 mg GAE/g. The antioxidant activity measured by the DPPH method, with an electron donation or hydrogen atom transfer mechanism [10], yielded an IC_{50} value of 137.721 µg/ml for the 70% ethanol extract of G. *dulcis* and 481.948 µg/ml for G. *forbesii* [11]. The antioxidant activity of G. *dulcis* is better than G. *forbesii*, as indicated by the smaller IC_{50} value, which means greater antioxidant activity [12].

Another specific and sensitive antioxidant test can be conducted on various types of free radicals such as ABTS (2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) [13]. ABTS measurements can be performed on forming radicals in both hydrophilic and lipophilic media [14]. In the human body, oxidative reactions that trigger the formation of free radicals can occur in both the aqueous and lipid compartments. Thus, the ABTS antioxidant activity can function more complexly than DPPH. In addition, serum gel preparations applied to the skin are more effective when delivered through hydrophilic molecules, as they work on intercellular and intracellular pathways that can enhance hydrophilic and lipophilic permeation [15].

In previous research, the ethanol extract of *Garcinia mangostana* L. using the maceration method exhibited antioxidant activity with a DPPH method IC_{50} value of 35.80 µg/ml. This extract was then formulated into a serum gel at concentrations of 3%, 4%, and 5%, resulting in DPPH method IC_{50} values of 169.3 µg/ml, 38.76 µg/ml, and 31.92 µg/ml, respectively. These results indicate that the antioxidant activity present in the G. *mangostana* extract is retained in the serum cosmetic formulation [16].

Thus, due to its antioxidant activity and anti-elastase properties, *Garcinia dulcis* has the potential as a skin care agent. Its ability to protect cells from oxidative damage and inhibit the enzyme elastase can slow down the aging process and help maintain skin elasticity. Therefore, in this study, serum gel containing extract ethanol of *Garcinia dulcis* was formulated into a serum gel. The antioxidant activity test was conducted using the ABTS method, and the serum gel was also evaluated, including pH, viscosity, and spreadability.

Methods

Materials

Mundu (*Garcinia dulcis* (Roxb.) Kurz) fruit extract (the fruits from Bogor, Indonesia), Carbomer 940 (BOC Sciences, USA), Propylene Glycol (Keanchem, Shanghai), Triethanolamine (PT Laju Usaha Gemilang, Indonesia), Sodium Metabisulfite (Henan Fengbai Industrial Co., Ltd., China), Potassium Sorbate (Topinchem, China), Distilled Water (PT. Anugrah Visi Cemerlang, Indonesia), ABTS (SIGMA-ALDRICH, USA, 30931-67-0), Potassium Persulfate (Hebei Fiza Technology Co., Ltd.), Elastase from Porcine Pancreas (SIGMA-ALDRICH, USA, 39445-21-1), N-Succinyl-Ala-Ala-Ala-p-nitroanilide elastase substrate (SIGMA-ALDRICH, USA, 52299-14-6), Trizma® base – Primary Standard and Buffer (SIGMA-ALDRICH, USA, 77-86-1).

Preparation of Mundu (Garcinia dulcis Roxb. Kurz.) Fruit Extract

Extraction was conducted using a microwave-assisted extraction (MAE) (Sharp-in modified, R-230R(S), Thailand) method with a power of 30% from 399 W (119.7 W). This is done by dissolving the simplicia of mundu fruit in 50% ethanol and then stirring for 10 minutes.

Evaluation of Mundu Fruit Extract (Garcinia dulcis Roxb. Kurz.)

Evaluation of mundu fruit extract was done by organoleptic test, pH (HANNA, H2211, English), homogeneity, viscosity, and spreadability. The homogeneity test was performed by looking at particles of prepared glass. Viscosity and flow properties were carried out using a Brookfield LV viscometer (USA), and spreadability was carried out by weighing 0.5 grams of the sample and then placing it on a spreadability test tool with a weight of 100 grams, 150 grams, or 200 grams, then let stand for 1 minute.

Antioxidant Activity Test of Mundu Fruit Extract (Garcinia dulcis Roxb. Kurz.) using the ABTS (2,2-azinobis (3-ethylbenthiazoline-6-sulfonic acid)) Method

The ABTS reagent was prepared by weighing seven mM ABTS liquified in 5 ml of distilled water, then weighing 2.45 mM $K_2S_2O_8$ dissolved in 5 ml of distilled water, putting the mixture in a dark glass bottle, and then observing for 12 to 16 hours. 1 ml of ABTS solution was pipetted, and pro-analysis ethanol was added until it reached a volume of 5 ml.

Then, 20 µl of the extract was mixed with 180 µl of ABTS solution, incubated at room temperature, and protected from light for 45 minutes. Absorption measurements were carried out using a microplate reader (ELISA Reader, China) at a wavelength of 734 nm. The antioxidant activity is done using the ABTS method tested Mundu fruit extract, with vitamin C as a positive control [17]. The concentrations used in the positive control are 20, 30, 40, 50, and 60 ppm. The concentrations used in the gel serum extract were 600, 700, 800, 900, and 1000 ppm.

Anti-elastase Activity Test of Mundu Fruit Extract (Garcinia dulcis Roxb. Kurz.)

Tris HCl buffer, N-Suc-$(Ala)_3$-pNA 4.4 mM substrate, and elastase enzyme were prepared. The sample activity was done by pipetting 140 µl of 0.1 M Tris HCl buffer, pH 8.0, into a 96-well microtiter plate. Then, pipetting 20 µl of sample and 20 µl of elastase enzyme solution was carried out. Incubation was carried out for 15 minutes at 25°C. After that, 20 µl of N-Suc-$(Ala)_3$-pNA substrate was added and then incubated for 15 minutes at 25°C [11]. The concentration of mundu fruit extract was 3000, 3500, 4000, 4500, and 5000 ppm.

% Inhibition of Elastase : (C-S)/C x 100% [18].

Description :

C = Absorbance of the control (without sample addition)

S = Absorbance of the sample (S_1) - the sample blank (S_0)

S_1 = Absorbance of the sample (sample + enzyme)

S_0 = Absorbance of the sample blank (sample without enzyme)

IC_{50} is calculated using a linear regression equation, where the x represents the sample concentration (in logarithm) and the y represents (% inhibitions) thus y = a + bx.

Optimization Process of Serum Gel Preparations

The speed optimization of the serum gel was performed by weighing Carbomer 940, then adding it gradually to distilled water (in a ratio of 1 20), allowed to stand for 24 hours, developing carbomer with a stirrer, and then adding triethanolamine gradually to form a gel base, then added propylene glycol and stirred, added potassium sorbate and sodium metabisulfite dissolved in distilled water to the gel base, speed optimization was performed at 100, 300, 400 rpm, and stirring time optimization was performed at 5, 10, and 15th minute.

Preparation of Gel Serum Formulation

The formulation of the Mundu fruit extract gel serum is shown in Table 1. The procedure begins with preparing and weighing the required materials. Gradually add carbomer 940 into distilled water at a ratio of 1:20 and let it sit for 24 hours until it fully swells. After swelling, homogenize the carbomer 940 using a stirrer. Slowly add Triethanolamine until the pH is neutral, allowing the carbomer 940 to expand and form a gel base fully. Next, propylene glycol is added to the gel base, stirring continuously until homogeneous. Dissolve potassium sorbate and sodium metabisulfite in distilled water, stirring until fully dissolved, and then add this solution to the prepared gel base. Finally, add the mundu fruit extract, pre-dissolved in pure water, and stir at 300 rpm for 10 minutes. Until the mixture is homogeneous, once the gel serum preparation is complete, proceed with the evaluation test.

Evaluation of Gel Serum Formulation from Mundu Fruit Extract (Garcinia dulcis (Roxb.)Kurz.,)

Organoleptic Test

The organoleptic test conducted included observing

Table 1. Formulation of serum gel of mundu fruit extract (*Garcinia dulcis* L.).

Raw Materials	Concentrations (%)			
	Blank	Formula 1	Formula 2	Formula 3
Mundu fruit extract	-	100xIC_{50}	200xIC_{50}	300xIC_{50}
Carbomer 940	0.3	0.3	0.3	0.3
Propylene glycol	10	10	10	10
Triethanolamine	0.3	0.3	0.3	0.3
Sodium metabisulfite	0.1	0.1	0.1	0.1
Potassium sorbate	0.1	0.1	0.1	0.1
Oleum rose	0.1	0.1	0.1	0.1
Distilled water	ad 100			

Table 2. Stirring optimization of serum gel base.

Stirring time (minutes)	Stirring speed (Rpm)	Observation results
5	300	TH (-)
	100	TH (-)
10	300	H (-)
	400	H (+)
15	300	H (+)

Description: TH: Not homogeneous -: Not bubbly
H : Homogeneous + : Bubbly

the color, smell, and shape of the gel serum preparation [19].

Homogeneity Test

The homogeneity test is conducted by applying the gel serum preparation onto a glass slide and then observing the coarse particles by touch [19].

Viscosity and Flow Properties Test

This is conducted using a Brookfield LV viscometer. A certain amount of gel serum is placed into a container as a glass cylinder (beaker), and the appropriate spindle number 3 is installed up to a predetermined limit, then rotated at a specific speed until the viscometer needle indicates a constant value on a scale [20]. The flow characteristics can be determined by creating a curve between rpm and force (dyne/cm) based on the obtained data, which is then plotted on graph paper with force (x) and rpm (y), after which the flow properties are determined.

Spreadability Test

The spread test is conducted to ensure the distribution of the gel serum on the skin. A sample of gel serum weighing 0.5 grams is placed on a spreading test apparatus consisting of a round glass plate or another transparent material along with weights so that the total weight of the round glass plate or transparent material and the weights is 100 grams 150 grams, and 200 grams. It is left for 1 minute, then the spreading diameter is recorded [21].

Stability Testing of Mundu Fruit Extract Gel Serum (Garcinia dulcis)

The stability test was conducted through an accelerated test at a temperature of 40 °C. The mundu fruit extract gel serum was evaluated weekly for four weeks. The evaluation included organoleptic test, homogeneity, viscosity, spreadability, and pH.

Result and Discussion

The result of the antioxidant test of positive control (Vitamin C) was the IC_{50} value of 4.68 ppm. The IC_{50} value shows the concentration of the sample solution used as 50% inhibition of ABTS free radicals [22]. The IC_{50} value of less than 50 ppm indicates that the antioxidant is very strong [23]. Then, the extract of Mundu fruit was carried out in which the reaction shown by a decrease in the intensity of the green-blue to colorless in the sample [24]. The IC_{50} value of extract Mundu fruit was 28.81 ppm, which is classified as very strong antioxidant ability. The smaller the IC_{50} value obtained, the greater the ABTS radical capture activity.

This study tested anti-elastase activity because anti-elastase can maintain skin elasticity by reducing elastin

Table 3. The result of serum gel evaluation.

Formula	Evaluations		
	pH value	Viscosity(cps)	Spreadability (mm^2)
Blank	5.98 ± 0.01	4888.5 ± 3166.95	2376.79
Formula 1	5.72 ± 0.02	4335.71 ± 2771.09	3422.57
Formula 2	5.62 ± 0.01	4020 ± 2550.84	3850
Formula 3	5.40 ± 0.02	3675.71 ± 2241.31	4419.64

Table 4. IC_{50} values of ABTS antioxidant and anti-elastase serum gel preparations of Mundu fruit extracts.

Activity	Formula 1 IC_{50} (µg/ml)	Formula 2 IC_{50} (µg/ml)	Formula 3 IC_{50} (µg/ml)
Antioxidant	88.61	71.47	66.26
Anti-elastase	150.32	134.47	111.48

degradation and using luteolin as the standard [25]. The concentrations used were 62.5, 125, 250, 500, and 1000 ppm, with an IC_{50} value of 63.32 ppm. This indicates that luteolin has a strong anti-elastase activity ability. The IC_{50} value of the mundu fruit extract was 82.21 ppm. They noted that mundu fruit extract has a strong ability in anti-elastase activity [26]. The antioxidant and anti-elastase activity test results on mundu fruit extract showed very strong IC_{50} values. Consequently, mundu fruit extract can be an anti-aging agent by shielding the skin from reactive oxygen species (ROS) and preventing UV-induced cell damage [15].

Before the preparation of the serum gel, the stirring speed of the serum gel base was optimized, as seen in Table 2. The optimization results show that a good stirring speed is found at 300 rpm because the good results are homogeneous and not bubbly. In addition, the stirring time of the serum gel base was also optimized, which can be observed in Table 2. Then, the serum gel base was stirred at 300 rpm for 10 minutes.

The result for the evaluated serum gel extract is three formulas. The organoleptic test findings are semi-solid, with a yellow color and the smell of oleum rose. The pH test findings are displayed in Table 3. A suitable pH on the skin ranges from 4.0 to 7.0 [27]. Based on Table 3, it is known that the pH values of the three formulas' satisfy the specifications. Thus, formula 3 has the most acidic pH value, so a more acidic pH can protect the skin from bacterial growth. At the same time, dryness and irritation might result in a somewhat alkaline skin pH. In addition, a homogeneity evaluation was carried out, obtaining homogeneous results in the three formulas. After that, a viscosity evaluation was carried out, which can be observed in Table 3. In all three formulas, the viscosity value meets the requirements.

Meanwhile, the viscosity requirement is 2.000 to 4.000 cps [21]. If the viscosity value obtained is too large, it will cause a small spreadability, making it challenging to apply to the skin [20]. The findings of the spreadability assessment are displayed in Table 3. The requirements for spreadability are 50 mm to 70 mm [28]. The spreadability test is designed to evaluate how well the preparation can spread on the skin; the more significant this ability, the larger the surface area it can cover [20]. The flow properties of the preparation are plastic thixotropic.

The antioxidant and anti-elastase activity were tested on the three formulas. The IC_{50} results on the three formulas can be seen in Table 4. The smaller the IC_{50} value, the greater the antioxidant activity. Based on the appearance of Table 4, it is concluded that formula 3 has higher antioxidant activity and is included in the potent antioxidant ability. This shows that the serum gel preparation of mundu fruit extract still maintains antioxidant activity despite adding other excipients. In addition, the excipients added to this serum gel are found to be antioxidant agents, namely sodium metabisulfite [29].

In addition, an anti-elastase activity test was conducted, which can be observed in Table 4. This is positively correlated to the results of antioxidant activity, which shows the best activity in formula 3. The evaluation results of the preparation confirm the pH value, viscosity, and spreadability. Stability testing was carried out on the

Tabel 5. Results of pH stability evaluation on serum gel preparation of mundu fruit extract

Time (Week)	Blank	Formula 1	Formula 2	Formula 3
0	5.98	5.72	5.62	5.40
1	5.79	5.66	5.50	5.31
2	5.78	5.65	5.49	5.30
3	5.77	5.64	5.48	5.28
4	5.75	5.63	5.47	5.27

Tabel 6. Results of viscosity stability evaluation on serum gel preparation of mundu fruit extract

Formula	Viscosity (cps) Time (Week)				
	0 ± SD	1 ± SD	2 ± SD	3 ± SD	4 ± SD
Blank	4888.57 ± 0	4510 ± 141.42	4052.86 ± 0.70	3861.43 ± 1.41	3478.57 ± 0.71
1	4335.7143 ± 0	3988.57 ± 70.71	3605.71 ± 70.71	3230 ± 0.71	2832.86 ± 6.36
2	4020 ± 0	3527.14 ± 0,07	3132.86 ± 4.24	2921.43 ± 70.71	2512.86 ± 70.71
3	3675.7143 ± 0	3175.71 ± 3.53	2690 ± 70.71	2444.29 ± 3.53	2225.71 ± 70.71

four-week preparation at 40 ℃. The stability test aims to test the durability of product quality determined during the period of use and storage to ensure a product's strength, quality, and purity [30].

The results of the stability evaluation for three formulas on the organoleptic preparation remained the same color, shape, and odor from week one to week four. Furthermore, the pH test was carried out on the preparation stability test, observable in Table 5. The gelling agent is acidic, so the TEA cannot compensate for this acidic nature during storage [31]. The reduction in pH of the preparation remains within the skin's pH range, which is still acceptable. The gel preparation is homogeneous, with a qualified viscosity and good spreadability value. The values of viscosity and spreadability can be seen in Tables 6 and 7.

As *Garcinia dulcis* has a chromophore group that can absorb UV light, its structure has a conjugated aromatic system [32]. That results in a very strong antioxidant ability, which helps counteract free radicals caused by UV exposure. In addition, anti-elastase activity testing was carried out, showing strong activity. This demonstrates that mundu fruit extract has the potential to the prevention of self-aging due to its antioxidant and anti-elastase activities. After this, it was still demonstrated that the best formula had the highest extract concentration.

Formula 3 has a pH value close to the normal skin pH, precisely 5.40, and a wider spreadability compared to Formula 1 and Formula 2, with a coverage area of 4,419.64 mm^2. Antioxidant activity tests indicated that Formula 3 exhibited the best IC_{50} value at 66.26 µg/ml and anti-elastase activity at 111.48 µg/ml. The antioxidant activity was classified as strong, while the anti-elastase activity was moderate [23].

One of the primary factors contributing to skin aging is exposure to ultraviolet radiation (UVR). UVR can increase ROS production and inhibit the skin's natural antioxidant mechanisms, leading to the degradation of collagen and elastin. This results in skin structure and elasticity changes, which can lead to premature aging [33] antioxidants function by stabilizing and deactivating free radicals, which helps to inhibit or delay the oxidation process [34].

The gel serum derived from the mundu fruit also demonstrates anti-elastase activity. Elastase is an enzyme that breaks down elastin, a protein that maintains skin elasticity. Prolonged UV exposure can cause collagen and elastin damage in the dermis, ultimately leading to the formation of wrinkles and premature aging. This process also induces the production of matrix metalloproteinases (MMP) enzymes [35]. By inhibiting elastase activity, skin aging can be effectively prevented. So the gel serum extract

Tabel 7. Results of spreadability stability evaluation on serum gel preparation of mundu fruit extract

Formula	Spreadability (mm2) Time (Week)				
	0	1	2	3	4
Blank	2376.79	2828.57	3118,5	3422.57	3850
1	3422.57	3850	4419.64	4780.29	5283.14
2	3850	4419.64	4903.64	5544	6364.29
3	4419.64	5028.57	5676.79	6364.29	6795.64

demonstrates excellent activity on the skin, offering strong antioxidant and moderate anti-elastase properties that effectively protect against oxidative stress and premature aging.

Conclusion

In conclusion, Mundu fruit extract exhibits strong antioxidant and anti-elastase activities. The serum gel containing mundu fruit extract also showed strong antioxidant and moderate anti-elastase activities. This study found that a higher extract concentration in the serum gel resulted in better antioxidant and anti-elastase activity, as demonstrated by the F3 formulation (300xIC_{50} value). Furthermore, F3 displayed the best physical properties regarding pH, viscosity, and spreadability.

Conflict of Interest

The authors declare that they have no conflict of interest.

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References

[1]. Kciuk M, Marciniak B, Mojzych M, Kontek R. Focus on uv-induced dna damage and repair—disease relevance and protective strategies. Int J Mol Sci. 2020;21(19):1–33. https://doi.org/10.3390/ijms21197264

[2]. Salminen A, Kaarniranta K, Kauppinen A. Photoaging: UV radiation-induced inflammation and immunosuppression accelerate the aging process in the skin. Inflamm Res. 2022;71(7–8):817–31. https://doi.org/10.1007/s00011-022-01598-8

[3]. Papaemmanouil CD, Peña-garc J, Jes A, Kostagianni AD, Gerothanassis IP, Horacio P, et al. ANTIAGE-DB : A Database and Server for the Prediction of Anti-Aging Compounds Targeting Elastase , Hyaluronidase , and Tyrosinase. Antioxid MDPI. 2022;11:2268. https://doi.org/https://doi.org/10.3390/antiox11112268

[4]. Warraich U, Hussain F, Ur H, Kayani R. Aging - Oxidative stress , antioxidants and computational modeling. Heliyon. 2020;6(March):e04107. https://doi.org/10.1016/j.heliyon.2020.e04107

[5]. Firdausia RS, Sholehah K, Kurniasih I, Diani A, Rusmeilina R. Analisis Potensi Antioksidan Daun Kayu Bulan (Pisonia alba Span .) sebagai Agen Anti Penuaan DIni. Chim Nat Acta. 2023;11(1):22–8. https://doi.org/https://doi.org/10.24198/cna.v11.n1.43034

[6]. Mechchate H, Allam A El, Omari N El, Hachlafi N El, Shariati MA, Wilairatana P, et al. Vegetables and Their Bioactive Compounds as Anti-Aging Drugs. Molecules. 2022;27(7). https://doi.org/10.3390/molecules27072316

[7]. Samosir SR. Isolasi dan Identifikasi Senyawa Flavonid dari Daun Tumbuhan Mundu (Garcinia dulcis (Roxb) kurz). JIFI (Jurnal Ilm Farm Imelda). 2022;5(2):65–72. https://doi.org/10.52943/jifarmasi.v5i2.764

[8]. Sutaryono S, Budiman H, Styawan AA, Hidayati N, Ainus D. Formulasi Gel Hand Sanitizer Ekstrak Etanol Daun Murbei (Morus Alba L.). Urecol Journal Part D Appl Sci. 2021;1(1):17–24. https://doi.org/10.53017/ujas.37

[9]. Santosa D, Priya Haresmita P. Antioxidant Activity Determination Garcinia dulcis (Roxb.) Kurz, Blumeamollis (D.Don) Merr., Siegesbeckia orientalis L., AND Salvia riparia H.B.K which Collected from Taman Nasional Gunung Merapi using DPPH (2,2-diphenyl-1-PIKRIL-HIDRAZIL) and Thin Layer . Tradit Med J. 2015;20(1):2015.

[10]. Mardani-Ghahfarokhi A, Farhoosh R. Antioxidant activity and mechanism of inhibitory action of gentisic and α-resorcylic acids. Sci Rep. 2020;10(1):1–11. https://doi.org/10.1038/s41598-020-76620-2

[11]. Siti N, Ambarwati S. Garcinia dulcis and Garcinia forbesii King fruit peel extract : Secondary metabolite composition , antioxidant , and elastase inhibitory activity evaluation. J Adv Pharm Technol Res. 2024;15(1):8–12. https://doi.org/10.4103/japtr.japtr

[12]. Islamiyati R, Mugitasari D., Nafiah L., I.Jayanto. Uji Aktivitas Antioksidan Ekstrak Etil Asetat Daun Matoa Menggunakan Radikal Bebas DPPH (Difenilpikrilhidrazil). Pharmacon. 2024;13(2):611–8. https://doi.org/10.35799/pha.13.2024.55951

[13]. Lee KJ, Oh YC, Cho WK, Ma JY. Antioxidant and Anti-Inflammatory Activity Determination of One Hundred Kinds of Pure Chemical Compounds Using Offline and Online Screening HPLC Assay. Evidence-based Complement Altern Med. 2015;2015:2–13. https://doi.org/10.1155/2015/165457

[14]. Cano A, Maestre AB, Hernández-Ruiz J, Arnao MB. ABTS/TAC Methodology: Main Milestones and Recent Applications. Processes. 2023;11(1):2–10. https://doi.org/10.3390/pr11010185

[15]. Kim B, Cho H-E, Moon SH, Ahn H-J, Bae S, Cho H-D, et al. Transdermal delivery systems in cosmetics. Biomed Dermatology. 2020;4(1):1–12. https://doi.org/10.1186/s41702-020-0058-7

[16]. Maulina SN, Zebua NF, Salsabila D. Antioxidant Activity Testing of Garcinia mangostana L Skin Extract in Serum Preparation with DPPH Method. J Pharm Sci. 2022;5(2):372–80. https://doi.org/10.36490/journal-jps.com.v5i2.129

[17]. Wulan W, Yudistira A, Rotinsulu H. Uji Aktivitas Antioksidan dari Ekstrak Etanol Daun Mimosa pudica Linn. Menggunakan Metode DPPH. Pharmacon. 2019;8(1):106. https://doi.org/10.35799/pha.8.2019.29243

[18]. Shirzad M, Hamedi J, Motevaseli E, Modarressi MH. Anti-elastase and anti-collagenase potential of Lactobacilli exopolysaccharides on human fibroblast. Artif Cells, Nanomedicine Biotechnol. 2018;46(sup1):1051–61. https://doi.org/10.1080/21691401.2018.1443274

[19]. Nurrohim S, Harjanti R, Dewi Purnamasari NA. Formulasi dan Evaluasi Serum Anti-Aging Hesperetin dalam Sistem NLC (Nanostructured Lipid Carriers) dengan Metode Emulsifikasi-Sonikasi. Media Farm Indones. 2022;17(1):25–35. https://doi.org/10.53359/mfi.v17i1.195

[20]. Tungadi R, Sy. Pakaya M, D.as'ali PW. Formulasi dan Evaluasi Stabilitas Fisik Sediaan Krim Senyawa Astaxanthin. Indones J Pharm Educ. 2023;3(1):117–24. https://doi.org/10.37311/ijpe.v3i1.14612

[21]. Irianto IDK, Purwanto P, Mardan MT. Aktivitas Antibakteri dan Uji Sifat Fisik Sediaan Gel Dekokta Sirih Hijau (Piper betle L.) Sebagai Alternatif Pengobatan Mastitis Sapi. Majalah Farmaseutik. 2020;16(2):202. https://doi.org/10.22146/farmaseutik.v16i2.53793

[22]. Azizah Rauf A, Saranani S. Penetapan Kadar Polifenol Total Dan Tanin Total Dari Ekstrak Etanol Buah Senggani (melastoma malabathricum L.) Serta Uji Aktivitas Antioksidan Dengan Metode ABTS Determination Of Total Polyphenols And Total Tannins From The Ethanol Extract Of Senggani Fru. J Pharm Mandala Waluya. 2023;2(6):2829–6850. https://doi.org/https://doi.org/10.54883/jpmw.v2i6.60

[23]. Zamzani I. Limpasu Pericarpium : an Alternative Source of Antioxidant From Borneo with Sequential Maceration Method. J Kedokt dan Kesehat. 2021;15(1):61–8. https://doi.org/10.33533/jpm.v15i1.2820
[24]. Alinkina E, Don E, Gizitdinova O, Samsonova L, Petrova A, Stepanov G, et al. A novel technique for studying the effects of technologically processed antibodies by evaluating the rate of oxidation of ascorbic acid during the reduction of the green-blue ABTS + radical. Spectrochim Acta A Mol Biomol Spectrosc. 2024;5(304). https://doi.org/10.1016/j.saa.2023.123323
[25]. Swandiny GF, Desmiaty Y, Rahmah HU. Aktivitas Antioksidan dan Anti- aging dari Ekstrak Buah dan Daun Zodia (Evodia suaveolens J . R . Forst & G . Forst). J Jamu Indones. 2022;7(1):20–4. https://doi.org/https://doi.org/10.29244/jji.v7i1.169 Aktivitas
[26]. Zamzani I, Triadisti N. Limpasu Pericarpium : an Alternative Source of Antioxidant From Borneo with Sequential Maceration Method. J Profesi Med J Kedokt dan Kesehat. 2021;15(1):60–8. https://doi.org/10.33533/jpm.v15i1.2820
[27]. Sehgal A, Singh A. The influence of PH on skin ' s surface. J Pharm Negat Results. 2022;13(1):2012–23. https://doi.org/10.47750/pnr.2022.13.S01.236
[28]. Rohma D, Widyasanti A, Filianty F. Pengaruh Variasi Konsentrasi CMC Terhadap Sifat Fisikokimia Gel Pembersih Tangan dari Ekstrak Etanol Daun Mimba (Azadirachta Indica). Teknotan. 2021;15(2):75–80. https://doi.org/10.24198/jt.vol15n2.2
[29]. Tonthawi M, Musfiroh I. Review: Peningkatan Stabilitas Vitamin C dalam Sediaan Kosmetika. Majalah Farmasetika. 2023;8(3):194. https://doi.org/10.24198/mfarmasetika.v8i3.44462
[30]. Zothanpuli, R R, Selvakumar. a Review on Stability Testing Guidelines of Pharmaceutical Products. Asian J Pharm Clin Res. 2020;13(10):3–9. https://doi.org/10.22159/ajpcr.2020.v13i10.38848
[31]. Zam Zam AN, Musdalifah M. Formulasi dan Evaluasi Kestabilan Fisik Krim Ekstrak Biji Lada Hitam (Piper nigrum L.) Menggunakan Variasi Emulgator. J Syifa Sci Clin Res. 2022;4(2):304–13. https://doi.org/10.37311/jsscr.v4i2.14146
[32]. Salatiana S, Sayekti E, Gusrizal G. Aktivitas Tabir Surya Fraksi Metanol dari Daun Simpur (Dillenia indica Linn) dan Karakterisasi Senyawa Isolat. Indones J Pure Appl Chem. 2023;6(1):27. https://doi.org/10.26418/indonesian.v6i1.63085
[33]. He X, Gao X, Guo Y, Xie W. Research Progress on Bioactive Factors against Skin Aging. Int J Mol Sci. 2024;25(7):1–19. https://doi.org/10.3390/ijms25073797
[34]. Varesi A, Chirumbolo S, Campagnoli LIM, Pierella E, Piccini GB, Carrara A, et al. The Role of Antioxidants in the Interplay between Oxidative Stress and Senescence. Antioxidants. 2022;11(7):1–42. https://doi.org/10.3390/antiox11071224
[35]. Azmi N, Hashim P, Hashim DM, Halimoon N, Majid NMN. Anti elastase, Anti Tyrosinase and matrix metalloproteinase inhibitory activity of earthworm extracts as potential new anti aging agent. Asian Pac J Trop Biomed. 2014;4(Suppl 1):3–7. https://doi.org/10.12980/APJTB.4.2014C116.