Utilization of Kappaphycus alvareezii and Sargassum plagyophyllum from Banten as cosmetic creams

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Abstract. Kappaphycus alvareezii and Sargassum plagyophyllum are marine commodities from Banten, containing vitamin C, vitamin E and bioactive compounds (alkaloids, terpenoids, steroids, flavonoids, saponins, and tannins), which are thought to have antioxidant and tyrosinase enzyme inhibitory activities. The use of seaweed slurry is chosen because it is cheap, easy to apply and environmentally friendly. The aim of this research was to obtain the selected cream preparation based on antioxidant activity, tyrosinase inhibition and physical characteristics of cream preparation. K. alvareezii and S. plagyophyllum slurry had antioxidant activity (IC₅₀) 598.86±1.494 μg/mL and 595.08±0.995 μg/mL, respectively with L-ascorbic acid 6.56±0.069 μg/mL. The selected cream was formula adding combination slurry of K. alvareezii and S. plagyophyllum (1:1) 20% which had the highest antioxidant activity (IC₅₀) and percent inhibition of tyrosinase enzyme (L-DOPA substrate and 6,000 μg/mL test concentration) 370.44±0.854 μg/mL and 26.139±0.984%, respectively. Cream preparations showed good homogeneity, stable against storage of various temperatures, cycling test, and mechanics with no phase separation and discoloration and pH value of cream fulfilling the pH range of human skin balances and Indonesian National Standard (SNI). Cream preparations did not show significant changes in viscosity value until 8 weeks with the thixotropic plastic rheology.

Keywords: L-DOPA substrate, stability, thixotropic, viscosity

1. Introduction

Melanin pigment is a major defense mechanism against ultraviolet light and plays an important role in the prevention of sun-induced skin damages (Maack and Pegard 2016). However, considering that Indonesia is a tropical country with intense solar radiation, melanin production in the skin can be triggered so that it can cause hyperpigmentation. Melanin pigments are produced in melanocyte cells. Melanin formation (through browning reactions) in human skin occurs in the presence of a catalyst (a tyrosinase enzyme form) and UV light, which can lead to hyperpigmentation (Chang 2009). Tyrosinase enzymes catalyze two different reactions using oxygen: tyrosine hydroxylation to 3,4-dihydroxyphenylalanine or DOPA (o-diphenol) (monophenolase) and oxidation from DOPA to
dopaquinone (o-quinone) (diphenolase), before becoming eumelanin or pheomelanin (Chang and Ki 2004). The antioxidant and tyrosinase inhibitory mechanisms can be used as skin lightening agents by inhibiting the melanin formation process. The use of synthetic compounds has been banned by the Food and Drug Supervisory Agency because of their carcinogenic properties, irritation, and ochronosis. Therefore, it is necessary to use safer bioactive compounds.

Seaweed is an abundant quantity of marine commodities in Indonesia. The amount of seaweed that has been identified is 550 species, but the bioactive content of seaweed is not yet known. The bioactive compounds of seaweed have antioxidant activity and tyrosinase inhibition. One species from the Phaeophyta Division is *S. plagiophyllum*. Potency of extracts and seaweed slurry from *S. plagiophyllum* as a source of antioxidants have been reported by previous researchers (Nurjanah et al 2016, Nurjanah et al 2017, Diachanty et al 2017, Arifianti et al 2017, Dolorosa et al 2017, Gazali et al 2017, Gazali et al 2019). Brown seaweed *Sargassum* sp. contains vitamin C, vitamin E and bioactive compounds (Nurjanah et al 2017, and Dolorosa et al 2017), total phenolic content (Diachanty et al 2017), potential as a tyrosinase inhibitor (Arifianti et al 2017 and Dolorosa et al 2019) and anti-collagenase activity (Mansauda et al 2018). Seaweed can also be processed into seaweed salt extract that had antioxidant activity *K. alvarezi* (*E. cottonii*) is red seaweed that has bioactive compounds, vitamin C, vitamin E (Nurjanah et al 2017), total phenolic content (Nufus et al 2017) and potential as antioxidant activity and tyrosinase inhibitor (Chang and Teo 2016, Dolorosa et al 2019).

Seaweed is a plant producing hydrocolloid alginate (brown seaweed) and carrageenan (red seaweed). This hydrocolloid can be used as a stabilizer, thickener, gel maker, emulsifier and water binder which can be developed in the cosmetics field. Carrageenan shows the ability to spread and has the capacity to hold water so that is used as a moisturizer (Suparmi and Sahri 2009). The combination of brown and red seaweed has been used in cosmetic preparations that have antioxidant activity, antibacterial activity (Nurjanah et al 2018) and sunscreen (Pratama et al 2019). Based on data, the bioactive compounds and hydrocolloid contained in *K. alvarezi* and *S. plagiophyllum* make this type of seaweed potential to be developed as a natural raw material in making skin lightening creams.

Cosmetic manufacturing nowadays uses active extracts added to cosmetic preparations (e.g. cream preparations). The active extract is obtained from the extraction using a solvent that results in not being environmentally friendly and the product price is quite expensive. Research carried out using seaweed slurry. Seaweed slurry is obtained by mixing seaweed and deionized water so that it is safer, inexpensive and easy to apply. Slurry preparations used all raw materials by utilizing bioactive compounds and hydrocolloid.

2. Materials and methods

2.1. Materials

The main materials, used in this research, were two types of seaweed *S. plagiophyllum* and *K. alvarezi*. *K. alvarezi* was obtained from community cultivation results of Lontar village and *S. plagiophyllum* was obtained from Pasauran Coastal Waters with a depth of 1.5 to 3 m, Serang, Banten. Cream materials included Emulglade®, cethyl alcohol, liquid paraffin, stearic acid, triethanolamine (TEA), glycerin, butyl hydroxytoluene (BHT), nipagin, fragrance (aroma) and demineralized water. The instruments were the UV VIS spectrophotometer type 1601 (Shimadzu), microplate ELISA reader (EPOCH BioTek Instruments, VT 05404-0998), viscometer (Brookfield viscometer type V1-0325 HAT 200), digital penetrometer controller (Precision Scientific Petroleum Instruments with corn aluminum), centrifugation (Beckman models J2-21, 5000 rpm, temperature 4°C), glassware (Pyrex), blender (Philips), vortex (Stuart SA8 Vortex Mixer, 230V, 50-60Hz, 20-2500 rpm), analytical scales (Sartorius), digital scales (Tanita KD-160), oven (Memmert, Germany), pH meter type 510 (Eutech Instrument, Singapore) and instruments that support analysis.
2.2. Methods

2.2.1. Preparation of seaweed slurry. *K. alvarezi* was sun-dried until the moisture less than 30% while *S. plagyophyllum* was wind-dried for 5-6 days (Masduqi et al 2014) until the moisture reached 15%, so the sample can be stored for a long time. Identification of brown seaweed species was carried out by the Center for Oceanographic Research, Indonesian Institute of Sciences (LIPI) Ancol. Dried-seaweed raw materials of *K. alvarezi* and *S. plagyophyllum* were reduced in size by crumbling the seaweed using a dish meal tool, aiming to minimize the seaweed surface area (obtain the finer fibers by grinding the thallus of dried seaweed) and simplify the homogenization of seaweed slurry manufacturing (Dolorosa et al 2019). The next step was to sift using a 100 mesh sieve to obtain the powder. Calculation of seaweed powder yield was obtained by comparing the weight after and prior to size reduction and expressed in percentage form. A single seaweed slurry making was carried out by homogenizing seaweed powder and deionized water with a ratio of 1:4 (g/mL) for *S. plagyophyllum* and 1:8 (g/mL) for *K. alvarezi*. Homogenization used a blender for 3-5 minutes. The preparation of combined-seaweed slurry followed previous research (Nurjanah et al 2016). The combined-seaweed slurry of *K. alvarezi* and *S. plagyophyllum* 10%, 15% and 20% were made by weighing each single seaweed slurry with a ratio of 1:1 (*K. alvarezi* : *S. plagyophyllum*) (g/g) be 10%, 15%, and 20%.

2.2.2. Preparation of cream. The preparation of the cream followed previous research (Mishra et al 2014) with some modifications. Material cream dissolving in oil was mixed until homogeneous at a temperature ±75°C called by oil phase. Material cream dissolving in water were mixed until homogeneous at a temperature ±75°C called by liquid phase. The oil phase put into the liquid phase until a homogeneous base cream is formed (T±40°C). Seaweed slurry, BHT, nipagin and fragrance added into base cream (T±40°C).

2.2.3. Analysis of cream. Several analysis of cream included antioxidant activity (Blois 1958), tyrosinase inhibitory activity (Batubara et al 2010), physical evaluation of cream preparations like as consistency, viscosity, and rheology (Sinko and Singh 2011), homogeneity test (DEPKES RI 1995) and accelerated stability test (Cannel 1985, Budiman 2008).

2.2.4. Analysis of data. The experimental design used in this research was a Completely Randomized Design (CRD) in antioxidant and tyrosinase inhibitory activities using Statistical Tool for Agricultural Research (STAR) Nebula 2013 software. CRD in time was carried out for the value of viscosity and consistency at week-0 and 8 using the Statistical Analysis System (SAS) software type 9.4. CRD factorial in time was carried out for testing pH stability of creams every 2 weeks for 8 weeks using Statistical Analysis System (SAS) software type 9.4. Data were analyzed by variance and if it was significant (reject H0), it was further tested using Tukey test (Steel and Torrie 1989) with a confidence interval of 95%.

3. Results and discussion

3.1. Powder seaweed yields
Brown seaweed identification resulted by the Center for Oceanographic Research, Indonesian Institute of Sciences (LIPI) Ancol was confirmed as *S. plagyophyllum* (Mertens) J.G. Agardh. Powder yields of *K. alvarezi* and *S. plagyophyllum* were 15.05% and 20.08%, respectively. These results were higher than results from similar research reporting the *K. alvarezi* and *Sargassum* sp. yields from the manufacturing of powder using the same modification tool, followed by dry blender and sieve with 48 mesh size as being 8.33% and 7.94%, respectively (Chaidir 2006). *K. alvarezi* and *S. plagyophyllum* powders are shown in figure 1.
3.2. Antioxidant activity of the seaweed slurry and creams

The DPPH (1,1-diphenyl-2-picrylhydrazil) method was chosen because it is simple, easy, fast and sensitive and requires only a small number of samples (Hanani et al 2005). Color changes that occur due to a reaction between molecule 1,1-diphenyl-2-picrylhydrazyl (DPPH) with H atoms released by the molecule components of the test sample (antioxidant compounds) result in the compound 1,1-diphenyl-2-picrylhydrazine (DPPH) is formed in yellow (Biranti et al 2009). The antioxidant activity of seaweed slurry is expressed in IC\textsubscript{50} values. \textit{K. alvarezii} and \textit{S. plagyophyllum} slurry had antioxidant activity (IC\textsubscript{50}) 598.86±1.49 μg/mL and 595.08±1.00 μg/mL, respectively with L-ascorbic acid 6.56±0.07 μg/mL.

Variance analysis results showed that the treatment of \textit{K. alvarezii} and \textit{S. plagyophyllum} seaweed slurry addition with different concentrations had a significant effect on the antioxidant activity of creams expressed in IC\textsubscript{50} values (p<0.05). Several studies on the potential of combined-seaweed slurry added to cosmetic preparations had antioxidant activity including: cream with addition of \textit{Sargassum} sp. and \textit{K. alvarezii} (1:1) 10% 83.4 μg/mL; \textit{Padina australis} and \textit{K. alvarezii} (1:1) 10% 103.76 μg/mL (Maharani 2018); \textit{Sargassum} sp. and \textit{K. alvarezii} (1:1) 7% 185±0.02 mg/mL (Nurjanah et al 2019); \textit{K. alvarezii} and \textit{Kaempferia galanga} (zingiberaceae) (1:1) 30% 20.32±6.23 μg/mL (Pratama et al 2019); lip balm with addition of \textit{Sargassum} sp. and \textit{K. alvarezii} (1:1) 30% 576.41 μg/mL (Nurjanah et al 2018).

UV light exposure and oxidative stress can induce an increase in reactive oxygen species (ROS). ROS can increase melanin synthesis and melanocyte proliferation. Antioxidant acts as a ROS scavenger thereby reducing hyperpigmentation (Sugiharto et al 2012). Antioxidants mechanism as skin lightening is to inhibit the oxidation of tyrosine to dihydroxyphenylalanine (DOPA) and reduce free radicals in keratinocytes caused by ultraviolet exposure (Naidoo et al 2016). Antioxidant activity values of creams are shown in table 1.

3.3. Tyrosinase inhibitory activity of the creams

The tyrosinase inhibition test of the cream preparations at a concentration 6,000 μg/mL was carried out at a wavelength 475 nm, incubation time for 30 minutes, substrate concentration L-DOPA 2 mM, enzyme concentration 333 unit/mL, pH 6.5 and room temperature. The results of the analysis of variance showed that the treatment of \textit{K. alvarezii} and \textit{S. plagyophyllum} seaweed slurry addition with different concentrations had a significant effect on the tyrosinase inhibitory activity of creams expressed in percent inhibition (p<0.05). The higher the concentration of slurry added, the higher the tyrosinase inhibition percentage against L-DOPA. The IC\textsubscript{50} value (antioxidant) was inversely proportional to the percentage inhibition of the tyrosinase enzyme, this indicated that antioxidant activity increased with an increase in tyrosinase inhibition. Skin lightening agents are associated with antioxidant activity that can protect the skin against oxidative stress due to UV exposure which can cause skin irritation. Skin that is exposed to UV light will activate ROS. ROS can activate melanocytes to increase melanin production. The depigmentation mechanism of phenol (flavonoids) is that flavonoids can directly inhibit the activity of tyrosinase with an α-keto group which is almost similar to the dihydroxyphenyl group of DOPA (Sari et al 2019). Tyrosinase inhibition percentages of creams are shown in table 1.

![Figure 1. K. alvarezii (a) and S. plagyophyllum (b) powders.](image-url)
Table 1. Antioxidant and tyrosinase inhibitory activities values of creams.

| Cream formulation | Antioxidant activity (IC<sub>50</sub>) | Tyrosinase inhibition (%) |
|-------------------|--------------------------------------|---------------------------|
| K (control)       | 545.60±1.24<sup>a</sup>              | 11.46±0.09<sup>b</sup>    |
| A (S. plagyophyllum 15%) | 491.93±2.31<sup>c</sup>              | 20.00±4.65<sup>ab</sup>   |
| B (K. alvarezi 15%) | 502.47±3.33<sup>b</sup>              | 13.05±1.97<sup>b</sup>    |
| C (K. alvarezi and S. plagyophyllum 10%) | 423.35±2.32<sup>d</sup> | 3.64±3.28<sup>a</sup>    |
| D (K. alvarezi and S. plagyophyllum 15%) | 405.78±1.29<sup>c</sup> | 25.06±2.15<sup>a</sup>    |
| E (K. alvarezi and S. plagyophyllum 20%) | 370.44±0.85<sup>f</sup> | 26.14±0.98<sup>a</sup> |

3.4. Physical characteristics of the creams

3.4.1. Consistency. Consistency measurements were performed on creams stored at room temperature (week-0 and 8) using an aluminum cone-shaped penetrometer. The results of the variance analysis showed that the treatment of addition of K. alvarezi and S. plagyophyllum seaweed slurry with different concentrations, time and interaction of treatment with time had an effect on the consistency of creams. The addition of cetyl alcohol can affect the consistency of the creams. Cetyl alcohol can function as a thickener, stabilizer, and emulsifier. Cetyl alcohol application with a concentration of 2-10% and combined with liquid paraffin serves as a hardener (Erungan et al 2009). The consistency values of creams are shown in table 2.

3.4.2. Viscosity and rheology. Cream viscosity was measured with a Brookfield (HA) viscometer with spindle number 6 at a speed of 20 rpm (cream preparations K, A, C, D, and E) and spindle number 5 on cream preparation B. The results of the variance analysis showed that there was no significant difference between the viscosity at week 0 and 8 (sig = 0.1709) and was not significantly different among the interaction of the seaweed slurry addition treatment with time (sig = 0.4160). This showed that there was viscosity stability in cream preparations. Viscosity is influenced by several factors including mixing, stirring, surfactant selecting and thickening (Djayadisastra and Amin 2012). The viscosity values of creams are shown in table 2.

The rheology of each creams at week-0 and 8 did not change, remained a thixotropic plastic which indicated a decrease to the left of the ascending curve indicating the material had lower consistency in each rate of shares on a descending curve compared to an ascending curve, so that the viscosity decreased with the increasing rate of share. The rheology of cream preparations with the addition of Glycine max soybean extracts (2-8%) did not change until 8 weeks which were plastic thixotropic (Dewi et al 2014). Thixotropic is the expected rheology in pharmaceutical preparations, that is, with high consistency in the pot but can be poured and easily spread.

3.4.3 Homogeneity. The homogeneity test is one of the tests to look and know the mixing of cream ingredients by observing the color of the cream preparation and the absence of parts that are not mixed. The results of the examination on cream preparations had good homogeneity, did not change and there were no clods. The homogeneity test was performed on creams from Solanum torvum Swartz ethanol extract were made homogeny because there were no beads when rubbed on the hands (Wibowo et al 2017). The homogeneity observation of creams is shown in figure 2.

3.4.4 Accelerated stability test. Accelerated physical stability testing was carried out in three methods, namely storage of various temperatures, cycling, and centrifugal test. The results of the analysis of variance showed that the addition of slurry, the difference in temperature and duration of storage had a significant effect on the pH value of the creams (p<0.05). The results of the analysis of variance also showed a significant relation or interaction among the addition of seaweed slurry with temperature and...
time, temperature with time, and the interaction of the three (p<0.05). pH value of creams fulfilling the pH range of human skin balances 4.6-6.5 and Indonesian National Standard (SNI) 4.5-8 (BSN 1996). The pH value must not be too acidic, which can cause skin irritation (wrinkled skin). However, skin pH that is too alkaline can cause scaly skin. The pH of the whitening cream containing Artocarpus heterophyllus jackfruit bark extract 1.5% and 2% had a pH of 6.48 and 6.35 (pH towards the acid), this was caused by the extracted content in the form of weak acidic polyphenol compounds (Juwita et al 2013). Cream pH stability values are shown in table 2. The observation of cream preparations color on different temperatures for 8 weeks showed that the color tended to be stable with no discoloration. Cream K and B were white, cream A, C, D, and E were light brown.

**Table 2. Physical characteristic results of creams for 8 weeks.**

| Cream formulation | Consistency (mm/10g/5s) | Viscosity value (cps) | Range pH | Centrifugal results |
|-------------------|-------------------------|----------------------|----------|---------------------|
|                   | Week-0                  | Week-8               | Week-0   | Week-8              | 8 weeks |                     |
| K                 | 28.15±0.212             | 26.35±0.212          | 49500    | 48750               | 4±2°C→5.92-6.06 |
|                   |                         |                      | 27±2°C→5.92-6.12 |                    | 40±2°C→5.92-6.24 |
| A                 | 22.45±0.071             | 20.85±0.071          | 89800    | 88750               | 4±2°C→5.77-5.95 |
|                   |                         |                      | 27±2°C→5.78-6.03 |                    | 40±2°C→5.78-6.21 |
| B                 | 33.45±0.071             | 30.20±0.141          | 17900    | 17700               | 4±2°C→5.7-5.91 |
|                   |                         |                      | 27±2°C→5.71-5.99 |                    | 40±2°C→5.65-6.06 |
| C                 | 25.95±0.636             | 23.50±0.141          | 47000    | 46250               | 4±2°C→6.01-6.05 |
|                   |                         |                      | 27±2°C→6.01-6.07 |                    | 40±2°C→6.01-6.16 |
| D                 | 23.85±0.212             | 23.55±0.071          | 74300    | 73750               | 4±2°C→5.72-5.91 |
|                   |                         |                      | 27±2°C→5.72-5.93 |                    | 40±2°C→5.72-5.89 |
| E                 | 21.15±0.071             | 20.85±0.071          | 74500    | 73750               | 4±2°C→5.61-6.05 |
|                   |                         |                      | 27±2°C→5.61-6.15 |                    | 40±2°C→5.61-6.26 |

**Figure 2.** Homogeneity observation of creams.

Cyclic testing was carried out with two different temperatures, namely at low temperatures 4±2°C and high temperatures 40±2°C during 6 cycles (12 days). The normal effect of storing an emulsion at higher temperatures is the accelerating coalescence and creaming and at lower temperatures is the viscosity changes. The results of the cycling test showed no phase separation in the emulsion cream preparations,
no crystallization occurred and no discoloration or odor. This showed that substances acted as emulsifiers (surfactants) can combine the two phases well so that they were homogeneous and stable. This study used a ratio of stearic acid and TEA (4:1), with an initial pH range of 5.61-6.02 and a final pH of 5.88-6.24 which fulfilled in the normal pH range of the skin. The use of anionic emulsifiers (TEA and stearic acid) in a ratio of 1:5 provided better cream stability against stress conditions compared to the use of nonionic emulsifiers (Tween 60 and Span 60) with no creaming formed (Nonci et al 2016). Surfactants reduced tension interfaces between phases, thus increasing the emulsification process during mixing (DEPKES RI 1995). The interface tension reduction is important in the homogenization process because it will result in the breakdown of the emulsion to be a smaller size droplet and prevents droplets from aggregation (Estiasih et al 2016). The cycling test observation of creams is shown in figure 3.

Centrifugation testing or mechanical testing was carried out by rotating using centrifugation with a speed of 5,000 rpm for 30 minutes with temperature regulation of 4°C. Mechanical tests are used as an indicator of the physical stability of semisolid cosmetic preparations against the gravity rotation (Setiawan 2010). The cream that is stored will obtain the gravity force and according to Stokes law, the force will affect the stability of cream. The centrifugal force is considered equivalent to the gravitational force received by the cream during a year of storage. There was no phase separation between the dispersed phase and dispersion one and discoloration of six cream preparations. The results indicated the six cream preparations were stable to the effects of gravity and assumed the shelf life of cream preparations for one year. The results of mechanical tests are shown in figure 4.

![Figure 3. Cycling test observation of creams.](image3)

![Figure 4. Observation of creams after a centrifugal test.](image4)
4. Conclusion

The selected cream was formula adding combination slurry of K. alvarezii and S. plagyophyllum (1:1) 20% which had the highest antioxidant activity (IC50) and percent inhibition of tyrosinase enzyme (L-DOPA substrate and 6,000 μg/mL test concentration) 370.44±0.854 μg/mL and 26.139±0.984%, respectively. Cream preparations showed good homogeneity; stable against the storage of various temperatures, cycling test, and mechanics with no phase separation and discoloration and pH value of cream fulfilling the pH range of human skin balances and Indonesian National Standard (SNI). Cream preparations did not show significant changes in viscosity value until 8 weeks with the thixotropic plastic rheology.

References

Arifianti A E, Anwar E and Nurjanah 2017 Aktivitas penghambatan tirosinase dan antioksidan serbuk rumput laut dari Sargassum plagyophyllum segar dan kering JPHPI 20 488-493
Batubara I, Darusman L K, Mitsunaga T, Rahminiwati M and Dja’hari E 2010 Potency of Indonesian medicinal plants as tyrosinase inhibitor and antioxidant agent J. Bio. Scie. 10 138-144
Blois M S 1958 Antioxidant Determinations by The Use of a Stable Free Radical (Nature)
Biranti F, Nursid M and Cahyono B 2009 Analisis kuantitatif B-karoten dan uji aktivitas karotenoid dalam alga cokelat Turbinaria decurrens J. Sains & Mat. 17 98-104
Budiman M H 2008 Uji stabilitas fisik dan aktivitas antioksidan sediaan krim yang mengandung ekstrak kering tomat (Solanum lycopersicum L.) [Undergraduate thesis] (Depok: University of Indonesia)

BSN 1996 Sediaan Tabir Surya (Jakarta: Badan Standardisasi Nasional)
Cannel J S 1985 Fundamentals of stability testing Int. J. Cos. Sci. 7 291-303
Chaidir A 2006 Kajian rumput laut sebagai sumber serat alternatif untuk minuman berserat [Thesis] (Bogor: IPB University)
Chang T 2009 An updated review of tyrosinase inhibitor Intern. J. of Mol. Scie. 10 2440-2475
Chang H J and Ki H S 2004 Tyrosinase inhibitor isolated from the leaves of Zanthoxylum piperitum Biosci. Biotechnol. Biochem. 68 1984-1987
Chang V S and Teo S S 2016 Evaluation of heavy metal, antioxidant and anti-tyrosinase activities of red seaweed (Eucheuma cottonii) IFRI 23 2370-2373
Dewi R, Anwar E and Yunita K S 2014 Uji stabilitas fisik formula krim yang mengandung ekstrak kacang kedelai (Glycine max) Pharm. Sci. Res. 1 194-208
Diachanty S, Nurjanah and Abdullah A 2017 Aktivitas antioksidan berbagai jenis rumput laut cokelat dari Perairan Kepulauan Seribu JPHPI 20 305-318
Dolorosa M T, Nurjanah, Purwaningsih S, Anwar E and Hidayat T 2017 Kandungan senyawa bioaktif bubur rumput laut Sargassum plagyophyllum dan Eucheuma cottonii sebagai bahan baku krim penceralah kulit JPHPI 20 633-644
Dolorosa M T, Nurjanah, Purwaningsih S, Anwar E and Hidayat T 2019 Tyrosinase inhibitory activity of Sargassum plagyophyllum and Eucheuma cottonii methanol extracts IOP Conf. Ser.: Earth Environ. Sci. 278 012020
DEPKES RI Departemen Kesehatan Republik Indonesia 1995 Farmakope Indonesia Ed ke-4 (Jakarta: Departemen Kesehatan Republik Indonesia)
Erungan A C, Purwaningsih S and Anita S B 2009 Aplikasi karagenan dalam pembuatan skin lotion JPHPI 12 128-143
Estiasih T, Harijono, Waziroh E and Fibrianto K 2016 Kimia dan Fisik Pangan (Jakarta: Bumi Aksara)

Gazali M, Nurjanah and Zamani N P 2018 Eksplorasi senyawa bioaktif alga cokelat Sargassum sp. Agardh sebagai antioksidan dari Pesisir Barat Aceh JPHPI 21 167-178
Gazali M, Zamani NP, Nurjanah 2019 The potency of green algae Chaetomorpha crassa Agardh as antioxidant agent from the coastal of Lhok Bubon, West Aceh. IOP Conf. Series: Earth and
Environmental Science 278 (2020) 012029
Hanani E, Munim A and Sekarini R 2005 Identifikasi senyawa antioksidan dalam Spons Cllyspongia sp. dari Kepulauan Seribu Majalah Kefarmasian 2 127-133
Juwita N K, Djajadisastra J and Azizahwati 2013 Uji penghambatan tirosinase dan stabilitas fisik sedienan krim penuhih yang mengandung ekstrak kulit batang nangka (Artocarpus heterophyllus) Majalah Ilmu Kefarmasian 8 57-124
Maack A and Pegard A 2016 Populus nigra (Salicaceae) absolute rich in phenolic acids, phenylpropanoids and flavonoids as a new potent tyrosinase inhibitor Fitoterapia 111 95-101
Maharany F 2018 Karakteristik krim tabir surya dari bubur rumput laut Padina australis dan Eucheuma cottonii [Thesis] (Bogor: IPB University)
Maharany F, Nurjanah, Suwandi R, Anwar and Hidayat T 2017 Kerundangan senyawa bioaktif rumput laut Padina australis dan Eucheuma cottonii sebagai bahan baku krim tabir surya JPHPI 20 10-17
Mansauda K L R, Anwar E and Nurhayati T 2018 Antioxidant and anti-collagenase activity of Sargassum plagiophyllum extract as an anti-wrinkle cosmetics ingredient Pharmacog. J. 10 932-936
Mishra A P, Saklani S, Milella L and Tiwari P 2014 Formulation and evaluation of herbal antioxidant face cream of Nardostachys jatamansi collected from Indian Himalayan region Asian Pac. J. Trop. Biomed. 4 679-682
Naidoo L, Khoza N and Dloma N C 2016 A fairer face, a fairer tommorrow? A review of skin lighteners Cosmetics 3 1-11
Nonci F Y, Tahar N and Aini Q 2016 Formulasi dan uji stabilitas fisik krim susu kuda Sumbawa dengan emulgator nononik dan anionik J FIK UINAM. 4 169-178
Nufus C, Abdullah A and Nurjanah 2019 Characteristics of green seaweed salt as alternative salt for hypertensive patients IOP Conf. Ser.: Earth Environ. Sci. 278 012050
Nurjanah, Nurilmala M, Hidayat T and Sudirdjo F 2016 Characteristics of Seaweed as Raw Materials for Cosmetics Aquat. Procedia 7 177-180
Nurjanah, Nurilmala M, Anwar E and Hidayat T 2016 Rasio bubur rumput laut Eucheuma cottonii dan Sargassum sp. sebagai formula krim tabir surya JPHPI 19 183-195
Nurjanah, Nurilmala M, Anwar E, Luthfiyana N and Hidayat T 2017 Identification of bioactive compounds of seaweed Sargassum sp. and Eucheuma cottonii Doty as a raw sunscreen cream Proceed. of Pakistan Academy of Sci. B. Life and Environ. Sci. 54 311-318
Nurjanah, Abdullah A and Nufus C 2018 Karakteristik sedienan garam Ulva lactuca dari Perairan Sekotong Nusa Tenggara Barat bagi pasien hipertensi JPHPI 21 109-117
Nurjanah, Luthfiyana N, Hidayat T, Nurilmala M and Anwar E 2019 Utilization of seaweed porridge Sargassum sp. and Eucheuma cottonii as cosmetic in protecting skin IOP Conf. Ser.: Earth Environ. Sci. 278 012055
Nurjanah, Abdullah A, Fachrozan R and Hidayat T 2018 Characteristics of seaweed porridge Sargassum sp. and Eucheuma cottonii as raw materials for lip balm IOP Conf. Ser. Earth. Environ. Sci. 196
Nurjanah, Aprilia B E, Fransiskayana A, Rahmawati M and Nurhayati T 2018 Senyawa bioaktif rumput laut dan ampas teh sebagai antibakteri dalam formula masker wajah JPHPI 21 304-316
Pratama G, Yauantari R, Ilhamdy A F and Suhana M P 2019 Formulation of sunscreen cream from Eucheuma cottonii and Kaempferia galanga (zingiberaceae) IOP Conf. Ser.: Earth Environ. Sci. 278 012062
Sari D M, Anwar E, Nurjanah and Arifianti A E 2019 Antioxidant and tyrosinase inhibitor activities of ethanol extracts of brown seaweed (Turbinaria conoides) as lightening ingredient Pharmacog. J. 11 379-382
Setiawan T 2010 Uji stabilitas fisik dan penentuan nilai SPF krim tabir surya yang mengandung ekstrak daun teh bijau (Camellia sinensis L.), otkit metoksisinamat dan titanium dioksida [Undergraduate Thesis] (Depok: University of Indonesia)
Sinko P J and Singh Y 2011 Martin’s Physical Pharmacy and Pharmaceutical Science Ed ke-6 (Baltimore: Lippincott Williams and Wilkins)
Steel R G D and Torrie J H 1989 *Prinsip dan Prosedur Statistika* trans. Sumantri B (Jakarta: Gramedia Pustaka Utama)

Sugiharto, Ariff A, Ahmad S and Hamid M 2012 Efektivitas kurkumin sebagai antioksidan dan inhibitor melanin pada kultur sel B16-F1 *Berk. Penel. Hayati* 17 173-176

Suparmi and Sahri A 2009 Mengenal potensi rumput laut : kajian pemanfaatan sumber daya rumput laut dari aspek industri dan kesehatan *Sultan Agung XLIV* 118 95-116

Wibowo S A, Budiman A and Hartanti D 2017 Formulasi dan aktivitas anti jamur sediaan krim M/A ekstrak etanol buah takokak (*Solanum torvum* Swartz) terhadap *Candida albicans* *JRST* 1 15-21

Yanuarti R, Nurjanah, Anwar E and Hidayat T 2017 Profil fenolik dan aktivitas antioksidan dari ekstrak rumput laut *Turbinaria conoides* dan *Eucheuma cottonii* *JPHPI* 20 230-237