cosmetics

MDPI

Article

Formulation and Physicochemical Evaluation of Green Cosmeceutical Herbal Face Cream Containing Standardized Mangosteen Peel Extract

Puay Luan Tan *, Mogana Rajagopal *, Sasikala Chinnappan, Malarvili Selvaraja *, Mun Yee Leong, Lee Fang Tan and Vi Lien Yap

Faculty of Pharmaceutical Sciences, UCSI University, UCSI Heights 1, Jalan Puncak Menara Gading, Taman Connaught, Cheras, Kuala Lumpur 56000, Malaysia; sasikala@ucsiuniversity.edu.my (S.C.); 1001540110@ucsiuniversity.edu.my (M.Y.L.); 1001747603@ucsiuniversity.edu.my (L.F.T.); 1001748119@ucsiuniversity.edu.my (V.L.Y.)

* Correspondence: 1001645248@ucsiuniversity.edu.my (P.L.T.); mogana@ucsiuniversity.edu.my (M.R.); malarvili@ucsiuniversity.edu.my (M.S.)

Abstract: The widely reported adverse effects of synthetic ingredients encourage the development of green cosmeceuticals to achieve Sustainable Development Goal (SDG) 3. The waste product of mangosteen (mangosteen peel) was utilized in the formulation to reduce waste production corresponding to SDG 12, in addition to its anti-aging and pigmentation control effects. This study aimed to formulate and evaluate novel herbal face creams containing standardized mangosteen peel extract. The mangosteen creams were formulated using natural ingredients and were evaluated for their organoleptic characteristics, rheology, spreadability and pH. Furthermore, an accelerated stability study, freeze–thaw stability study and centrifugation test were conducted. In addition, 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical scavenging assays were conducted to assess its antioxidant effects, whereas tyrosinase inhibitory assay was conducted to determine its anti-tyrosinase activity. The formulated creams appeared light yellowish-brown and homogenous without phase separation. The creams displayed shear-thinning behavior and optimal pH which was ideal for topical application. The creams were stable after being subjected to various stability tests and were shown to have antioxidant and anti-tyrosinase activity. In conclusion, the development of mangosteen-based green cosmeceutical face cream is in line with SDG 3 and 12. It is expected to be used as a safe and effective alternative to synthetic products.

Keywords: mangosteen; *Garcinia mangostana*; cream; anti-aging; whitening; pigmentation control; green cosmeceutical; sustainable development

Citation: Tan, P.L.; Rajagopal, M.; Chinnappan, S.; Selvaraja, M.; Leong, M.Y.; Tan, L.F.; Yap, V.L. Formulation and Physicochemical Evaluation of Green Cosmeceutical Herbal Face Cream Containing Standardized Mangosteen Peel Extract. *Cosmetics* **2022**, *9*, 46. https://doi.org/10.3390/cosmetics9030046

Academic Editor: Enzo Berardesca

Received: 17 February 2022
Accepted: 22 March 2022
Published: 27 April 2022

1. Introduction

Skin is the largest organ in humans and one that plays a role in protection, regulation and sensation. It is the first line of defense against microorganisms, chemicals and radiations [1]. However, aging, genetics and environmental factors such as ultraviolet radiation, infection, smoking and other air pollutants cause skin aging [2,3]. Among these, exposure to ultraviolet radiation contributes to 80% of skin aging cases. Skin aging is defined as the accumulation of molecular damages over time and can be explained by the micro-inflammatory model developed by Giacomoni et al. [4]. Clinical manifestation of skin aging includes reduced elasticity, sagging of the dermis and wrinkle formation.

Skin aging occurs when the generation of free radicals exceeds the antioxidative activity at the target site. Hence, topical antioxidants work by inhibiting free radical-mediated cellular damage pathways, eliminating oxidative stress and stimulating DNA repair [5]. For instance, retinoids such as tretinoin and tazarotene are commonly used as antioxidants in the cosmetics field. However, topical application of retinoids is reported to

cause skin itchiness, redness and scaling [6]. Furthermore, the limitation to sun exposure is vital due to its photosensitive features. The use of retinoids is also contraindicated in pregnant women due to their teratogenicity.

On the other hand, melanogenesis causes skin pigmentation. In general, skin pigmentation helps to protect our skin from detrimental ultraviolet irradiation. However, a high level of melanin leads to melasma, skin cancer, DNA damage and gene mutation. Since tyrosinase is the key enzyme in melanogenesis, the role of tyrosinase inhibitor is crucial to inhibit melanogenesis. For instance, hydroquinone, arbutin, kojic acid and azelaic acid are well known in the market as tyrosinase inhibitors. However, the chronic use of hydroquinone is carcinogenic and causes ochronosis and nail discoloration. Furthermore, skin whitening agents such as mercury are strictly banned due to the risk of nephrotoxicity, skin rashes, mental disorder and skin discoloration [7].

Moreover, synthetic ingredients such as Sodium Lauryl Sulphate (SLS), parabens, sulfides and alcohol cause skin dryness and irritation. The widely reported adverse effects of synthetic ingredients encourage the development of green cosmeceuticals to achieve Sustainable Development Goal (SDG) 3: Good Health and Well-being. Green cosmeceuticals are defined as 'products that will not pollute the earth or deplete natural resources and can be recycled or conserved' [8]. Green cosmeceuticals are safer, less toxic and environmentally friendly. The sustainability of green cosmeceuticals is achieved by the use of natural resources and reusable packaging materials [9]. Furthermore, the production of green cosmeceuticals requires less consumption of water, material and energy [10]. Besides, the manufacturing of green cosmeceuticals helps to reduce waste production and the cost of manufacturing in addition to its ecological, economic and social benefits [11]. The knowledge about biotechnology, chemistry, pharmaceutical technology and toxicology is becoming increasingly important to optimize the features of green cosmeceuticals [12]. For instance, the emerging use of nanotechnology in the cosmetic field provides targeted or controlled action. Moreover, nanocosmetics improve the efficacy, dispersibility, quality and texture of the final product [13]. However, the application of nanotechnology in green cosmeceuticals is not well studied.

Mangosteen (*Garcinia mangostana*) is mainly cultivated in Southeast Asia. However, it is being consumed worldwide due to its sweet and juicy texture. It is one of the major tropical fruits in Malaysia. Thus, the 9th Malaysia Development Plan (2006–2010) emphasized the importance of mangosteen for the domestic and export market [14]. The whole fruit consists of the outer pericarp, inner pericarp, flesh and cap. The food industry processes the mangosteen to obtain their fruit juices, concentrates and dried fruits. At the same time, the remaining waste of the mangosteen, such as peel, leads to environmental issues [15]. The potential use of mangosteen peel in the medical field is extensively studied. It was proven to have antimicrobial, antidiabetic, anticancer, antihistamine and anti-inflammatory activity [16]. Moreover, mangosteen peel extract was found to have anti-motility and anti-spasmodic effects, which are beneficial for the treatment of diarrhea [17]. The medicinal benefits of mangosteen peel extract are attributed to the presence of α-mangostin, γ-mangostin, gartanin, garcinone E, garcixanthones B and garcixanthones C [18]. In this study, novel herbal face creams were formulated with natural ingredients without the incorporation of synthetic ingredients. Mangosteen peel was utilized in the formulation to reduce waste production corresponding to SDG 12: Responsible Consumption and Production, in addition to its anti-aging, anti-wrinkle and pigmentation control effects. Polyphenols present in mangosteen peel extract demonstrate antioxidant properties that inhibit the production of advanced glycation end products. Consequently, improvement in skin elasticity and skin hydration is observed [19–21]. Natural antioxidants derived from natural sources such as mangosteen peel are preferable to synthetic antioxidants due to the undesirable side effects of synthetic antioxidants. Hence, the objective of this study is to formulate and evaluate novel herbal face creams containing mangosteen peel extract that was standardized to 10% α-mangostin.

2. Materials and Methods

2.1. Materials

Mangosteen peel extract standardized to 10% α-mangostin (multiple extraction; extracting solvent: ethanol) was purchased from Chemtron Biotechnology Sdn. Bhd. (Kuala Lumpur, Malaysia). Certified pure organic refined shea butter, organic aloe vera gel, vegetable glycerine solution, hyaluronic acid solution (big molecular weight) and rose geranium essential oil were purchased from Iko Nature Sdn. Bhd (Seremban, Malaysia). D-panthenol (USP Grade), baby powder fragrance oil and Olivem 1000 were purchased from Future Food (Selangor, Malaysia). Refined avocado oil and Optiphen BD were purchased from The Soap Cellar Sdn. Bhd. (Penang, Malaysia). Additionally, 2,2-Diphenyl-1-picrylhydrazyl (DPPH), 2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and tyrosinase inhibitor screening kit (Catalog number: MAK257) were purchased from Sigma Aldrich, United States. Methanol for analysis of EMSURE® ACS and dimethyl sulfoxide for analysis of EMSURE® ACS were purchased from Merck, Germany. Ethanol 95%, denatured, ChemAR was purchased from Systerm, Malaysia. Potassium persulphate was purchased from Kollin Chemicals. Sail brand microscope slides, glass beaker, mortar and pestle, amber glass container, Eppendorf multichannel pipettes, pipette tips, 96-well flat-bottom clear microtiter plate and reagent reservoir were available at the research institution.

2.2. Equipments

Equipments included an analytical balance (AB204-S, Mettler Toledo, Switzerland), waterbath (WB14, Memmert, Schwabach, Germany), Young Ji homogenizer (HMZ-20DN, Hana Instruments, Korea), Discovery Series Hybrid Rheometer (DHR-2, TA Instruments, New Castle, Delaware), pH meter (CyberScan PC300, Eutech Instruments, Singapore), 100 g and 200 g calibration weight (Mettler Toledo, Switzerland), humidity chamber (M200, Capromax Sdn. Bhd., Selangor, Malaysia), Heraeus Labofuge 400 R Centrifuge (Thermo Scientific, Germany) and microplate reader (FLUOstar Omega, BMG Labtech, Germany).

2.3. Physical Compatibility Test

Physical compatibility of mangosteen peel extract with excipients was determined before the formulation of creams. Mangosteen peel extract was mixed with each excipient in a 1:1 ratio using mortar and pestle for five minutes. Then, the mixtures were transferred into separate vials and kept in a stability chamber at 40 °C and 75% relative humidity (RH). The mixtures were observed initially and weekly for any color or physical changes such as changes in texture, homogeneity, odor or phase separation for one month [22–24]. A 1:1 ratio was used to maximize the probability of interactions between mangosteen peel extract and excipients [25].

2.4. Formulation of Cream Bases

The cream bases were formed by mixing the oil phase, water phase, actives and excipients, as shown in Table 1, without incorporation of mangosteen peel extract. First, the ingredients of the oil phase were weighted in beaker A, whereas the ingredients of the water phase were weighted in beaker B. Both beakers were heated to 75 °C over a water bath. Then, the water phase was added into the oil phase gradually and mixed at 2000 rpm for 15 min using Young Ji homogenizer (HMZ-20DN, Hana Instruments, Korea) [26]. D-panthenol, hyaluronic acid solution and excipients were weighted and added at 35–40 °C due to their heat sensitivity and volatility. The speed of the homogenizer was subsequently reduced to 1000 rpm for five minutes and further reduced to 500 rpm for another five minutes [26].

Table 1. Formulation of mangosteen creams.

Composition	Quantity for 100 g (%)	
	Male Cream (M1)	**Female Cream (F1)**
Actives		
Mangosteen peel extract (10% α-mangostin)	0.5	0.5
D-panthenol (USP Grade)	3	3
Hyaluronic acid solution	2	2
Excipients		
Optiphen BD	0.3	0.3
Baby powder fragrance oil	0.1	-
Rose geranium essential oil	-	0.1
Oil phase		
Refined shea butter	10	10
Refined avocado oil	8	8
Olivem 1000	3	3
Water phase		
Organic aloe vera gel	24	24
Vegetable glycerine solution	5	5
Distilled water	q.s. to 100 g	q.s. to 100 g

2.5. Formulation of Mangosteen Creams

Mangosteen peel extract was weighed and incorporated into the cream bases by trituration in mortar and pestle. Trituration was continued until a uniform cream was obtained, as shown in Figure 1. Male (M1) and female (F1) mangosteen cream were packaged in an amber glass container and kept at room temperature for further analysis.

Figure 1. Formulation of mangosteen cream.

2.6. Organoleptic Characteristics

The formulated creams were observed for physical appearance, color, texture, phase separation, homogeneity and odor [27]. A small amount of cream was pressed between the thumb and index finger to check for the consistency and presence of coarse particles. In addition, the stiffness, grittiness and greasiness of the creams upon application were evaluated [28].

2.7. Determination of Type of Cream (Dilution Test)

The creams were diluted with water. Oil in water (o/w) type cream shows good miscibility with water, whereas water in oil (w/o) type cream shows poor miscibility with water [29].

2.8. Washability

A total of 0.1 g of the cream was applied to the skin and washed under running tap water with minimal force [30]. Good washability of the cream is demonstrated when the applied cream is easily removed from the area of application, leaving a non-greasy skin surface.

2.9. Rheology

The viscosity of creams was measured using Discovery Series Hybrid Rheometer (DHR-2, TA Instruments, New Castle, Delaware) at 25 °C, over a shear rate of 0.5–100 s^{-1}. The cream was placed between a parallel plate of 40 mm diameter [31]. The graph of shear stress (Pa) vs. shear rate (s^{-1}) and viscosity (Pa.s) vs. shear rate (s^{-1}) was plotted.

2.10. Spreadability

A total of 0.5 g of the cream was measured and placed within a 1 cm diameter circle which was previously marked on the center of the glass slide. Another glass slide was placed on the cream. A series of weights (100 g and 200 g) was allowed to rest on the upper glass slide for two minutes at room temperature (25 °C) [32]. The diameter of the spread of the cream (cm) was measured in triplicate to obtain the average diameter of spread ± standard deviation (SD) [33]. Spreadability was assessed initially and monthly for three months [34].

2.11. pH Determination

The pH meter was calibrated with pH 4, 7 and 10 standard buffers before use. A total of 10% w/v of the cream suspension was prepared for pH measurement at room temperature (25 °C). The pH measurement was repeated in triplicate to obtain the average pH ± SD of the cream suspension [33]. pH was measured initially and monthly for three months [34].

2.12. Accelerated Stability Study

The creams were filled into amber glass containers and covered with aluminum foil for light protection. According to ICH guidelines, accelerated stability study was conducted at 40 ± 2 °C and 75 ± 5% RH in the stability chamber for three months [35,36]. Organoleptic characteristics (color, texture, odor, phase separation), spreadability and pH of the creams were observed initially and monthly thereafter [36].

2.13. Freeze–Thaw Stability

A total of 2 g of the cream were weighed and filled into several vials before being subjected to the freeze–thaw cycle [37]. The creams were stored at −20 °C for 48 h, then thawed at room temperature (25 °C) for another 48 h. The freeze–thaw was repeated for three cycles. Physical stability, pH and spreadability of the cream were observed initially and after the completion of each freeze–thaw cycle [37].

2.14. Centrifugation Test

The centrifugation test was conducted at zero, one, two and three months of storage at 40 ± 2 °C and 75 ± 5% RH. A total of 2 g of the cream was centrifuged at 25 °C and 5000× g rpm for two runs of 10 min. The stability, phase separation and appearance of the cream after centrifugation were observed after each run [38,39]. The percentage of emulsion stability was calculated according to Equation (1) [40].

$$\text{Emulsion stability } (\%) = \frac{\text{Height of emulsion separation}}{\text{Total height of emulsion}} \times 100\% \quad (1)$$

2.15. 2,2-Diphenyl-1-picrylhydrazyl (DPPH) Radical Scavenging Assay

DPPH radical scavenging assay was conducted according to the method previously described by Mogana et al. [41]. Mangosteen peel extract, hyaluronic acid, panthenol and mangosteen cream were tested for their antioxidant capacity. The stock solution of test samples was prepared in a suitable solvent (DMSO or distilled water). In a 96-well microtiter plate, 100 µL of various concentrations of test samples were plated out in triplicate. Then, 100 µL of 0.1 mM DPPH solution was added to the test samples, whereas 100 µL of methanol was added as the control of the test samples. The plate was covered with aluminum foil

for light protection, shaken for 2 min and incubated for 30 min in the dark. The percentage decolorization was obtained spectrophotometrically at 550 nm.

A graph of percentage decolorization against the concentration of the test samples was plotted. Prism 9 software was used to determine the EC_{50} values of the test samples. DPPH radical scavenging activity increases with the reduction in DPPH absorbance. The percentage of DPPH radical scavenging activity was calculated according to Equation (2) [41].

$$\text{DPPH radical scavenging activity } (\%) = \frac{\text{Abs control} - \text{Abs sample}}{\text{Abs control}} \times 100 \quad (2)$$

where Abs control is the absorbance of DPPH radical without test samples; Abs sample is the absorbance of DPPH radical + test samples.

2.16. 2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) Assay

ABTS assay was conducted according to the method previously described by Mogana et al. [41]. First, 7 mM of ABTS solution (180 mg ABTS in 50 mL purified water) and 2.4 mM potassium persulfate solution (32.4 mg in 50 mL purified water) were prepared and mixed in a 1:1 ratio to form the working solution. The working solution was kept in dark for 12–16 h before use and was stable for 2–3 days in the dark. This solution was diluted with 95% ethanol to obtain the absorbance of 0.70 ± 0.01 at 734 nm before conducting the assay. Briefly, 100 µL of test samples at various concentrations were plated out in triplicate in a 96-well microtiter plate. Then, 100 µL of ABTS●+ solution was added to the test samples to determine their antioxidant capacity. For the negative control, 95% ethanol was used. The solutions were incubated at 37 °C for 7 min, after which the absorbance was read at 734 nm. A graph of percentage decolorization against the concentration of the test samples was plotted. Prism 9 software was used to determine the EC_{50} values of the test samples. The percentage of ABTS radical scavenging activity was calculated according to Equation (3) [41].

$$\text{ABTS radical scavenging activity } (\%) = \frac{\text{Abs control} - \text{Abs sample}}{\text{Abs control}} \times 100 \quad (3)$$

where Abs control is the absorbance of ABTS radical without test samples; Abs sample is the absorbance of ABTS radical + test samples.

2.17. Tyrosinase Inhibitory Assay

Tyrosinase inhibitory activity was determined using a tyrosinase inhibitor screening kit (Catalog number: MAK257) from Sigma Aldrich, United States. Mangosteen peel extract was dissolved in dimethyl sulfoxide (DMSO) and diluted to five times concentration using tyrosinase assay buffer. The concentration of mangosteen peel extract was ranged from 0.625 µg/mL to 10 µg/mL. Kojic acid (0.67 µg/mL to 10.66 µg/mL) was used as the positive control. Then, 20 µL of diluted mangosteen peel extract (S), diluted positive control (P), tyrosinase assay buffer (EC) or DMSO (SC) was plated out in duplicate in a 96-well microtiter plate. Next, 50 µL of tyrosinase enzyme solution (48 µL tyrosinase assay buffer + 2 µL tyrosinase) was added into each well, mixed well and incubated for 10 min at 25 °C. Then, 30 µL of tyrosinase substrate solution (23 µL tyrosinase assay buffer + 2 µL tyrosinase substrate + 5 µL tyrosinase enhancer) was added into each well and mixed well. The absorbance was measured in kinetic mode every 2 min for 30 min at 510 nm. The slope for S, P, EC and SC was calculated by dividing the net ΔAbs (Abs2–Abs1) by the ΔTime (T2–T1) in the linear range of the plot. The percentage relative inhibition was calculated according to Equation (4).

$$\text{Relative inhibition } (\%) = \frac{\text{Slope (EC)} - \text{Slope (S)}}{\text{Slope (EC)}} \times 100 \quad (4)$$

2.18. Statistical Analysis

All data were recorded, edited and entered using IBM SPSS Statistics Version 20 (Chicago, IL, USA). The data obtained were expressed in average ± standard deviation (SD). The significant difference between groups was analyzed using one-way ANOVA followed by Tukey's HSD test or independent samples t-test where applicable. p-value < 0.05 was considered statistically significant.

3. Results and Discussion

3.1. Physical Compatibility Test

The physical compatibility test demonstrated that all the combinations of mangosteen peel extract and excipients did not have characteristic changes as compared to the control, as shown in Table 2. This shows that mangosteen peel extract is compatible with other excipients. A compatibility study is vital to detect any possible incompatibility between the active ingredient and excipients in the final formulation. Hence, it plays an important role in the product development process to select appropriate excipients and ensure active ingredients' stability [42].

Table 2. Physical compatibility of mangosteen peel extract and excipients.

No.	Combination of Ingredients	Duration (Weeks)			
		1	2	3	4
1	MG	NCC	NCC	NCC	NCC
2	MG:AO	NCC	NCC	NCC	NCC
3	MG:AO:SB	NCC	NCC	NCC	NCC
4	MG:AO:SB:O	NCC	NCC	NCC	NCC
5	MG:AO:SB:O:H_2O:G	NCC	NCC	NCC	NCC
6	MG:AO:SB:O:H_2O:G:AV	NCC	NCC	NCC	NCC
7	MG:AO:SB:O:H_2O:G:AV:HA	NCC	NCC	NCC	NCC
8	MG:AO:SB:O:H_2O:G:AV:HA:P	NCC	NCC	NCC	NCC
9	MG:AO:SB:O:H_2O:G:AV:HA:P: Opt.	NCC	NCC	NCC	NCC

Abbreviations: NCC: No characteristic changes as compared to control; MG: Mangosteen peel extract (10% α-mangostin); AO: Refined avocado oil; SB: Refined shea butter; O: Olivem 1000; H_2O: Distilled water; G: Vegetable glycerine solution; AV: Aloe vera gel; HA: Hyaluronic acid solution; P: D-Panthenol; Opt.: Optiphen BD.

3.2. Organoleptic Characteristics

The organoleptic characteristics of creams were shown in Table 3. Both male (M1) and female (F1) creams appeared light yellowish-brown with visible debris which is the characteristic color of mangosteen peel extract. Their organoleptic characteristics were similar in terms of flow property, texture, homogeneity and consistency. The only difference between M1 and F1 was the odor due to the incorporation of different essential oil or fragrance oil into the creams.

Table 3. Organoleptic characteristics of creams.

	Male Cream (M1)	Female Cream (F1)
Odor	Baby powder scent	Rose scent
Color	Light yellowish-brown with visible debris	
Flow property	No flow when inverted 180°	
Texture	Smooth, creamy, thick	
Homogeneity	Homogenous	
Consistency	Good	
Phase separation	Absent	
Coarse particles	Absent	
Stiffness	Absent	
Grittiness	Absent	
Greasiness	Absent	
Absorption	Within 1–2 min	

3.3. Determination of Type of Cream (Dilution Test)

Both M1 and F1 showed good miscibility with water. They were confirmed as oil in water (o/w) type creams. o/w type creams are more cosmetically acceptable due to their superior washability and relatively less greasiness as compared with water in oil (w/o) type creams [43].

3.4. Washability

Both M1 and F1 showed good washability under running tap water.

3.5. Rheology

The rheological behavior of creams was shown in Figures 2 and 3. Both M1 and F1 showed pseudoplastic or shear-thinning behavior. Pseudoplastic behavior is explained by the decrease in viscosity when the shear rate increases [44]. The rheological behavior of the creams will affect their spreadability and extrudability upon application [36,45]. For instance, the flow of pseudoplastic cream increases proportionally with the shear rate/rubbing force and forms a thin layer on the site of application [45,46]. This is attributed to the alteration of both microstructure and arrangement of particles when force is applied [45].

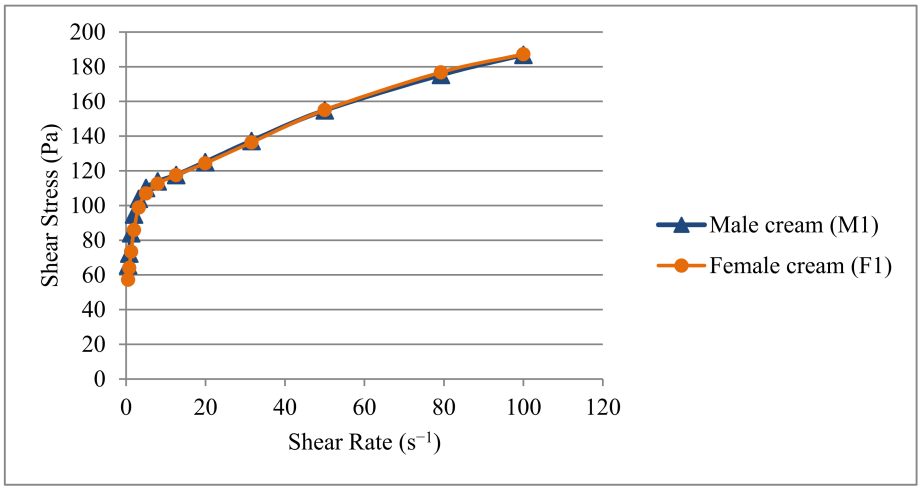

Figure 2. Graph of Shear stress (Pa) vs. Shear rate (s^{-1}).

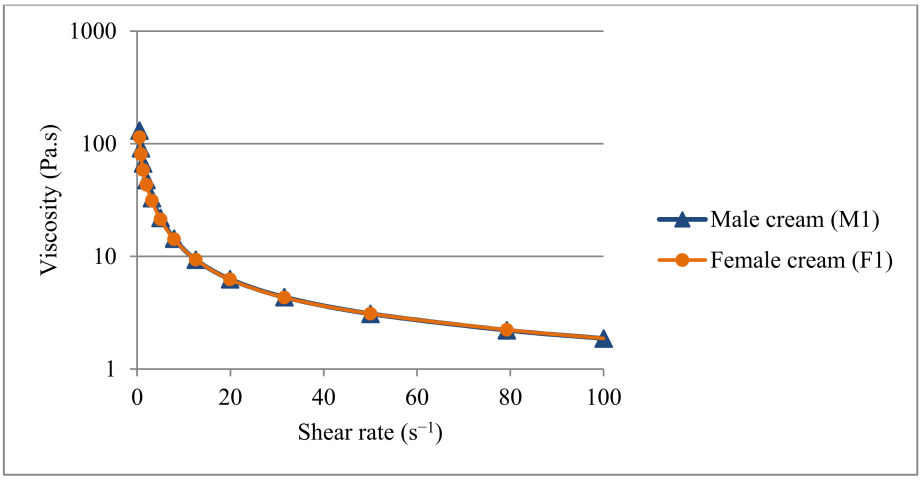

Figure 3. Graph of Viscosity (Pa.s) vs. Shear rate (s^{-1}).

3.6. Spreadability and pH at Room Temperature and Accelerated Stability Study

The spreadability and pH of creams at room temperature were shown in Table 4. The spreadability of M1 ranged from 4.10 cm to 6.30 cm, whereas the spreadability of F1 ranged from 3.50 cm to 6.65 cm. The diameter of the spread of the creams represents the spreadability of the creams [36]. For instance, cream with good spreadability spreads over a larger area [47]. Hence, an ideal cream should be easily spread with a small force applied. Furthermore, good spreadability improves consumer compliance and helps in the uniform application of topical formulations [48]. Spreadability of the creams reduced with the increase in storage duration. Since viscosity is closely associated with spreadability, these changes in spreadability may be due to the change in the particle size, shape and distribution of dispersed phase, continuous phase and emulsifier [49].

Table 4. Spreadability and pH of creams at room temperature and accelerated stability study.

Formulation	Duration (months)	Room Temperature			Accelerated Stability Study		
		Spreadability [a] (cm) ± SD		pH[a] ± SD	Spreadability [a] (cm) ± SD		pH [a] ± SD
		100 g	200 g		100 g	200 g	
Male Cream (M1)	0	5.05 ± 0.05 [c,d,e]	6.30 ± 0.26 [c,d,e]	5.16 ± 0.01 [d,e]	5.05 ± 0.05 [d,e]	6.30 ± 0.26 [d,e]	5.16 ± 0.01 [c,d,e]
	1	4.50 ± 0.05 [b,d,e]	5.70 ± 0.20 [b,e]	5.17 ± 0.01 [d,e]	4.70 ± 0.20 [d,e]	5.90 ± 0.20 [e]	5.26 ± 0.01 [b,d,e,f]
	2	4.20 ± 0.10 [b,c]	5.30 ± 0.10 [b]	5.31 ± 0.01 [b,c,e]	4.20 ± 0.10 [b,c]	5.50 ± 0.10 [b]	5.41 ± 0.01 [b,c,e,f]
	3	4.10 ± 0.10 [b,c]	5.20 ± 0.15 [b,c]	5.36 ± 0.01 [b,c,d]	4.10 ± 0.15 [b,c]	5.10 ± 0.15 [b,c]	5.45 ± 0.01 [b,c,d,f]
Female Cream (F1)	0	5.40 ± 0.10 [c,d,e]	6.65 ± 0.05 [c,d,e]	5.19 ± 0.01 [d,e]	5.40 ± 0.10	6.65 ± 0.05 [c,d,e]	5.19 ± 0.01 [c,d,e]
	1	4.30 ± 0.10 [b,d,e]	5.10 ± 0.20 [b,d,e]	5.18 ± 0.01 [d,e]	5.10 ± 0.10 [f]	6.20 ± 0.20 [b,f]	5.27 ± 0.01 [b,d,e,f]
	2	3.60 ± 0.10 [b,c]	4.40 ± 0.20 [b,c]	5.41 ± 0.01 [b,c]	5.10 ± 0.10 [f]	6.10 ± 0.10 [b,f]	5.41 ± 0.00 [b,c,e]
	3	3.50 ± 0.06 [b,c]	4.25 ± 0.15 [b,c]	5.42 ± 0.01 [b,c]	5.30 ± 0.15 [f]	6.30 ± 0.10 [b,f]	5.45 ± 0.01 [b,c,d,f]

[a] Average of 3 readings. One-way ANOVA followed by Tukey's HSD test was used to detect significant differences between duration (months), where p-value < 0.05 was considered significant. [b] There was a statistically significant difference as compared with the result at 0 month. [c] There was a statistically significant difference as compared with the result at 1 month. [d] There was a statistically significant difference as compared with the result at 2 months. [e] There was a statistically significant difference as compared with the result at 3 months. Independent Samples t-test was used to detect significant differences between storage condition (accelerated stability study vs. room temperature), where p-value < 0.05 was considered significant. [f] There was a statistically significant difference as compared with the result at room temperature (25 °C).

The physiological pH of human skin falls between 4 and 6. Thus, the pH of topical formulation or cosmetics should be adjusted nearly to the physiological pH to avoid skin irritation [46,50]. Despite the significant change in pH between duration (months), the average pH of the creams at room temperature was ranged from 5.16 to 5.42, which was ideal for topical application.

Both M1 and F1 were stable with no phase separation and no significant changes in color, texture and odor after being subjected to 40 ± 2 °C and 75 ± 5% RH for three months. However, both creams showed significant differences in spreadability and pH between duration (months), as shown in Table 4. Although these significant differences were observed, the overall spreadability and average pH were acceptable for topical application.

The spreadability of F1 at room temperature and stability chamber was statistically significantly different due to the difference in storage temperature [51]. This was attributed to the presence of shea butter in the cream that reduces the hardness and improves the spreadability of the creams at a higher temperature. Hence, the cream tends to spread rapidly at higher skin temperatures. Besides that, the application behaviors of the consumers may affect the spreadability of the cream. For instance, the rubbing of cream on the skin increases the blood flow and skin temperature which subsequently improves the spreadability of cream [52].

3.7. Freeze–Thaw Stability

The spreadability of the creams at 100 g and 200 g was significantly different between freeze–thaw cycles. This may be due to the change in the properties of the emulsifier when

it is subjected to stress conditions [53]. However, no phase separation was observed in the creams. Thus, both M1 and F1 were thermodynamically stable according to Table 5.

Table 5. Spreadability, pH and physical stability of creams throughout freeze–thaw cycles.

Formulation	Cycles	Spreadability [a] (cm) ± SD		pH [a] ± SD	Phase Separation
		100 g	200 g		
Male Cream (M1)	0	5.05 ± 0.05 [c,d,e]	6.30 ± 0.26 [c,d,e]	5.16 ± 0.01 [c,e]	Absent
	1	4.15 ± 0.05 [b]	5.15 ± 0.05 [b]	5.25 ± 0.00 [b,d,e]	Absent
	2	4.05 ± 0.05 [b]	5.10 ± 0.00 [b]	5.17 ± 0.01 [c,e]	Absent
	3	4.10 ± 0.10 [b]	4.90 ± 0.00 [b]	5.21 ± 0.01 [b,c,d]	Absent
Female Cream (F1)	0	5.40 ± 0.10 [c,d,e]	6.65 ± 0.05 [c,d,e]	5.19 ± 0.01 [e]	Absent
	1	4.20 ± 0.20 [b,e]	4.80 ± 0.10 [b]	5.20 ± 0.00 [e]	Absent
	2	4.15 ± 0.15 [b,e]	4.95 ± 0.05 [b,e]	5.19 ± 0.00 [e]	Absent
	3	3.70 ± 0.10 [b,c,d]	4.65 ± 0.15 [b,d]	5.17 ± 0.01 [b,c,d]	Absent

[a] Average of 3 readings. One-way ANOVA followed by Tukey's HSD test was used to detect significant differences between cycles, where p-value < 0.05 was considered significant. [b] There was a statistically significant difference as compared with the result at cycle 0. [c] There was a statistically significant difference as compared with the result at cycle 1. [d] There was a statistically significant difference as compared with the result at cycle 2. [e] There was a statistically significant difference as compared with the result at cycle 3.

The average pH of the creams before and after each freeze–thaw cycle was consistent. The average pH of M1 falls around 5.16 to 5.25, whereas the average pH of F1 falls around 5.17 to 5.20. Despite the significant differences in pH between freeze–thaw cycles, the average pH of both M1 and F1 was near to the physiological pH (4–6) of the human skin. Hence, it does not cause skin irritation [46,50].

3.8. Centrifugation Test

The emulsion stability of M1 and F1 was 100% for two runs of 10 min at 0, 1, 2 and 3 months. They remained stable with no observable phase separation after centrifugation. This may be attributed to the similarity in density between the oil and water phase or the strong interfacial interaction between the ingredients. Centrifugation is a type of stability test that applies strong centrifugal force to the sample and separates the ingredients with different densities [38]. Creaming, coalescence, caking and phase separation normally occur as a result of product instability [38,54].

3.9. 2,2-Diphenyl-1-picrylhydrazyl (DPPH) Radical Scavenging Assay

DPPH free radical scavenging assay is commonly used to study the free radical scavenging activity of natural antioxidants. It is expressed in EC_{50} which is known as the effective substrate's concentration that reduces the DPPH color by 50% [55]. Furthermore, EC_{50} is inversely proportional to the free radical scavenging activity of antioxidants. The EC_{50} of test samples was shown in Table 6.

In this study, the EC_{50} of mangosteen peel extract (37.31 µg/mL) was lower than the EC_{50} of ascorbic acid (46.54 µg/mL), butylated hydroxytoluene (BHT) (49.50 µg/mL) and Trolox (57.75 µg/mL) [56,57]. Hence, the antioxidant capacity of mangosteen peel extract was stronger than the positive controls. BHT is commonly used as an antioxidant and preservative in cosmetic products. However, it may cause skin irritation and pulmonary toxicity. In addition, further studies are required to evaluate the long-term efficacy and safety of BHT for topical application [58]. In contrast, mangosteen peel extract is a natural antioxidant that is relatively safe and effective as compared to BHT. Antioxidants are widely incorporated in anti-aging cosmetics due to their free radical scavenging activity that helps to reduce or prevent skin oxidative stress.

Table 6. Antioxidant capacity of test samples.

Test Samples	EC_{50} [a] ± SD		*p*-Value *
	DPPH Assay	ABTS Assay	
Mangosteen peel extract (10% α-mangostin)	37.31 ± 4.73 μg/mL	21.02 ± 2.92 μg/mL	0.007
Mangosteen cream (0.5% mangosteen peel extract)	9.05 ± 4.14 mg/mL	5.96 ± 2.77 mg/mL	0.343
Hyaluronic acid	>100 mg/mL	>100 mg/mL	-
Panthenol	>100 mg/mL	>100 mg/mL	-

[a] Average of 3 readings. * Independent Samples *t*-test was used to detect significant differences between DPPH and ABTS assay, where *p*-values < 0.05 was considered significant.

The antioxidant activity of mangosteen peel extract is attributed to the presence of phenolic compounds such as α-mangostin, flavonoids, epicatechins and tannins. Jung et al. [21] demonstrated that α-mangostin, γ-mangostin, smeathxanthone A, gartanin and 8-hydroxycudraxanthone G had potent antioxidant activity. Among these, α-mangostin is the major xanthone present in the mangosteen peel. However, different types of mangosteen peel extract affect the level of phenolic compounds and, subsequently, the radical scavenging activity. This is due to the utilization of different extracting solvents that have distinct affinities for compounds and the ability of sample penetration during extraction [59–61]. For instance, the EC_{50} of mangosteen peel extract ranged from 12.84 μg/mL to 154.7 μg/mL [61–65]. Hence, the mangosteen peel extract used in this study was standardized to 10% α-mangostin to impart their antioxidant effects to the mangosteen cream.

The development of a green cosmeceutical from fruit waste such as mangosteen peel is in line with Sustainable Development Goal (SDG) 12: Responsible Consumption and Production. The ultimate goals of the United Nations are to reduce waste production and promote efficient use of natural resources and sustainable living [66].

The DPPH free radical scavenging activity of hyaluronic acid (HA) was concentration-dependent. At 100 mg/mL, the average free radical scavenging activity of HA was 27.54 ± 2.64%. Hence, the antioxidant activity of HA was lower than mangosteen peel extract. In contrast, Ke et al. [67] demonstrated that 1600 μg/mL low molecular weight hyaluronic acid-1 (LMWHA-1), HA and LMWHA-2 showed DPPH radical scavenging activity of 59.38%, 53.65% and 50.23%, respectively. The differences in free radical scavenging activity of HA may be due to the variation in their molecular weight. In this study, the molecular weight of HA was 8–15 kDa, whereas Ke et al. [67] utilized LMWHA-1, LMWHA-2 and HA with molecular weights of 1.45×10^5 Da, 4.52×10^4 Da and 1.05×10^6 Da, respectively. However, the relationship between antioxidant activity and the molecular weight of HA requires further investigation.

The average DPPH scavenging activity of panthenol at a concentration of 100 mg/mL was 21.81 ± 4.81%. Panthenol is commonly used in cosmetic products as a humectant that minimizes transepidermal water loss and provides skin protective effects [68]. In addition, panthenol promotes wound healing and rarely causes skin irritation after application [69]. However, further studies should be conducted to discover the antioxidant effect of panthenol.

The EC_{50} of mangosteen cream was 9.05 ± 4.14 mg/mL. Due to the weak antioxidant effects of hyaluronic acid and panthenol, the antioxidant effect of mangosteen cream is mainly attributed to the 0.5% of mangosteen peel extract. Besides, the concentration of mangosteen peel extract in the cream was approximately 5 mg/mL, which is higher than the EC_{50} of mangosteen peel extract alone (37.31 μg/mL). Natural antioxidants derived from natural sources such as mangosteen peel are preferable to synthetic antioxidants due to the undesirable side effects of synthetic ingredients. Moreover, the mangosteen cream was free from synthetic color, sulfide, alcohol, parabens and SLS in addition to the utilization of natural surfactant and fragrance. Besides, the ingredients incorporated in the formulation have a long history of safe use in cosmetics and are used within the concentration range specified by Cosmetic Ingredient Review (CIR).

Mangosteen peel extract, aloe vera gel, glycerine, panthenol and hyaluronic acid work synergistically to prevent, slow down and treat skin aging. Aloe vera gel is rich in antioxidants such as ascorbic acid and vitamin A, which helps in the reversal of skin aging. Furthermore, it is widely used to treat eczema, psoriasis and promotes wound healing due to its moisturizing and soothing effects [70]. On the other hand, glycerine and panthenol act as humectants and skin protectants that promote skin hydration and provide skin protection. Furthermore, HA is commonly used in anti-aging skin care products due to its skin conditioning effects.

3.10. 2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) Assay

The EC_{50} of mangosteen peel extract was 21.02 µg/mL, which is close to the EC_{50} reported by Widowati et al. (15.93 µg/mL) [71] and Li et al. (24.6 µg/mL) [64]. This demonstrated that mangosteen peel extract was having stronger free radical scavenging effects than α-tocopherol (EC_{50}: 38.51 µg/mL), Trolox (EC_{50}: 58.14 µg/mL), BHT (EC_{50}: 73.1 µg/mL) and ascorbic acid (EC_{50}: 75.15 µg/mL) [72–74]. The mangosteen peel extract used in this study was standardized to 10% α-mangostin. α-mangostin is well known as the active ingredient in mangosteen due to its antioxidant effects [75]. Despite its antioxidant properties, batch-to-batch variation may occur due to the growth conditions and geographical, environmental and genetic factors of *G. mangostana*. Thus, standardization is required to ensure the quality, safety, efficacy, consistency and reproducibility of mangosteen peel extract by implementing Good Manufacturing Practices (GMP). The herbal extract comprises a complex build-up of constituents that work synergistically for their desired medicinal effects. However, some of the constituents remain unknown, which makes the quality control of herbal products much more challenging [76].

At 100 mg/mL, HA demonstrated ABTS radical scavenging activity of 9.98 ± 1.39%. The ABTS radical scavenging activity of HA (EC_{50} > 100 mg/mL) was lower than mangosteen peel extract ($EC_{50:}$ 21.02 µg/mL). In contrast, the ABTS radical scavenging activity of HA isolated from bivalve mollusk, *Amussium pleuronectus* was 71.35% at 1 mg/mL [77]. According to Braga et al. [78], 900 kDa of hyaluronic acid manufactured by Equality demonstrated significant concentration-dependent ABTS free radical scavenging activity, from 0.62 mg/mL (14.04 ± 0.94%) to 2.5 mg/mL (47.22 ± 2.91%). In addition, both in vitro and in vivo studies reveal the antioxidant activity of HA.

Panthenol demonstrated ABTS radical scavenging activity of 27.29 ± 3% at 100 mg/mL. However, further studies should be conducted to evaluate the role of panthenol as an antioxidant.

The EC_{50} of mangosteen cream was 5.96 ± 2.77 mg/mL. The antioxidant effects of mangosteen cream are strongly attributed to the 0.5% mangosteen peel extract incorporated into the cream base, since HA and panthenol showed weak antioxidant effects. Furthermore, the concentration of mangosteen peel extract in the cream was approximately 5 mg/mL, which is higher than the EC_{50} of mangosteen peel extract alone (21.02 µg/mL). The formulation of green cosmeceutical mangosteen herbal face cream with free radical scavenging effects helps to improve skin appearance and alleviate skin conditions. According to McEachern et al., green cosmeceuticals are crucial for environmental protection, animal welfare and species preservation by the responsible use of non-renewable resources [79].

As shown in Table 6, the EC_{50} of mangosteen peel extract obtained via ABTS assay was significantly lower than the EC_{50} obtained via DPPH radical scavenging assay ($p < 0.05$). This may be due to the variation in steric accessibility of the compounds to the active sites of the radicals [80,81]. On the other hand, the EC_{50} of mangosteen cream via ABTS and DPPH assay was not significantly different.

3.11. Tyrosinase Inhibitory Assay

Mangosteen peel extract (IC_{50}: 1.603 µg/mL) strongly inhibits tyrosinase enzyme as compared with kojic acid (IC_{50}: 3.57 µg/mL), as shown in Figure 4. In contrast, Widowati et al. [82] reported that γ-mangostin (IC_{50}: 50.35 µg/mL) showed more potent tyrosinase inhibitory activity than garcinone C (IC_{50}: 65.66 µg/mL), α-mangostin (IC_{50}: 70.92 µg/mL),

garcinone D (IC_{50}: 107.86 µg/mL) and mangosteen peel extract (IC_{50}: 181.08 µg/mL). Meanwhile, Arif et al. [62] demonstrated that 50 µg/mL of ethyl acetate mangosteen peel extract inhibits tyrosinase by 61.66%, whereas 200 µg/mL of methanolic mangosteen peel extract inhibits tyrosinase by 7.46%. The anti-tyrosinase activity is attributed to the structural similarity between *G. mangostana* derived xanthones and tyrosine or dihydroxyphenylalanine (DOPA) [62,83].

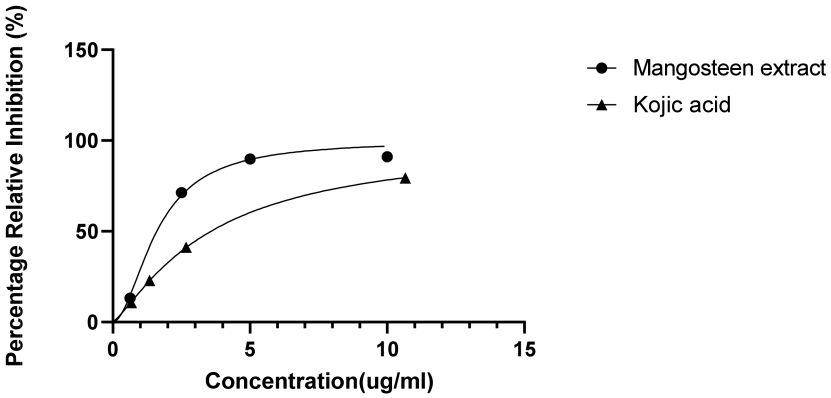

Figure 4. Tyrosinase inhibitory activity of mangosteen peel extract and kojic acid.

There are a few limitations in this study. Firstly, the information about mangosteen fruit such as origin, growth conditions and maturity level are limited. In addition, the method of mangosteen fruit harvesting, processing and drying temperature is not known. All these factors contribute to the variation in phenolic content and subsequently the antioxidant capacity of mangosteen peel extract. Thus, the reproducibility of the study will be impossible without standardization. Standardization is required to ensure the quality, safety, efficacy and reproducibility of mangosteen peel extract. Furthermore, the organoleptic characteristics such as texture, greasiness and absorption are subjective and may vary from person to person. Hence, it is impossible to generalize the results to the whole population.

4. Conclusions

Green cosmeceutical herbal face creams containing standardized mangosteen (*Garcinia mangostana*) peel extract which are skin-friendly and physically stable were successfully formulated. The uniqueness of the mangosteen creams was demonstrated by the absence of SLS, sulfides, parabens and alcohol that frequently cause skin irritation. In addition, natural surfactants and fragrances were used to improve their stability and acceptability. The development of green cosmeceutical mangosteen herbal face cream helps to boost the local economy and increase the chance of international collaboration. Furthermore, the utilization of fruit waste such as mangosteen peel reduces waste generation and achieves sustainability development goals advocated by the United Nations. This study demonstrated that mangosteen peel extract shows antioxidant and anti-tyrosinase activity. Hence, mangosteen-based cream is expected to be used as a safe and effective alternative to synthetic antioxidant and whitening products. However, randomized controlled trials should be conducted to evaluate the anti-aging and pigmentation control effects of mangosteen-based facial cream.

Author Contributions: Conceptualization, formal analysis, investigation, methodology, visualization and writing—original draft preparation, P.L.T. and M.Y.L.; funding acquisition, M.R.; project administration, supervision and resources, M.R. and S.C.; validation, L.F.T. and V.L.Y.; writing—review and editing, M.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by UCSI University for Pioneer Science Incentive Fund (PSIF), Proj-2019-In-FPS-019.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Ruddy, E.; Zhu, G.; Idowu, O.; Birch-Machin, M.A. Skin aging and mitochondria. In *Mitochondrial Dysfunction and Nanotherapeutics*; de Oliveira, M.R., Ed.; Academic Press: Cambridge, MA, USA, 2021; pp. 237–259, ISBN 978-032-385-666-9.
2. Giacomoni, P.U.; Declercq, L.; Hellemans, L.; Maes, D. Aging of human skin: Review of a mechanistic model and first experimental data. *IUBMB Life* **2000**, *49*, 259–263. [CrossRef] [PubMed]
3. Giacomoni, P.U.; Rein, G. Factors of skin ageing share common mechanisms. *Biogerontology* **2001**, *2*, 219–229. [CrossRef] [PubMed]
4. Giacomoni, P.U.; D'Alessio, P. Skin Ageing. In *Molecular Gerontology*; Rattan, S.I.S., Toussaint, O., Eds.; Springer: Boston, MA, USA, 1996; pp. 177–192, ISBN 978-1-4615-5889-7. [CrossRef]
5. Poljšak, B.; Dahmane, R. Free radicals and extrinsic skin aging. *Dermatol. Res. Pract.* **2012**, *2012*, 135206. [CrossRef] [PubMed]
6. Callender, V.D.; Baldwin, H.; Cook-Bolden, F.E.; Alexis, A.F.; Stein Gold, L.; Guenin, E. Effects of topical retinoids on acne and post-inflammatory hyperpigmentation in patients with skin of color: A clinical review and implications for practice. *Am. J. Clin. Dermatol.* **2022**, *23*, 69–81. [CrossRef]
7. World Health Organization. Preventing Disease Through Healthy Environments: Mercury in Skin Lightening Products. Available online: https://apps.who.int/iris/rest/bitstreams/1262414/retrieve (accessed on 3 October 2020).
8. Shamdasani, P.; Chon-Lin, G.O.; Richmond, D. Exploring green consumers in an oriental culture: Role of personal and marketing mix factors. In *NA—Advances in Consumer Research*; McAlister, L., Rothschild, M.L., Eds.; Association for Consumer Research: Provo, UT, USA, 1993; Volume 20, pp. 488–493.
9. Chin, J.; Jiang, B.C.; Mufidah, I.; Persada, S.F.; Noer, B.A. The investigation of consumers' behavior intention in using green skincare products: A pro-environmental behavior model approach. *Sustainability* **2018**, *10*, 3922. [CrossRef]
10. Amberg, N.; Fogarassy, C. Green consumer behavior in the cosmetics market. *Resources* **2019**, *8*, 137. [CrossRef]
11. Paul, J.; Modi, A.; Patel, J. Predicting green product consumption using theory of planned behavior and reasoned action. *J. Retail. Consum. Serv.* **2016**, *29*, 123–134. [CrossRef]
12. Lopez-Hortas, L.; Florez-Fernandez, N.; Torres, M.D.; Ferreira-Anta, T.; Casas, M.P.; Balboa, E.M.; Falque, E.; Domínguez, H. Applying seaweed compounds in cosmetics, cosmeceuticals and nutricosmetics. *Mar. Drugs* **2021**, *19*, 552. [CrossRef]
13. Dubey, S.K.; Dey, A.; Singhvi, G.; Pandey, M.M.; Singh, V.; Kesharwani, P. Emerging trends of nanotechnology in advanced cosmetics. *Colloids Surf. B Biointerfaces* **2022**, 112440. [CrossRef]
14. Salleh, M.M.; Yusof, M.R. Tropical fruits and vegetables in Malaysia: Production and impact on health. In Proceedings of the Fruits and Vegetables for Health Workshop, Seoul, Korea, 15–16 August 2006; pp. 1–5.
15. Ibrahim, U.K.; Kamarrudin, N.; Suzihaque, M.U.H.; Abd Hashib, S. Local fruit wastes as a potential source of natural antioxidant: An overview. In *IOP Conference Series: Materials Science and Engineering, 29th Symposium of Malaysian Chemical Engineers (SOMChE), Miri, Sarawak, Malaysia, 1–3 December 2016*; IOP Publishing: Bristol, UK, 2017; Volume 206, p. 012040. [CrossRef]
16. Ansori, A.N.M.; Fadholly, A.; Hayaza, S.; Susilo, R.K.; Inayatillah, B.; Winarni, D.; Husen, S.A. A review on medicinal properties of mangosteen (*Garcinia mangostana* L.). *Res. J. Pharm. Technol.* **2020**, *13*, 974–982. [CrossRef]
17. Ching, M.O.Y.; Sasikala, C.; Mogana, R. In vitro anti-motility and antispasmodic effects of *Garcinia mangostana* extracts in isolated chicken ileum preparation. *Int. J. Res. Pharm. Sci.* **2019**, *10*, 1444–1447. [CrossRef]
18. Aizat, W.M.; Jamil, I.N.; Ahmad-Hashim, F.H.; Noor, N.M. Recent updates on metabolite composition and medicinal benefits of mangosteen plant. *PeerJ* **2019**, *7*, e6324. [CrossRef] [PubMed]
19. Im, A.R.; Kim, Y.M.; Chin, Y.W.; Chae, S. Protective effects of compounds from *Garcinia mangostana* L. (mangosteen) against UVB damage in HaCaT cells and hairless mice. *Int. J. Mol. Med.* **2017**, *40*, 1941–1949. [CrossRef] [PubMed]
20. Ohno, R.I.; Moroishi, N.; Sugawa, H.; Maejima, K.; Saigusa, M.; Yamanaka, M.; Nagai, M.; Yoshimura, M.; Amakura, Y.; Nagai, R. Mangosteen pericarp extract inhibits the formation of pentosidine and ameliorates skin elasticity. *J. Clin. Biochem. Nutr.* **2015**, *57*, 27–32. [CrossRef] [PubMed]
21. Jung, H.A.; Su, B.N.; Keller, W.J.; Mehta, R.G.; Kinghorn, A.D. Antioxidant xanthones from the pericarp of *Garcinia mangostana* (mangosteen). *J. Agric. Food Chem.* **2006**, *54*, 2077–2082. [CrossRef]
22. Jamadar, M.J.; Husen Shaikh, R. Preparation and evaluation of herbal gel formulation. *J. Pharm. Res. Educ.* **2017**, *1*, 201–224.
23. Bynum, K.C. Preformulation and early phase method development. In *Separation Science and Technology*; Ahuja, S., Scypinski, S., Eds.; Academic Press: Cambridge, MA, USA, 2011; Volume 10, pp. 361–396, ISBN 978-012-375-680-0. [CrossRef]
24. Narang, A.S.; Rao, V.M.; Raghavan, K.S. Excipient compatibility. In *Developing Solid Oral Dosage Forms*; Qiu, Y., Chen, Y., Zhang, G.G.Z., Liu, L., Porter, W.R., Eds.; Academic Press: Cambridge, MA, USA, 2009; pp. 125–145, ISBN 978-044-453-242-8. [CrossRef]
25. De Barros Lima, Í.P.; Lima, N.G.P.B.; Barros, D.M.C.; Oliveira, T.S.; Mendonça, C.M.S.; Barbosa, E.G.; Raffin, F.N.; De Lima, E. Moura, T.F.A.; Gomes, A.P.B.; Ferrari, M.; et al. Compatibility study between hydroquinone and the excipients used in semi-solid pharmaceutical forms by thermal and non-thermal techniques. *J. Therm. Anal. Calorim.* **2015**, *120*, 719–732. [CrossRef]

26. Soumya, A.; Rasheed, S.; Manjunath, S. Formulation and evaluation of herbal cream containing extracts of *Murraya koenigii* and *Cajanus cajan*. *Int. J. Res. Phytochem. Pharmacol. Sci.* **2020**, *1*, 58–63. [CrossRef]
27. Navindgikar, N.N.; Kamalapurkar, K.A.; Chavan, P.S. Formulation and evaluation of multipurpose herbal cream. *Int. J. Curr. Pharm. Res.* **2020**, *12*, 25–30. [CrossRef]
28. Chen, M.X.; Alexander, K.S.; Baki, G. Formulation and evaluation of antibacterial creams and gels containing metal ions for topical application. *J. Pharm.* **2016**, *2016*, 1–10. [CrossRef]
29. Ahmed, A.A.; Nath, B. Formulation and in vitro evaluation of poly-herbal anti-ageing face cream of *Coriandrum sativum* and rose hip oil. *Int. J. Curr. Pharm. Res.* **2017**, *9*, 75–78. [CrossRef]
30. Mahawar, V.; Patidar, K.; Joshi, N. Development and evaluation of herbal antiaging cream formulation containing *Annona squamosa* leaf extract. *Asian J. Pharm. Clin. Res.* **2019**, *12*, 210–214. [CrossRef]
31. Glusac, J.; Davidesko-Vardi, I.; Isaschar-Ovdat, S.; Kukavica, B.; Fishman, A. Gel-like emulsions stabilized by tyrosinase-crosslinked potato and zein proteins. *Food Hydrocoll.* **2018**, *82*, 53–63. [CrossRef]
32. Berenguer, D.; Sosa, L.; Alcover, M.; Sessa, M.; Halbaut, L.; Guillén, C.; Fisa, R.; Calpena-Campmany, A.C.; Riera, C. Development and characterization of a semi-solid dosage form of meglumine antimoniate for topical treatment of cutaneous leishmaniasis. *Pharmaceutics* **2019**, *11*, 613. [CrossRef]
33. Maru, A.D.; Lahoti, S.R. Formulation and evaluation of moisturizing cream containing Sunflower wax. *Int. J. Pharm. Pharm. Sci.* **2018**, *10*, 54–59. [CrossRef]
34. Razi, M.; Khan, U.; Raza, S.M.; Hussain, M. Formulation and in vitro evaluation of cream containing diclofenac sodium and *Curcuma longa* for the management of rheumatoid arthritis. *Int. J. Pharma Sci.* **2014**, *4*, 654–660.
35. Ambala, R.; Vemula, S.K. Formulation and characterization of ketoprofen emulgels. *J. Appl. Pharm. Sci.* **2015**, *5*, 112–117. [CrossRef]
36. Netto MPharm, G.; Jose, J. Development, characterization, and evaluation of sunscreen cream containing solid lipid nanoparticles of silymarin. *J. Cosmet. Dermatol.* **2018**, *17*, 1073–1083. [CrossRef]
37. Sungpud, C.; Panpipat, W.; Chaijan, M.; Yoon, A.S. Techno-biofunctionality of mangostin extract-loaded virgin coconut oil nanoemulsion and nanoemulgel. *PLoS ONE* **2020**, *15*, e0227979. [CrossRef]
38. Mohsin, S.; Akhtar, N.; Mahmood, T.; Khan, H.; Mustafa, R. Formulation and stability of topical water in oil emulsion containing corn silk extract. *Trop. J. Pharm. Res.* **2016**, *15*, 1115–1121. [CrossRef]
39. Santhanam, R.K.; Akhtar, M.T.; Ahmad, S.; Abas, F.; Ismail, I.S.; Rukayadi, Y.; Shaari, K. Utilization of the ethyl acetate fraction of *Zanthoxylum rhetsa* bark extract as an active ingredient in natural sunscreen formulations. *Ind. Crops Prod.* **2017**, *96*, 165–172. [CrossRef]
40. Restu, W.K.; Sampora, Y.; Meliana, Y.; Haryono, A. Effect of accelerated stability test on characteristics of emulsion systems with chitosan as a stabilizer. *Procedia Chem.* **2015**, *16*, 171–176. [CrossRef]
41. Mogana, R.; Teng-Jin, K.; Wiart, C. Anti-inflammatory, anticholinesterase, and antioxidant potential of scopoletin isolated from *Canarium patentinervium* Miq. (Burseraceae Kunth). *Evid.-Based Complementary Altern. Med.* **2013**, *2013*, 734824. [CrossRef]
42. Simões, A.; Veiga, F.; Vitorino, C.; Figueiras, A. A tutorial for developing a topical cream formulation based on the quality by design approach. *J. Pharm. Sci.* **2018**, *107*, 2653–2662. [CrossRef]
43. Mishra, A.P.; Saklani, S.; Milella, L.; Tiwari, P. Formulation and evaluation of herbal antioxidant face cream of *Nardostachys jatamansi* collected from Indian Himalayan region. *Asian Pac. J. Trop. Biomed.* **2014**, *4*, S679–S682. [CrossRef]
44. Rapp, B.E. Fluids. In *Microfluidics: Modelling, Mechanics and Mathematics*; Rapp, B.E., Ed.; Elsevier: Oxford, UK, 2017; pp. 243–263, ISBN 978-145-573-141-1. [CrossRef]
45. Kwak, M.S.; Ahn, H.J.; Song, K.W. Rheological investigation of body cream and body lotion in actual application conditions. *Korea Aust. Rheol. J.* **2015**, *27*, 241–251. [CrossRef]
46. Aremu, O.; Olayemi, O.; Ajala, T.; Isimi, Y.; Oladosu, P.; Ekere, K.; John, J.; Emeje, M. Antibacterial evaluation of *Acacia nilotica* lam (Mimosaceae) seed extract in dermatological preparations. *J. Res. Pharm.* **2020**, *24*, 170–181. [CrossRef]
47. Estanqueiro, M.; Amaral, M.H.; Sousa Lobo, J.M. Comparison between sensory and instrumental characterization of topical formulations: Impact of thickening agents. *Int. J. Cosmet. Sci.* **2016**, *38*, 389–398. [CrossRef]
48. Yadav, N.P.; Rai, V.K.; Mishra, N.; Sinha, P.; Bawankule, D.U.; Pal, A.; Tripathi, A.K.; Chanotiya, C.S. A novel approach for development and characterization of effective mosquito repellent cream formulation containing Citronella oil. *Biomed Res. Int.* **2014**, *2014*, 786084. [CrossRef]
49. Miner, P.E. Emulsion rheology: Creams and lotions. In *Rheological Properties of Cosmetics and Toiletries*; Laba, D., Ed.; Marcel Dekker: New York, NY, USA, 2017; pp. 313–370, ISBN 978-0-8247-9090-5. [CrossRef]
50. Al-Busaid, M.M.; Akhtar, M.S.; Alam, T.; Aly Shehata, W. Development and evaluation of herbal cream containing curcumin from *Curcuma longa*. *Pharm. Pharmacol. Int. J.* **2020**, *8*, 285–289. [CrossRef]
51. Deuschle, V.C.K.N.; Norbert Deuschle, R.A.; Bortoluzzi, M.R.; Athayde, M.L. Physical chemistry evaluation of stability, spreadability, in vitro antioxidant, and photo-protective capacities of topical formulations containing *Calendula officinalis* L. leaf extract. *Braz. J. Pharm. Sci.* **2015**, *51*, 63–75. [CrossRef]
52. Barry, B.W.; Grace, A.J. Sensory testing of spreadability: Investigation of rheological conditions operative during application of topical preparations. *J. Pharm. Sci.* **1972**, *61*, 335–341. [CrossRef] [PubMed]

53. Jumaa, M.; Müller, B.W. Parenteral emulsions stabilized with a mixture of phospholipids and PEG-660-12-hydroxy-stearate: Evaluation of accelerated and long-term stability. *Eur. J. Pharm. Biopharm.* **2002**, *54*, 207–212. [CrossRef] [PubMed]
54. National Health Surveilance Agency. Cosmetic Products Stability Guide. Available online: http://portal.anvisa.gov.br/documents/106351/107922/guidestabilityseries.pdf/5f90ee5b-c77b-4c1e-91f9-5fa680b05022 (accessed on 20 May 2021).
55. Shahidi, F.; Zhong, Y. Measurement of antioxidant activity. *J. Funct. Foods* **2015**, *18*, 757–781. [CrossRef]
56. Kalin, P.; Gülçin, İ.; Gören, A.C. Antioxidant activity and polyphenol content of cranberries (*Vaccinium macrocarpon*). *Rec. Nat. Prod.* **2015**, *9*, 496–502.
57. Yao, X.; Zhang, T.; Tang, H.; Wang, H.; Chen, W. Free radical-scavenging, nitrite-scavenging, and N-nitrosamine formation inhibitory activities of extracts from Kunlun compositae tea (*Coreopsis tinctoria* Nutt.). *J. Food Nutr. Res.* **2015**, *3*, 587–592. [CrossRef]
58. Lanigan, R.S.; Yamarik, T.A. Final report on the safety assessment of BHT (1). *Int. J. Toxicol.* **2002**, *21*, 19–94. [CrossRef]
59. Ngawhirunpat, T.; Opanasopi, P.; Sukma, M.; Sittisombut, C.; Kat, A.; Adachi, I. Antioxidant, free radical-scavenging activity and cytotoxicity of different solvent extracts and their phenolic constituents from the fruit hull of mangosteen (*Garcinia mangostana*). *Pharm. Biol.* **2010**, *48*, 55–62. [CrossRef]
60. Tjahjani, S.; Widowati, W.; Khiong, K.; Suhendra, A.; Tjokropranoto, R. Antioxidant properties of *Garcinia mangostana* L (mangosteen) rind. *Procedia Chem.* **2014**, *13*, 198–203. [CrossRef]
61. Weecharangsan, W.; Opanasopit, P.; Sukma, M.; Ngawhirunpat, T.; Sotanaphun, U.; Siripong, P. Antioxidative and neuroprotective activities of extracts from the fruit hull of mangosteen (*Garcinia mangostana* Linn.). *Med. Princ. Pract.* **2006**, *15*, 281–287. [CrossRef]
62. Arif, N.; Yahya, A.; Hamid, M.; Yaakob, H.; Zulkifli, R. Development of lightening cream from mangosteen pericarp extract with olivoil emulsifier. *Int. Proc. Econ. Dev. Res.* **2014**, *81*, 58. [CrossRef]
63. Shafy, G.M.; Jassim, A.M.N.; Mohammed, M.T. Study of phytochemical, antioxidant and anti-inflammatory of mangosteen (*G. mangostana*) and its ability to wound healing. *Plant Arch.* **2019**, *19*, 665–673.
64. Li, W.Q.; Xu, J.G. Profile of DNA damage protective effect and antioxidant activity of different solvent extracts from the pericarp of *Garcinia mangostana*. *J. Food Nutr. Sci.* **2015**, *3*, 1–6. [CrossRef]
65. Pothitirat, W.; Chomnawang, M.T.; Supabphol, R.; Gritsanapan, W. Free radical scavenging and anti-acne activities of mangosteen fruit rind extracts prepared by different extraction methods. *Pharm. Biol.* **2010**, *48*, 182–186. [CrossRef] [PubMed]
66. United Nations. Goal 12: Ensure Sustainable Consumption and Production Patterns. Available online: https://www.un.org/sustainabledevelopment/sustainable-consumption-production/ (accessed on 23 June 2021).
67. Ke, C.; Sun, L.; Qiao, D.; Wang, D.; Zeng, X. Antioxidant acitivity of low molecular weight hyaluronic acid. *Food Chem. Toxicol.* **2011**, *49*, 2670–2675. [CrossRef]
68. Camargo, F.B., Jr.; Gaspar, L.R.; Maia Campos, P.M.B.G. Skin moisturizing effects of panthenol-based formulations. *J. Cosmet. Sci.* **2011**, *62*, 361–369.
69. Bergfeld, W.F.; Belsito, D.V.; Hill, R.A.; Klaassen, C.D.; Liebler, D.C.; Marks, J.G.; Shank, R.C.; Slaga, T.J.; Snyder, P.W.; Heldreth, B. Safety Assessment of Panthenol, Pantothenic Acid, and Derivatives as Used in Cosmetics. Available online: http://www.cir-safety.org/sites/default/files/PANTS012017.pdf (accessed on 20 May 2021).
70. Ijaz, N.; Durrani, A.I.; Rubab, S.; Bahadur, S. Formulation and characterization of Aloe vera gel and tomato powder containing cream. *Acta Ecol. Sin.* **2022**, *42*, 34–42. [CrossRef]
71. Widowati, W.; Darsono, L.; Suherman, J.; Yelliantty, Y.; Maesaroh, M. High Performance Liquid Chromatography (HPLC) analysis, antioxidant, antiaggregation of mangosteen peel extract (*Garcinia mangostana* L.). *Int. J. Biosci. Biochem. Bioinf.* **2014**, *4*, 458–466. [CrossRef]
72. Haddouchi, F.; Chaouche, T.M.; Ksouri, R.; Medini, F.; Sekkal, F.Z.; Benmansour, A. Antioxidant activity profiling by spectrophotometric methods of aqueous methanolic extracts of *Helichrysum stoechas* subsp. *rupestre and Phagnalon saxatile subsp. saxatile*. *Chin. J. Nat. Med.* **2014**, *12*, 415–422. [CrossRef]
73. Deveci, E.; Çayan, F.; Tel-Çayan, G.; Duru, M.E. Structural characterization and determination of biological activities for different polysaccharides extracted from tree mushroom species. *J. Food Biochem.* **2019**, *43*, e12965. [CrossRef]
74. Atolani, O.; Oguntoye, H.; Areh, E.T.; Adeyemi, O.S.; Kambizi, L. Chemical composition, anti-toxoplasma, cytotoxicity, antioxidant, and anti-inflammatory potentials of Cola gigantea seed oil. *Pharm. Biol.* **2019**, *57*, 154–160. [CrossRef]
75. Lim, C.V.; Sasikala, C.; Mogana, R. Antioxidant activity of *Garcinia mangostana* L and alpha mangostin: A review. *Res. J. Pharm. Technol.* **2021**, *14*, 4466–4470. [CrossRef]
76. Kunle, O.F.; Egharevba, H.O.; Ahmadu, P.O. Standardization of herbal medicines—A review. *Int. J. Biodivers. Conserv.* **2012**, *4*, 101–112. [CrossRef]
77. Kanchana, S.; Arumugam, M.; Giji, S.; Balasubramanian, T. Isolation, characterization and antioxidant activity of hyaluronic acid from marine bivalve mollusc *Amussium pleuronectus* (Linnaeus, 1758). *Bioact. Carbohydr. Diet. Fibre* **2013**, *2*, 1–7. [CrossRef]
78. Braga, P.C.; Dal Sasso, M.; Lattuada, N.; Greco, V.; Sibilia, V.; Zucca, E.; Stucchi, L.; Ferro, E.; Ferrucci, F. Antioxidant activity of hyaluronic acid investigated by means of chemiluminescence of equine neutrophil bursts and electron paramagnetic resonance spectroscopy. *J. Vet. Pharmacol. Ther.* **2015**, *38*, 48–54. [CrossRef]
79. McEachern, M.G.; McClean, P. Organic purchasing motivations and attitudes: Are they ethical? *Int. J. Consum. Stud.* **2002**, *26*, 85–92. [CrossRef]

80. Prior, R.L.; Wu, X.; Schaich, K. Standardized methods for the determination of antioxidant capacity and phenolics in foods and dietary supplements. *J. Agric. Food Chem.* **2005**, *53*, 4290–4302. [CrossRef]
81. Suvarnakuta, P.; Chaweerungrat, C.; Devahastin, S. Effects of drying methods on assay and antioxidant activity of xanthones in mangosteen rind. *Food Chem.* **2011**, *125*, 240–247. [CrossRef]
82. Widowati, W.; Ginting, C.N.; Lister, I.N.E.; Girsang, E.; Amalia, A.; Wibowo, S.H.B.; Kusuma, H.S.W.; Rizal. Anti-aging effects of mangosteen peel extract and its phytochemical compounds: Antioxidant activity, enzyme inhibition and molecular docking simulation. *Trop. Life Sci. Res.* **2020**, *31*, 127–144. [CrossRef]
83. Briganti, S.; Camera, E.; Picardo, M. Chemical and instrumental approaches to treat hyperpigmentation. *Pigment Cell Res.* **2003**, *16*, 101–110. [CrossRef]