Current Trends in Biotechnology and Pharmacy
Vol. 17 (4A) 61 - 69, October 2023, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2023.4s.91

An Expedition Towards Formulating Natural Face Serum with *Garcinia mangostana* (Mangosteen)

Ashok Kumar Janakiraman[1], Saiqa Afroze[1]*, Yik Ling Chew[1], Yap Jeck Yee[1], Cheng Zenli[1], Vetriselvan Subramaniyan[2], and Saminathan Kayarohanam[3]

[1 & 2]Pharmacology Unit, Jeffrey Cheah School of Medicine and Health Sciences, Monash University Malaysia, Jalan Lagoon Selatan, Bandar Sunway, 47500 Selangor Darul Ehsan, Malaysia

[3]Faculty of Bioeconomics, Food and Health Sciences, University Geomatika Malaysia (UGM), Kuala Lumpur 54200, Malaysia

*Corresponding author: 1002162848@ucsiuniversity.edu.my

Abstract

The fast development of different industries has a negative impact on public health and the environment. Where the admiration for healthy skin has encouraged the cosmeceutical industry to develop quickly, the use of synthetic and harmful substances in many skin care products causes skin reactions like irritations, redness, and itching. As a result, the necessity for 100% natural formulation for skin health motivated the researchers to recognize it. This research aimed to formulate mangosteen anti-acne face serums using 100% natural excipients (green product) and evaluate their physicochemical properties. A combination of magnetic stirring and homogenization techniques was used for the serum formulation at room temperature. The stability of the formulation was satisfactory based on redispersion and pH (4.71) stability results. The serum provided good coverage with around 52% occlusive properties. The product was able to show an impressive antioxidant effect with an IC_{50} of 0.19mg/mL. Its antibacterial properties were observed against *Staphylococcus aureus* and *Staphylococcus epidermidis* where the *Staphylococcus aureus* was inhibited with a zone of inhibition of 18.03 mm. In the next stages, *in-vivo* studies of the product will help to move forward with commercialization.

Keywords: Face serum, Mangosteen, Anti-acne, Antioxidant, Antibacterial.

Introduction

In recent decades, the cosmeceutical industries have experienced major shift through the evaluation of science. Nowadays, scientists are more focused on developing natural-based products than synthetic ones (1). The causes of this shift in formulations include a wide range of accessible natural components, their exceptional pharmacological benefits, and a number of reporting incidents on adverse effects of artificial ingredients on health, the environment, and the economy (2). Such include side effects on the skin or hair, allergic responses, microplastic contamination, and exorbitant product prices because of costly production methods (3). In the majority of cases, the existing cosmeceutical formulations have one or more artificial ingredients like polyethylene glycol, retinol, alcohols, sulfites, and many more (4). These can cause skin burning, itching, and photosensitivity. Some researchers are also directing their research on the long-term use of synthetic cosmeceuticals and chronic immunological disorders (5). The presence of microplastics in those cosmeceutical products in the form of microbeads contaminates the water while washing these off. In addition to polluting the environment, these microplastics can get into the human body through different routes and cause carcinogenicity (6). Returning to natural products is the only way to resolve these catastrophic events.

Cosmeceutical serums are the finest option for delivering active ingredients. It is a highly concentrated water or oil-based product. Serums contain active ingredients ten times more than conventional creams and lotions. Furthermore, the serum offers delivery of micro molecules of the formulation's constituents. As a result, it ensures product distribution in the deeper skin layers is faster and more effective (7). The serum provides the skin with a firmer, smoother texture, makes pores seem smaller, and boosts moisture levels. Because of the benefits of serums, it is an ideal tool for treating acne (8, 9).

Acne or acne vulgaris is one of the most prevalent dermatological conditions. The etymology behind acne is still unclear. But some of the well-known factors involved are bacterial infection by *Staphylococcus aureus (S. aureus)*, inflammation, lack of moisture, and diet (10). *Garcinia mangostana*, often known as mangosteen in Southeast Asia, is a nutritious and delightful fruit. Mangosteen pericarps have traditionally been used to treat gonorrhea, bladder infections, diabetes, diarrhea, and skin rashes. According to the literature, the other parts of the fruit are full of oxygenated materials. Such as xanthone-like compounds (alpha, beta, and gamma mangostins), isomangostin, garcinone, and garcimangosone. The phytochemicals show antioxidant and antibacterial properties (11, 12). These activities are needed in anti-acne treatments. The antioxidants will prevent free radical formation, which helps reduce inflammation and promote skin rejuvenation by scar healing. The antibacterial properties are needed for protection against acne-causing bacteria (13,14). This study aims to formulate a face serum using only natural ingredients and utilizing the benefits of mangosteen peel extract for anti-acne properties that are safe for public health and the environment.

Material and Methods

Materials

Mangosteen peel extract powder was from Chemtron Biotechnology Sdn. Bhd. The organic aloe vera gel, vitamin C, hyaluronic acid, hydrolyzed collagen, allantoin, orange oil, xanthan gum tea tree oil, and glycerin were purchased from IKO Natural Beauty, Sdn. Bhd. While purchasing the materials, special attention was given, making sure they were in 100% natural form. The 2,2-Diphenyl-1-picrylhydrazyl were supplied by CHEMSOLN.

Instrumentations

A magnetic stirrer (Fisher Scientific) and homogenizer (YHANA Specification, model HMX-20DN) were used for formulations. A centrifuge, pH meter, and “Thermo Nicolet NEXUS” spectrometer were utilized for the characterization of the product. UV spectrophotometer (Secomam UviLine9400), incubator, and stability chamber were used for assessing the in-vitro properties.

Formulation of serum

The face serum was prepared in three stages. The first stage included mixing hyaluronic acid, hydrolyzed collagen, vitamin C, and aloe vera in a certain percentage, and in purified water. The second stage included adding all the essential oils. The third stage included the formulation of the base of the face serum. Here, xanthan gum and glycerin were added to purified water. Each stage was prepared using a magnetic stirrer in the speed range of 700-1100 rpm. The temperature used in each stage was dependent on the ingredients in it. The mangosteen extract was added at 0.1% concentration to the base along with the other ingredients. A homogenizer was used at the end of the process to ensure that the mixture was homogenous in texture.

Organoleptic characteristic

The color of the formulation was observed visually under appropriate light. The texture of the product was confirmed by touch. The smell of the serum was also observed.

Redispersion

The formulation was subjected to centrifugation at 3000 rpm for 5 min to check if

phase separation appears and the presence of any particulate matter. After centrifugation, visual observation was done under appropriate light.

pH

A calibrated pH meter was used to measure the pH of the face serum. 1 mL of the face serum was diluted in 10 mL of purified water for the test. It was essential to ensure the pH is appropriate for topical use (15)

Spreadability

As the face serum samples easily flow, the spreadability test would be significant for characterization. 0.1g of the sample was placed in the center of a 10 cm x 10cm cleaned transparent flat surface. 100g and 200g loads were placed and kept for 2 min. The diameters of the spread samples were measured. A good spreadability of the face serum was needed to give a nice coverage on minimal product usage (16).

Fourier-transform infrared spectroscopy (FTIR) study

FTIR spectra of the mangosteen extract and face serum formulation were obtained by "Thermo Nicolet NEXUS" spectrometer. The test was done at 20 scans with a resolution of $4cm^{-1}$. At a scanning range of 650 to 4000 cm^{-1}, the FTIR spectrum of each sample was observed and recorded. This test was done to observe any compatibility issues between active ingredients and excipients (17, 18).

2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay

DPPH radical scavenging assay was conducted to observe the antioxidant characteristics of the face serum (19). Different concentrations of the mangosteen peel extract and face serum test samples were prepared using suitable solvents. 100 µL of various concentrations of test samples were plated out in triplicate in a 96-well microtiter plate. Consequently, 100 µL of 0.1mM DPPH solution was added to the test samples, whereas 100 µL of methanol was added to the test samples as the control. The plate was shaken for 2 min followed by incubation for 30 min in the dark and protected from light with aluminum foil. At 520 nm, the proportion of decolorization was measured by a UV spectrometer (20, 21). Ascorbic acid was the positive control. The applied equation-

$$\text{Inhibition}(\%) = \frac{(\text{Abs control} - \text{Abs sample})}{\text{Abs control}} X\ 100$$

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

Anti-bacterial activity test

The agar disc diffusion method was used to evaluate the antibacterial efficacy of the serum against *S. aureus* ATCC 25923 and *S. epidermidis* ATCC 12228. The bacteria were cultured overnight in a broth solution. The discs of the samples were prepared by injecting 200 µL of the samples on the discs followed by air-drying for some time. Then, cotton swaps were used to spread the bacteria sample on a petri dish with Mueller–Hinton agar media. After placing the discs over the inoculated agar media, petri dishes were kept in the incubator overnight. The results were recorded the next day. Tetracycline was used as the positive control (22).

***In-vitro* occlusive test**

This test was done to observe the ability of the face serum to lock the internal moisture inside the skin. An empty beaker was taken and weighed. It was filled with a particular amount of purified water and weighed again. The opening of the beaker was covered with Whatman filter paper, and a specific amount of the sample formulation was spread on the filter paper. After some time, the beaker was weighed again to determine the water loss in percentage. The overall setup was placed in the stability chamber (40 °C, RH 75%) (23).

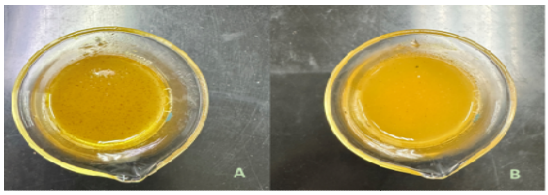

Figure: 1: Mangosteen face serum, before homogenization (A) after homogenization (B)

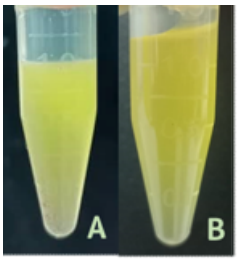

Figure: 2: Redispersion test 1 month (A) 6 months

Result and Discussion

Organoleptic

The organoleptic properties were consistent throughout the observation period of six months. The color of the face serum was yellow due to the incorporation of the mangosteen extract. The smell of the serum sample was of tea tree oil, for being high among the essential oils. The texture before and after the homogenizer was different, as shown in (Figure 1). The latter provided a smoother texture and homogenized formulation.

Redispersion

The redispersion test of the serum also showed satisfactory results with no extra layer of disposition of materials after centrifugation, as exhibited in (Figure 2). The homogeneity did not change even after 6 months.

pH

The following Table 1 shows the pH results of the mangosteen face serum on 1st day, one month, and six months at room temperature. Based on the results in Table 1, all the pH values were in the range of normal pH range applicable for topical use.

Table 1: pH study over six months of mangosteen face serum

Duration of storage	pH values ± SD
Initial	4.71± 0.016
1st month	4.62± 0.038
6 months	4.49± 0.031

Spreadability

The face serum showed a spreadability of 27.62 ± 0.27 cm^2 during a 100g load and 34.21 ± 0.19 cm^2 during a 200g load.

Fourier-transform infrared spectroscopy (FTIR) study

The compatibility between active ingredients and excipients was checked through this test (Figure: 3). The infrared spectrum of mangosteen extract showed some significant peaks in the range of 3243 cm^{-1} to 1079 cm^{-1}. These peaks represent the functional groups of phytochemicals present in the extract. For instance, peak 3243 cm^{-1} indicates -OH group and -COOH, 2973 cm^{-1} and 2910 cm^{-1} represent alkyl group by -CH stretching, C=O stretching at 1650 cm^{-1}, methyl group and carboxylic group in aromatic compounds can be indicated by the range of 1455cm^{-1} to 1372cm^{-1}. The C-O functional group can be involved in the peak of 1278 cm^{-1} to 1043 cm^{-1} range. As shown in Figure 3, the face serum formulation also showed such significant peaks (3282 cm^{-1}, 2939 cm^{-1}, 1644 cm^{-1}, and 1022 cm^{-1}) referring to the chemical integrity of the mangosteen extract phytochemicals that were intact in the formulation. There was no major shift in the spectrum between the active ingredient and the formulation. The FTIR spectrum of blank face serum does not show significant peaks from the mangosteen peel extract powder.

$$F = \frac{A - B}{A} X\ 100$$

Here, A= Amount of purified water taken in the beaker and B= Loss of water

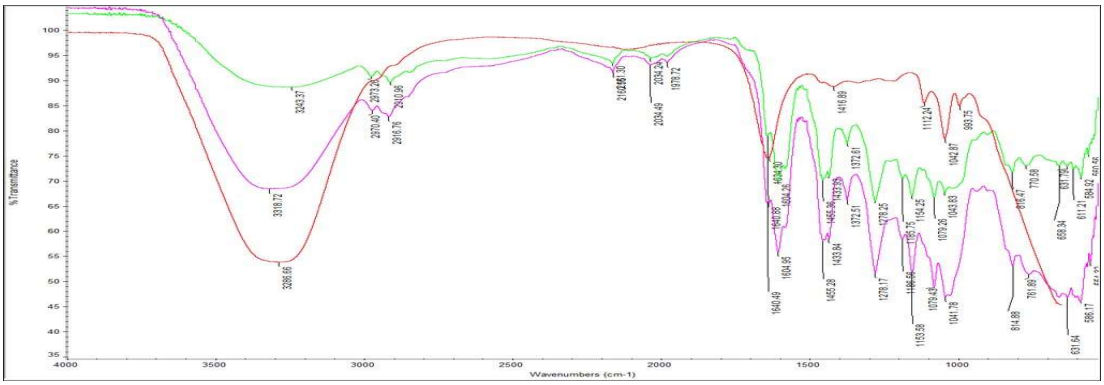

Figure: 3: FTIR spectrum comparison between mangosteen extract powder (green), blank (red), and face serum (purple)

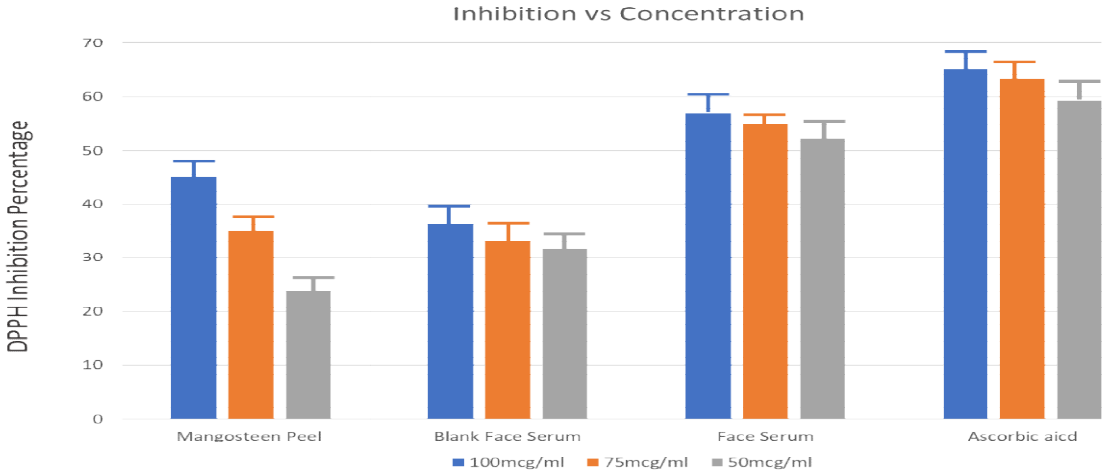

Figure: 4: Comparison of DPPH-free radical inhibition

2,2-Diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay

The serum sample exhibited significant antioxidant activity against DPPH. As shown in Figure 4, the DPPH scavenging capacity for face serum was higher than the mangosteen powder. The blank without the API also showed some inhibitory effect which indicates the main antioxidant property is from the API and the overall formulation shows a synergistic antioxidant effect. The IC_{50} of the formulation was lower than the IC_{50} of the active ingredient. The results are shown in the following (Table 2).

Antibacterial test

The antibacterial study of the face serum samples showed activity against *S. aureus* but not *S. epidermidis* (Figure 5). According to our study, the face serum sample was able to show a zone of inhibition at 18.03 ± 0.24 mm for *S. aureus* exhibited in (Table 3).

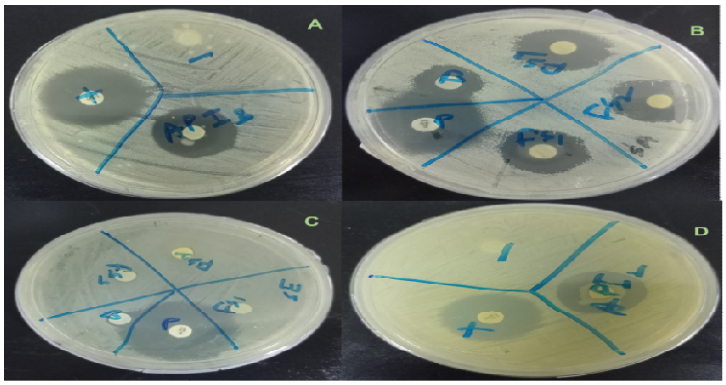

Figure: 5: Antibacterial activity against *S. aureus* A) mangosteen peel powder B) face serum, antibacterial activity against *S. epidermidis* C) face serum D) mangosteen peel powder.

Table: 2: IC_{50} value represents the antioxidant activity of the samples against DPPH free radical.

Sample	IC_{50}
Mangosteen peel extract powder	0.075 mg/mL
Face serum	0.019 mg/mL
Blank	0.198 mg/mL

Table: 3: Zone of inhibition against *S. aureus*

Sample name	Inhibition Zone (mm) ± Standard deviation
Tetracycline	25.2 ± 0.11
Mangosteen peel extract	23 ± 0.14
Face serum	18.03 ± 0.24

In-vitro occlusive test

In terms of occlusive functions, the mangosteen face serum prevented moisture loss by around 52%.

Discussion

The natural mangosteen face serum is developed with specific ingredients that contribute to the efficacy of the face serum. The use of a homogenizer not only provided a smoother texture but also (Figure 1) helped in reducing the size of the mangosteen powder so that it could be incorporated more effectively in the formulation. This production process was suitable for formulating an overall natural mangosteen face serum. The mangosteen peel extract contains valuable phenolic compounds like xanthone, isomangostin, garcinone, and garcimangosone. These contribute to the antioxidant functions that were also seen in this study. The better efficacy in this regard is due to the presence of vitamin C, aloe vera gel, hyaluronic acid, hydrolyzed collagen, and essential oils. These components are well known for their free radical scavenging properties (24, 25). All these provide a synergistic antioxidant effect. The face serum showed significant inhibitory action against *S. aureus*, consistent with other studies on mangosteen peel extract. In those studies, the peel extract is found to be rich in alpha mangostin (26, 11). The FTIR study also indicates the presence of this phenolic compound as these showed strong peaks for -OH, C-O, and C=O in Figure: 5. The presence of the -COOH group is also indicated in the study, which could be phenolic acids like protocatechuic acid and caffeic acid (27).

The pH of a topical formulation is very crucial. A range of 4-6 pH values is considered appropriate for application on the skin. Otherwise, it might cause itchiness, burning sensation, and even severe rashes. The use of

synthetic products like alpha hydroxy acids and beta hydroxy acids can alter the skin's pH and cause side effects as mentioned above. (28) According to the literature, a skin pH of 4-5 can prevent skin infection by many pathogens. This study focuses on using the natural ingredients appropriately to keep the formulation pH range under 5 (29). Hence, this new product can help maintain the skin's protective barrier against infectious microbes. The spreadability results are satisfactory in terms of topical formulation indicating the new face serum will give proper coverage during application and promote ease of application. Preventing moisture loss is another unique property of cosmeceuticals. A significant amount of moisture is needed for a healthy skin barrier which is important for acne treatment. On the other hand, excessive moisture trapped in the skin can cause moisture-associated skin damage (MASD) (30). The mangosteen face serum can prevent 52% moisture loss and provide a healthy balance of water in the skin. Therefore, this face serum formulation can be an effective alternative to the existing anti-acne treatments through its antioxidant properties and anti-bacterial protection against acne-causing bacteria.

Conclusion

Mangosteen is a miraculous fruit with therapeutic properties that can also be applied in the cosmeceutical industry. Developing a formulation that uses natural excipients is the most secure approach for the consumer to utilize the anti-acne benefits of the natural ingredient. The smooth texture and pleasant smell of the essential oils will provide serenity. Developed natural face serum works well for acne treatment owing to its antioxidant and antibacterial qualities. These products are made by avoiding expensive ingredients and machines. Therefore, after commercialization, this will be affordable to everyone in need. In addition to *in-vivo* testing, these compounds can be further tweaked and enhanced for greater efficacy and stability.

Acknowledgement

The authors extend their sincere appreciation to the Faculty of Pharmaceutical Sciences, UCSI University for conducting this study. The authors extend their appreciation to the PSIF grant at UCSI University for funding this work through the research project, under grant number Proj-2019-In-FPS-021.

Conflict of Interest

The authors declare no conflict of interest.

References

1 Omar, N. A., Abd Razak, F. S., Tang, C. H., Helal Uddin, A. B. M., Sarker, M. Z. I., Janakiraman, A. K., & Liew, K. bin. (2020). Development and evaluation of a cosmetic cream formulation containing annona muricata leaves extract. *Latin American Journal of Pharmacy*, *40*(2), 258–266.

2 Subramaniyan, V., Kayarohanam, S., Ashok Kumar, J., & Kumarasamy, V. (2019). Impact of herbal drugs and its clinical application. *International Journal of Research in Pharmaceutical Sciences*, *10*(2), 1340–1345.

3 Panico, A., Serio, F., Bagordo, F., Grassi, T., Idolo, A., de Giorgi, M., Guido, M., Congedo, M., de Donno, A. (2019). Skin safety and health prevention: An overview of chemicals in cosmetic products. Journal of Preventive Medicine and Hygiene, 60(1), E50–E57.

4 Bruusgaard□Mouritsen, M.A., Johansen, J.D. and Garvey, L.H. (2021) 'Clinical manifestations and impact on daily life of allergy to Polyethylene Glycol (PEG) in ten patients', Clinical & Experimental Allergy, 51(3), pp. 463–470.

5 Zuo, T. et al. (2018) 'Urbanization and the gut microbiota in health and inflammatory bowel disease', Nature Reviews Gastroenterology & Hepatology, 15(7), pp. 440–452.

6 Napper, I.E. et al. (2015) 'Characterisation, quantity and sorptive properties

of microplastics extracted from cosmetics', Marine Pollution Bulletin, 99(1–2), pp. 178–185.

7 Ojha Madan Mohan, S., Sinha, S., Chadha, H., Aggarwal, B., Ojha, S., das Chaudhuri, S., & Mahor Jain, S. (2019). Formulation And Evaluation Of Face Serum Containing Bee Venom And Aloe Vera Gel. *World Journal of Pharmaceutical Research*, *8*(2), 1100–1105.

8 Amnuaikit, T., Shankar, R., & Benjakul, S. (2022). Hydrolyzed Fish Collagen Serum from By Product of Food Industry: Cosmetic Product Formulation and Facial Skin Evaluation *Sustainability (Switzerland)*, *14*(24).

9 Juncan, A. M., Moisă, D. G., Santini, A., Morgovan, C., Rus, L. L., Vonica-Țincu, A. L., & Loghin, F. (2021). Advantages of Hyaluronic Acid and Its Combination with Other Bioactive Ingredients in Cosmeceuticals. *Molecules 2021, Vol. 26, Page 4429*, *26*(15), 4429.

10 Lynde, C.W. et al. (2014) 'Moisturizers and Ceramide-containing Moisturizers May Offer Concomitant Therapy with Benefits', The Journal of Clinical and Aesthetic Dermatology, 7(3), pp. 18–26.

11 Chaiwarit, T., Kantrong, N., Sommano, S. R., Rachtanapun, P., Junmahasathien, T., Kumpugdee-Vollrath, M., & Jantrawut, P. (2021). Extraction of Tropical Fruit Peels and Development of HPMC Film Containing the Extracts as an Active Antibacterial Packaging Material. *Molecules (Basel, Switzerland)*, *26*(8), 1–26.

12 Pothitirat, W., Chomnawang, M. T., Supabphol, R., & Gritsanapan, W. (2010). Free radical scavenging and anti-acne activities of mangosteen fruit rind extracts prepared by different extraction methods, *48*(2), 182–186.

13 Lueangarun, S., Sriviriyakul, K., Tempark, T., Managit, C., & Sithisarn, P. (2019). Clinical efficacy of 0.5% topical mangosteen extract in nanoparticle loaded gel in treatment of mild-to-moderate acne vulgaris: A 12-week, split-face, double-blinded, randomized, controlled trial. *Journal of Cosmetic Dermatology*, *18*(5), 1395–1403.

14 Mills, O. H., Criscito, M. C., Schlesinger, T. E., Verdicchio, R., & Szoke, E. (2016). Addressing Free Radical Oxidation in Acne Vulgaris. *The Journal of Clinical and Aesthetic Dermatology*, *9*(1), 25.

15 de Azevedo Ribeiro, R. C., Barreto, S. M. A. G., Ostrosky, E. A., da Rocha-Filho, P. A., Veríssimo, L. M., & Ferrari, M. (2015). Production and characterization of cosmetic nanoemulsions containing Opuntia ficus-indica (L.) mill extract as moisturizing agent. *Molecules (Basel, Switzerland)*, *20*(2), 2492–2509.

16 Mursyid, A. M., & Waris, R. (2021). Formulation And Evaluation Of Pharmaceuticaly Stable Serum Of *Duchesnea Indica* (Arbenan). *Universal Journal of Pharmaceutical Research*, *6*(1), 38–42.

17 Yusefi, M., Shameli, K., Yee, O. S., Teow, S. Y., Hedayatnasab, Z., Jahangirian, H., Webster, T. J., & Kuča, K. (2021). Green synthesis of fe3o4 nanoparticles stabilized by a garcinia mangostana fruit peel extract for hyperthermia and anticancer activities. *International Journal of Nanomedicine*, *16*(2021), 2515–2532.

18 Kurniawan, Y.S., Fahmi, M.R. and Yuliati, L. (2019) 'Isolation and optical properties of natural pigments from Purple Mangosteen peels', IOP Conference Series: Materials Science and Engineering, 833(1), pp. 1–8.

19 Jiea, C. K., Fuloria, S., Subrimanyan, V., Sekar, M., Sathasivam, K. v., Kayarohanam, S., Wu, Y. S., Velaga, V. S. S. R., Janakiraman, A. K., Maziz, M. N. H., & Fuloria, N. K. (2022). Phytochemical screening and Antioxidant activity of Cananga odorata extract. *Research Journal of Pharmacy and Technology*, *15*(3), 1230–1234.

20 Zhou, X., Dai, Q., Huang, X., & Qin, Z. (2021). Preparation and characterizations of antibacterial-antioxidant film from soy protein isolate incorporated with mangosteen peel extract. *E-Polymers*, *21*(1), 575–589.

21 Celiz, G., Renfige, M. and Finetti, M. (2020) 'Spectral analysis allows using the

DPPH* UV–VIS assay to estimate antioxidant activity of colored compounds', Chemical Papers, 74(9), pp. 3101–3109.

22 Ramesh, M., Anbuvannan, M. and Viruthagiri, G. (2015) 'Green synthesis of zno nanoparticles using solanum nigrum leaf extract and their antibacterial activity', Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 136, pp. 864–870.

23 Montenegro, L., Parenti, C., Turnaturi, R., & Pasquinucci, L. (2017). Resveratrol-Loaded Lipid Nanocarriers: Correlation between In Vitro Occlusion Factor and In Vivo Skin Hydrating Effect. *Pharmaceutics*, *9*(4).

24 Radha, M. H., & Laxmipriya, N. P. (2015). Evaluation of biological properties and clinical effectiveness of Aloe vera: A systematic review. *Journal of Traditional and Complementary Medicine*, *5*(1), 21–26.

25 Gocmen, G., Gonul, O., Oktay, N. S., Yarat, A., & Goker, K. (2015). The antioxidant and anti-inflammatory efficiency of hyaluronic acid after third molar extraction. *Journal of Cranio-Maxillofacial Surgery*, *43*(7), 1033–1037.

26 Sultan, O. S., Kantilal, H. K., Khoo, S. P., Davamani, A. F., Eusufzai, S. Z., Rashid, F., Jamayet, N. bin, Soh, J. A., Tan, Y. Y., & Alam, M. K. (2022). The Potential of α-Mangostin from Garcinia mangostana as an Effective Antimicrobial Agent—A Systematic Review and Meta-Analysis. *Antibiotics 2022, Vol. 11, Page 717*, *11*(6), 1–22.

27 Zarena, A.S. and Sankar, K.U. (2011) 'Phenolic acids, flavonoid profile and antioxidant activity in Mangosteen (garcinia mangostanaL.) pericarp', Journal of Food Biochemistry, 36(5), pp. 627–633.

28 Wulaningsih, T.I. (2023). Gluconolactone in Cosmetic (Review Article). KESANS : International Journal of Health and Science, 2(9), pp.1-16.

29 Nguyen, A.V. and Soulika, A.M. (2019) 'The dynamics of the skin's immune system', International Journal of Molecular Sciences, 20(8), pp. 1–53.

30 Voegeli, D., & Hillery, S. (2021). Prevention and management of moisture-associated skin damage. *British Journal of Nursing (Mark Allen Publishing)*, *30*(15), S40–S46.