Pouteria campechiana PULP ETHANOL-WATER EXTRACT AS A BIOACTIVE INGREDIENT FOR TOPICAL DELIVERY OF OIL-IN-WATER NANOEMULSION

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DEDICATION

This thesis is dedicated to beloved my mother, ***Piah binti Sarpah*** *and my beloved siblings, Hafizi, Hanis and Raihan. Thanks for your unconditional love, mentally and financially support towards me.*

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ABSTRACT

The aging process is an inevitable natural course of each human, affecting the entire body, notably the skin's surface. Numerous over-the-counter nanoformulations are available, but none has considered *Pouteria campechiana* (*Pc*) extract as a source of the active ingredient in the formulation. In this study, the hydrophilic fraction of the *Pc* fruit extract was used as an O/W formula for topical application to the human skin. Fatty acid analysis showed that over 18 types of fatty acids were present in the *Pc* pulp, with the *Pc* oil showing an acid value of 6.451. The proximate analysis gave an 8.4% moisture content, 1.7% ash, 4.0% protein, 1.0% fat, 84.9% carbohydrates, with a total energy value of 364.60 Kcal/100g. Next, ultrasonic-assisted extraction (UAE) used in this study facilitated satisfactory extraction of phenolic compounds from the *Pc* pulp. Under optimized UAE conditions (extraction time = 30 min, extraction temperature = 25 °C, ratio of ethanol:water = 60%, v/v), the experimental response surface methodology-assisted optimization, a maximum total phenolic content (TPC) of 1162.80 mg GAE/100 g (DW) was obtained. In the screening process, compositions of jojoba oil (JO), grapeseed oil (GSO), Tween 80, and glycerol (GLY) at 6–12%, 20–26%, 5–7%, and 25–27% gave good particle sizes and PdI between 280–420 nm and 0.18–0.44, respectively. The resultant *Pc* extract showed a percentage 2,2-diphenyl-1-picrylhydrazyl (DPPH) inhibition at 82.91%, IC_{50} of 2.344 mg/mL, ferric reducing antioxidant power (FRAP) value of 836.30±30.60 µmol/100 g DW, and total flavonoid content (TFC) of 813.29 mg QE/100 g. In the D-optimal Mixture Experimental Design experiment, the optimized *Pouteria campechiana* extract nanoemulsion (OPT-*Pc*E-Ne) formulation comprised JO amount (6.25%), GSO amount (34.38%), T80 (14.06%), and GLY (45.31%) at fixed 0.5% phenoxyethanol, 5% *Pc*E, 2% xanthan gum (XG), and 0.5% perfume oil. The OPT-*Pc*E-Ne yielded the lowest particle size at 222±0.61 nm and PdI of 0.16. The OPT-*Pc*E-Ne gave good organoleptic and stability profiles by remaining creamy white, without any color change for up to 90 days, with a zeta potential of –32.6±0.5 mV and an acceptable pH (4.81±0.02). The OPT-*Pc*E-Ne droplets were averagely sized at 93.46−183.13 nm in the transmission electron microscopy (TEM) micrograph and gave conductivity of 0.22 µS/cm. The OPT-*Pc*E-Ne rheology followed a Bingham plastic behavior, suggesting that the cream must be applied to the skin in successive layers. In the accelerated tests, phase separation in the OPT-*Pc*E-Ne was absent in the ultracentrifugation and freeze-thaw cycle studies. Next, samples stored for 6 weeks showed mean particle size and PdI between 155–315 nm and 0.16−0.28 for 4±2 °C, 415–150 nm and 0.16−0.26 for 28±2 °C and 125–295 nm and 0.14−0.45 for storage at 50±2 °C. The general non-linearity for the OPT-*Pc*E-Ne stored at 4±2 °C, 28±2 °C proved the system was not destabilized by coalescence but more so by Ostwald ripening when stored for long durations at 28±2 °C (R^2=0.7753). The OPT-*Pc*E-Ne exhibited a release of ~0.18% of *Pc*E in the 0–6 h duration, with a maximal level of 5.17% after 24 h. Pertinently, the OPT-*Pc*E-Ne was also free from microorganisms- and heavy metal contamination. In the sensory evaluation study, the OPT-*Pc*E-Ne exhibited the highest color and texture scores compared to other commercial lotions scoring 7.3 and 6.6, respectively. However, the scent was the lowest-rated factor at a collective scale of 6.1. The study findings supported the use of the *Pc*E as a natural-based ingredient in cosmeceuticals and the OPT-*Pc*E-Ne as a topical lotion on human skin.

ABSTRAK

Proses penuaan adalah kejadian semula jadi yang tidak dapat dielakkan oleh setiap manusia, ianya mempengaruhi seluruh tubuh, terutamanya permukaan kulit. Terdapat banyak nanoformulasi di kaunter, tetapi tidak ada yang mempertimbangkan ekstrak *Pouteria campechiana* (*Pc*) sebagai sumber bahan aktif di dalam formulasi. Dalam kajian ini, pecahan hidrofilik ekstrak buah *Pc* telah digunakan sebagai formula O/W untuk aplikasi topikal pada kulit manusia. Analisis asid lemak menunjukkan bahawa lebih daripada 18 jenis asid lemak wujud di dalam pulpa *Pc*, dengan minyak *Pc* menunjukkan nilai asid 6.451. Analisis proksimat memberikan kadar kelembapan 8.4%, abu 1.7%, protein 4.0%, lemak 1.0%, karbohidrat 84.9%, dengan nilai keseluruhan tenaga 364.60 Kcal/100g. Seterusnya, pengeskstrakan berbantukan ultrasonik (UAE) yang digunakan dalam kajian ini membantu pengekstrakan sebatian fenolik daripada pulpa *Pc* dengan memuaskan. Di bawah keadaan UAE yang optimum (masa pengekstrakan = 30 min, suhu pengekstrakan = 25 °C, nisbah etanol:air = 60%, v/v), pengoptimuman ujikaji berbantukan kaedah permukaan gerak balas, jumlah kandungan fenolik (TPC) maksimum 1162.80 mg GAE/100 g (DW) telah diperoleh. Dalam proses penyaringan, komposisi minyak jojoba (JO), minyak biji anggur (GSO), Tween 80, dan gliserol (GLY) pada 6–12%, 20–26%, 5–7%, dan 25–27% yang masing-masing memberikan ukuran partikel yang baik dan PdI antara 280–420 nm dan 0.18–0.44. Ekstrak *Pc* yang dihasilkan menunjukkan peratusan perencatan 2,2-difenil-1-pikrilhidrazil (DPPH) pada 82.91%, IC_{50} 2.344 mg/mL, nilai keupayaan antioksidan penurunan ferik (FRAP) 836.30±30.60 µmol/100 g DW, dan jumlah kandungan flavonoid (TFC) 813.29 mg QE/100 g. Dalam eksperimen Reka Bentuk Percampuran D-optimum, formulasi optimum nanoemulsi ekstrak *Pouteria campechiana* (OPT-*Pc*E-Ne) terdiri daripada jumlah JO (6.25%), jumlah GSO (34.38%), T80 (14.06%), dan GLY (45.31%) pada tetapan 0.5% fenoksietanol, 5% ekstrak *Pc* (*Pc*E), 2% gam xanthan (XG), dan 0.5% minyak wangi. OPT-*Pc*E-Ne menghasilkan saiz zarah terendah pada 222±0.61 nm dan PdI 0.16. OPT-*Pc*E-Ne memberikan profil organoleptik dan kestabilan yang baik dengan kekal putih berkrim, tanpa apa-apa perubahan warna sehingga 90 hari, dengan potensi zeta –32.6±0.5 mV dan pH yang boleh diterima (4.81±0.02). Titisan OPT-*Pc*E-Ne memberikan saiz purata 93.46-183.13 nm dalam mikrograf mikroskopi elektron penghantaran (TEM) dan memberikan kekonduksian 0.22 µS/cm. Reologi OPT-*Pc*E-Ne mematuhi kelakuan plastik Bingham yang mencadangkan bahawa krim ini mesti digunakan pada kulit secara lapisan berturut-turut. Dalam ujian dipercepatkan, pemisahan fasa OPT-*Pc*E-Ne tidak berlaku dalam kajian ultrasentrifugasi dan kitaran beku-cair. Seterusnya, sampel yang disimpan selama 6 minggu menunjukkan saiz zarah dan PdI min antara 155–315 nm dan 0.16–0.28 untuk suhu 4±2 °C, 415–150 nm dan 0.16–0.26 untuk 28±2 °C dan 125–295 nm dan 0.14 −0.45 untuk penyimpanan pada suhu 50±2 °C. Ketaklinearan umum untuk OPT-*Pc*E-Ne yang disimpan pada suhu 4±2 °C, 28±2 °C membuktikan sistem ini tidak ternyahstabil dengan penyatuan tetapi lebih kepada pematangan Ostwald apabila disimpan untuk jangka masa yang lama pada 28±2 °C (R^2=0.7753). OPT-*Pc*E-Ne menunjukkan pelepasan ~0.18% *Pc*E dalam jangka masa 0-6 jam, pada tahap maksimum 5.17% setelah 24 jam. Bersesuaian dengan itu, OPT-*Pc*E-Ne juga bebas daripada mikroorganisma dan pencemaran logam berat. Dalam kajian penilaian deria, OPT-*Pc*E-Ne mempamerkan skor warna dan tekstur tertinggi berbanding losyen komersial yang lain, masing-masing dengan skor 7.3 dan 6.6. Walau bagaimanapun, faktor bau mendapat penarafan terendah pada skala terkumpul 6.1. Hasil kajian ini menyokong penggunaan *Pc*E sebagai bahan asas semula jadi dalam kosmeseutikal dan OPT-*Pc*E-Ne sebagai losyen topikal pada kulit manusia.

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LIST OF ABBREVIATIONS

Pc	-	*Pouteria campechiana*
JO	-	Jojoba oil
GSO	-	Grapeseed oil
GLY	-	Glycerol
T80	-	Tween 80
MD	-	Mixture Design
RSM	-	Response Surface Methodology
PdI	-	Polydiversity Index
TPC	-	Total Phenolic Content
TFC	-	Total Flavonoid Content
GA	-	Gallic acid
OPT-*Pc*E-Ne	-	Optimized *Pouteria campechiana* Extract's Nanoemulsion
OVAT	-	One-Variable-at-Time
ANOVA	-	Analysis of Variances
CCD	-	Central Composite Design
O/W	-	Oil-in-water
W/O	-	Water-in-oil
UAE	-	Ultrasonic-assisted Extraction
TEM	-	Transmission electron microscopes
IUPAC	-	International Union of Pure and Applied Chemistry
PIT	-	Phase inversion temperature
AOAC	-	Association of Official Agricultural Chemists
BHT	-	Butylated hydroxytoluene
DPPH	-	2,2-diphenyl-1-picrylhydrazyl
FRAP	-	Ferric Reducing Antioxidant Power
NPRA	-	National Pharmaceutical Regulatory Agency

LIST OF SYMBOLS

°C	-	Degree Celsius
g	-	Gram
h	-	Hour
mg	-	Milligram
mL	-	Milliliter
nm	-	Nanometer
rpm	-	Rotation per minutes
%	-	Percentage
mM	-	Millimolar
v/v	-	Volume per volume
w/v	-	Weight per volume
µg	-	Microgram
µL	-	Microliter
min	-	Minute
s	-	Second
ppm	-	Parts per million

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CHAPTER 1

INTRODUCTION

1.1 Background of the Study

The aging process is an inevitable natural course of each human, affecting the entire body, notably the skin's surface. The changes gradually manifest as wrinkles and fine lines, alterations in skin pigmentation, skin appearing thinner due to epidermal and dermal atrophy (Holtz, 2008). Several other factors such as environmental and nutritional also contribute to the above said changes of human skin. There are claims that the biological aging process can be delayed by factors *viz.* consumption of natural antioxidants such as Vitamin E (Fata *et al.*, 2014, Hategekimana *et al.*, 2015, Shikh *et al.*, 2021), carnosine (McFarland and Holliday, 1994, Aldini *et al.*, 2020, Wu *et al.*, 2021) and garlic (Rahman, 2003, Ahangar-Sirous *et al.*, 2021). These components are believed to have a pro-longevity effect on the primary human cultures, thus their increasingly popular use as components in anti-aging products *viz.* cosmeceuticals and pharmaceuticals products. The market for cosmeceutical products has grown substantially because of increasing consumer awareness for dermatologically nutritional products (Royer *et al.,* 2013). The boundary between cosmetics and topical pharmaceutical products are now difficult to distinguish, with "cosmeceuticals" gaining popularity because these products lie between the grey zone of cosmetics and pharmaceuticals (Katz *et al.,* 2015). The applications of cosmeceuticals have now extended to skin protection, whitening, tanning, anti-aging and anti-wrinkling, deodorants, and for nail and hair care.

There are many undiscovered interesting phyto-active compounds for such products (Lee *et al.*, 2007, Patel *et al.,* 2009, Ghimeray *et al.*, 2015, F Maluf *et al.*, 2018, Averilla *et al.*, 2019). Natural compounds are preferred in cosmeceuticals due to reports of carcinogenicity of synthetic chemicals and other undesirable substances *viz.* reproductive toxins, skin penetrators, endocrine disrupters, and plasticizer in

cosmeceutical formulations (Wang *et al.*, 2015, Radice *et al.*, 2016, Bilal *et al.*, 2020, Sharma *et al.*, 2021). Polyphenolics in plants are naturally occurring antioxidants which include gallic acid and their derivatives favored for cosmeceuticals. Their structures have at least one aromatic ring and one or more hydroxyl groups (Monteiro e Silva *et al.*, 2017). Also, *in-silico* investigation by Romes and co-workers (2021), revealed the ability gallic acid and catechin in the oil palm leaves extract nanoemulsion to bind with the AQP-3 protein to promote skin moisturization, and increases the expression of the proteins to hydrate the human skin better (Romes *et al.*, 2021). Another in vivo study on GA-loaded cosmetic gel formulation demonstrated its efficacy for reducing lipid peroxides in the stratum corneum of the volunteers (Monteiro *et al.*, 2017). The data imply that it is possible to create a cosmetic formulation with antioxidant activity employing GA as the active cosmetic.

Malaysia is one of few countries in Southeast Asia with several species of underutilized fruits. The unfamiliarity of the fruits to consumers results in nearly zero demand (Ikram *et al.*, 2009, Lim, 2013, Fitriansyah *et al.*, 2021), and their nutritional content remaining undiscovered (Kong *et al.*, 2013, Aseervatham *et al.*, 2014). Among such forgotten fruits is the *Pouteria campechiana* (*Pc*) (Zhang *et al.*), a tropical fruit belonging to the family *Sapotaceae.* In Malay, it is commonly called 'Buah Kuning Telur' while it bears a simpler English name, "Canistel'. This fruit is found in Central America, some parts Asia such as Sri Lanka, Indonesia, and South Asian countries (de Lanerolle *et al.*, 2009, Silva *et al.*, 2009, Elsayed *et al.*, 2016, Fitriansyah *et al.*, 2021). The ovoid-shape *Pc* measures between 7.5 and 12.5 cm in length and 5 and 7.5 cm in breadth (Ma *et al.*, 2004) with a central yellow pulp that can consist of one to four hard seeds (Balerdi and Shaw). The richly textured *Pc* fruit contains a myriad of nutrients, *viz.* carbohydrates, vitamin A and minerals (Coronel *et al.*, 1986). Phytochemically, the *Pc* fruit consisted mainly of triterpenes and long chains or acetate esters of flavonoid derivatives (Ma *et al.*, 2004). The natural fatty acids from other Pouteria species, i.e., *Pouteria lucuma* nut, have been reported to promote skin regeneration (Rojo *et al.*, 2010), while extracts of *Pouteria ramiflora* are said to confer neuroprotective effects against oxidative damage. The versatility of the Pouteria species fruits is relatable by their abundance in biologically active polyphenolic antioxidants *viz.* gallic acid, myricitrin, (+)-gallocatechin, (+)-catechin, dihydromyricetin, (+)-catechin-3-O-gallate, and (−)-ikrai-epicatechin (Ma *et al.*,

2004). The Mexicans believed that the *Pc* contains antipyretic substances, and is used to treat skin eruptions in Cuba (Morton, 1987). Based on the literature, the study believes the *Pc* fruit extract could have a possible application in skin rejuvenating concoctions to view the natural abundance of polyphenolic antioxidants (Ma *et al.*, 2004, Elsayed *et al.*, 2016, Fitriansyah *et al.*, 2021). Conventional plant extraction methods include Soxhlet extraction, maceration, and hydro distillation are three methods for extracting phenolic compounds utilizing the liquid-liquid extraction method. However, the modern extraction method using ultrasonic-assisted Extraction (UAE) is better as cavitation bubbles around the samples' tissue rupture the cell wall and release more of the cell contents (Altemimi *et al.*, 2016). Hence, UAE is a good extraction method to obtain higher concentration of GA and catechins from the *Pc* pulp, in this study.

Nanoemulsions can be classified based on their morphology, wherein a 'water-based', or oil in water (O/W), corresponding to a system with water as the continuous phase and oil as the dispersed phase (Mason *et al.*, 2006, Singh *et al.*, 2017), whereas the inversed condition yields an 'oil-based' or water in oil (W/O) emulsion. The small droplet size of nanoemulsions allows uniform deposition and penetration of active ingredients through the skin surface (Sonnevilleaubrun, 2004), with better penetration efficacy of the active ingredients due to the large surface area and low surface tension of the emulsion system (Bouchemal *et al.*, 2004). Thus, only 3-10 % of surfactants is required during preparation (Tan *et al.*, 2006). As a result, nanoemulsions appear more fluid (at low oil concentrations), with display of appealing physical properties and skin feel, especially in the absence or the small use of thickeners. On a different note, particle sizes between 20-300 nm in nanoemulsions ns are consistently proven to be effective and show better penetration through the skin. The higher bioavailability of the active ingredients in nanoemulsions can better penetrate through the pores of the human skin over micron-sized ones (Effiong *et al.*, 2019, Upasani *et al.*, 2020). This is feature is advantage when the active ingredients are obtained in low quantities from plant sources or when drugs are too expensive to be formulated in large quantities. The key benefit of using nanotechnology in cosmeceutical applications are to improve stability of cosmetic ingredients, such as unsaturated fatty acids, vitamins, or antioxidants encapsulated within nanoparticles (Care *et al.*, 2017), increased penetration rate of certain ingredients, such as vitamins and other antioxidants (Katz

et al., 2015), and enhanced product aesthetics. Substantial leaps in nanotechnology have made possible for formulators to continually develop newer and more efficient topical delivery systems.

1.2 Statement of Problem

Concerns about the safety of synthetic chemicals, as well as their cancer-causing effects on human skin (Costa & Santos, 2017), necessitate the scientific community's ongoing attempts to identify safer alternatives. Considering the inevitable age-related deterioration of the human skin from constant exposures to pollutants and an unhealthy diet, as well as the possible long-term hazards that synthetic chemicals impart on our skin, the use of topically applied phyto-based nano lotions would be a better option. That said, this study proposes to use polyphenolics in plants with high levels of antioxidants GA and their derivatives as the viable option for this application. A good source is the *Pc* pulp extract, rich in such compounds, and obtainable in higher quantities through UAE. This new extraction approach has been shown to be more effective in extracting bioactive compounds in plants and fruits. However, conditions of *Pc* fruit extract for the maximum total phenolic content must first be discovered.

In this study, the hydrophilic fraction of the *Pc* fruit extract can be prepared as an O/W formula for topical application and better penetration through the human skin and improve the overall skin condition. The crude polyphenolic-rich *Pc* extract GA and its derivatives could effectively combat the unpleasant effects of environmental pollutants and physiological processes that deteriorate the overall quality of human skin. Consequently, for better delivery of the Pc extract through the skin, this study proposed an oil-in-water (O/W) nano-sized cream formulated from the polyphenolic rich *Pc* pulp extract's hydrophilic component. However, the composition, mixing protocol the in-vitro delivery efficacy remains unclear, and thus must be found for the *Pc* pulp extract to be effectively formulated into a topical nanoemulsion. It is hypothesized that the nano-sized, GA-rich Pc extract can better penetrate the stratum corneum and quench free radical scavengers in the skin.

The study first focused on the comprehensive physicochemical assessment of the *Pc* pulp EtOH:H_2O extract before formulating the nano cream for topical delivery through the skin. This part of the assessment is crucial to seek empirical confirmation on the hidden benefits and suitability of the *Pc* extracts for incorporation as an active ingredient into anti-aging nano-formulation. While numerous skin rejuvenating formulations are found on the open market, it is worth noting that none has considered the *Pc* extract as a source of the active ingredient in a nano lotion formulation. Moreover, the role of nano-formulated gallic acid for hydration effect through topical delivery through the skin is yet to be explored, and its benefits remain to be seen. The O/W of the gallic acid nano lotion system could improve the *Pc* extracts' bioavailability and efficacy for topical application. Moreover, literature has shown that nano-formulated lotions are an effective system to transport phyto-active compounds through the skin topically and are released at target sites in a sustained-release manner (Shah *et al.*, 2010, Santos *et al.*, 2019).

1.3 Objectives of the Study

The objectives of this research are as follows:

(a) To characterize the *Pc* fruit pulp and optimize the ultrasonic-assisted extraction (UAE) process for the *Pc* extract's highest total phenolic content and antioxidant activity.

(b) To formulate and optimize the *Pc* extract containing nano cream using the D-optimal Mixture Experimental Design (MED).

(c) To characterize the physicohemical characteristics of the optimized the *Pc*-based nanoemulsion.

(d) To evaluate *in vitro* efficacy study and sensory evaluation of the *Pc*-based nano lotion.

1.4 Hypotheses of Study

The UAE method to extract the antioxidants from the *Pc* pulp can yield satisfactorily good amounts of phyto-active compounds. The D-optimal MED-assisted optimization to prepare the *Pc* extract containing nano cream can produce a stable and effective O/W nanoemulsion system. The *Pc* extract nano lotion could improve the skin condition by imparting a better hydration effect.

1.5 Scopes of the Study

This study was split into four phases. The first involved the screening of variables for the UAE of the *Pc* pulp to obtain the crude extract using the One-Variable at-a-Time (OVAT) method for three relevant parameters *viz.* effect of time, temperature, and solvent ratio (EtOH:H_2O). Antioxidant tests for the *Pc* pulp crude extracts was done to monitor the total phenolic content (TPC), total flavonoid content (TFC), the 1,1-diphenyl-2-picrylhydrazyl radical scavenging activity (DPPH), and Ferric reducing antioxidant power (FRAP).

The second phase of this study revolved around the optimization of the *Pc* pulp extraction process and the characterization of the *Pc* pulp crude extracts. The UAE conditions were optimized for the response of high TPC by the method of response surface methodology (RSM). The variables monitored were extraction time (A), extraction temperature (B), the ratio of ethanol:water (C). The *Pc* crude extract was characterized for fatty acid composition and determination of acid value. Reverse-phase high-performance liquid chromatography (HPLC) was used to analyze the *Pc* crude extract. The ultra-high-performance liquid chromatography (UHPLC) was performed to diagnose the active compounds that contributed to the antioxidant activity in *Pc* extracts.

In the third phase, this study screened and optimized the protocol to prepare *Pc* extract containing oil in water (O/W) nano lotion system using a combined hot-hot process, ultrasonic and high-speed homogenization. The screening process identified

the suitable ranges of water and oils mixture, surfactant, co-surfactant(s), and thickening agent. The quality of the resultant nano lotions was monitored for particle size and PdI. The O/W nano lotions were also subjected to tests for stability and pH. In the subsequent D-optimal MD-assisted optimization to prepare the *Pc* extract containing nano cream, four relevant parameters that can influence the quality of the nano cream were considered: ratio such as Jojoba oil, grapeseed oil, Tween 80, and glycerol, for the response of particle size (R_1) and PDI (R_2).

The fourth phase characterized the MD-optimized *Pc* extract containing O/W nano lotions for several parameters. The tested parameters were particle size, PdI, zeta potential, pH assessment, conductivity, thermodynamic stability test, i.e. (a) accelerate study (freeze-thaw cycle, centrifugation studies, mechanical vibration test), (b) long term stability (temperature varied), rheology study, pH value, and organoleptic evaluation. Finally, the morphology of the optimized *Pc* extract containing nano cream was visualized by transmission electron microscopy (TEM). The safety evaluation for the *Pc* nano lotion was evaluated for heavy metal- and microbiological tests. Next, the in-vitro release study was done on the *Pc* extract containing nano lotion. This step was done to determine the effect of the *Pc* extract on the characteristics and performance of the nano lotion. The study's final part subjected the optimized *Pc* extract nano lotion to sensory profiling for customer product acceptance. The sensory evaluation was done to compare the *Pc* extract containing nano lotion with a comparable commercial hand lotion for texture, absorption, moisture, and after-feel characteristics. A total of 40 participants were involved in the assessment, and the data were analyzed based on Hedonic scale and by Microsoft Excel for comparative statistical relevance.

1.6 Significance of the Study

The polyphenolic-rich *Pc* extract containing nano cream developed by this study may confer a new lease of life in terms of possible uses for the forgotten fruit. Furthermore, *Pc* extract encapsulated within the nano-sized O/W the optimized nanoemulsion could successfully deliver the ingredients through the stratum corneum of the human skin. This, in turn, enhances the bioavailability of the antioxidants. Most

importantly, a lesser loading of the bioactive components in the formulation is needed due to the effective delivery technique. Also, the study findings could potentially turn the fruit into a commodity that has cosmeceutical relevance. Most interestingly, the applicability of the *Pc* extract nanoemulsion's efficacy to improve the human skin condition can be affirmed once and for all. Henceforth, the findings can be put to good use by the general public.

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