SOLID LIPID PARTICLES FOR IMPROVED DERMAL DELIVERY OF VIRGIN COCONUT OIL

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requirements for the award of the degree of
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Dedicated to my beloved Husband, Mohd Husni Yusoff, my mom, Wan Norhani Wan Mustaffa, my dad, Mohamed Noor Bin Ba Md Yunus and my children, Iman Syakirin and Nur Damia Safrina.

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ABSTRACT

Coconut oil has been recognized as a health oil in Ayurverdic medicine. Virgin Coconut Oil (VCO) is unique because it has a high degree of saturated fats, medium chain triglycerides, antioxidant activity and antimicrobials property. These factors make VCO a suitable lipophilic active ingredient in skin care products. VCO is usually extracted from well matured and fresh coconut through specialized process and is prepared in such a way that does not damage its natural structure or nutrition. Solid Lipid Particles (SLPs) is a novel delivery system of lipophilic functional cosmetic active ingredients. In this work, formulation, characterization and efficacy of VCO-SLPs have been studied. VCO-SLPs were prepared using ultrasonification of molten stearic acid and virgin coconut oil in an aqueous solution. From screening experiments, the best formula for VCO-SLPs was 1.78% Tween 80, 0.73% soy lecithin, 10% stearic acid, 5% VCO and 82.5% distilled water. Ultrasonicating was performed at several power intensities and different exposure times. The particle sizes of VCO-SLPs obtained were ranged from 0.608 µm to 44.265 µm. The zeta potentials of all the particles were from -43.2 mV to -47.5 mV showing that the particles obtained have good stability. The cumulative permeation of the VCO-SLPs range from 3.83 µg/cm^2 to 3.59 µg/cm^2 for VCO-SLPs in the range of 0.608 µm to 39.255 µm. VCO-SLPs with the particle size of 0.608 µm was chosen for subsequent study. Double blind skin evaluation test was conducted to analyze the performance of the VCO-SLPs incorporated moisturizing lotion. Moisturizing lotion incorporated with VCO-SLPs was found to increase skin hydration and skin elasticity by 24.8% and 2.60% respectively from day 0 to day 28. This shows that solid lipid particles has the potential to be utilized as a carrier for improved dermal delivery of VCO.

ABSTRAK

Minyak kelapa telah diiktiraf sebagai minyak kesihatan dalam perubatan Ayurverdic. Minyak Kelapa Dara (VCO) bersifat unik kerana ia mempunyai kandungan lemak tepu yang tinggi, rantai trigliserida sederhana, aktiviti antioksidan dan ciri-ciri antimikrobial. Faktor ini menjadikan VCO sebagai bahan lipofilik aktif yang sesuai digunakan di dalam produk penjagaan kulit. VCO kebiasaannya diekstrak daripada kelapa yang matang dan segar melalui beberapa proses bagi mengelakkan kerosakan kepada struktur dan nutrien semulajadinya. Partikel Lipid Pepejal (SLPs) adalah sistem penyampaian bagi bahan-bahan kosmetik bersifat lipophilik. Dalam kajian ini, formulasi, pencirian dan keberkesanan VCO-SLPs telah dikaji. VCO-SLPs telah disediakan menggunakan ultrasonifikasi asid stearik cair dan minyak kelapa dara dalam satu larutan akuas. Daripada eksperimen saringan, formula terbaik untuk VCO-SLPs mengandungi 1.78% Tween 80, lesitin soya 0.73%, 10% asid stearik, VCO 5% dan 82.5% air suling. Ultrasonikasi dijalankan pada kuasa dan masa pendedahan yang berbeza. Saiz zarah VCO-SLPs yang terhasil adalah 0.608 μm hingga 44.265 μm. Potensi zeta bagi semua zarah yang terhasil adalah dari -43.2 mV sehingga -47.5 mV yang menunjukkan bahawa zarah yang diperolehi mempunyai kestabilan yang baik. Penyerapan kumulatif VCO-SLPs adalah dari 3.83 μg/cm^2 sehingga 3.59 μg/cm^2 untuk partikel bersaiz 0.608 μm sehingga 39.255 μm. VCO-SLPs dengan saiz partikel 0.608 μm telah dipilih bagi kajian seterusnya. Penilaian pada kulit secara gelap ganda telah dijalankan bagi mengkaji keberkesanan losyen pelembab VCO-SLPs. Losyen pelembab yang mengandungi VCO-SLPs didapati telah meningkatkan hidrat dan keanjalan kulit masing-masing sebanyak 24.8% dan 2.60% dari hari 0 sehingga hari ke 28. Ini menunjukkan bahawa, partikel lipid pepejal berpotensi sebagai agen pembawa VCO yang lebih baik ke bahagian kulit.

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NOMENCLATURES

DLS	-	Dynamic light scattering
EDTA	-	Ethylenediaminetetraacetic acid
EE	-	Entrapment Efficiency
Fe	-	Ferum
GMP	-	Good Manufacturing Practices
GRAS	-	**G**enerally Recognized as Safe
HLB	-	Hydrophilic Lipophilic Balance
HPLC	-	High Performance Liquid Chromatography
LCFAs	-	Long chain fatty acids
LD	-	Laser diffraction
MCFAs	-	Medium chain fatty acids
MCT	-	Medium chain triglycerides
PBS	-	Phosphate buffer solution
PI	-	Polydispersity index
Q10	-	Coenzyme
RHLB	-	Required Hydrophilic-Lipophilic Balance
SC	-	Stratum corneum
SCFAs	-	Short chain fatty acids
SLM	-	Solid Lipid Microparticles
SLN	-	Solid Lipid Nanoparticles
SLP	-	Solid Lipid Particles
TEWL	-	Transepidermal Water Loss
UV	-	Ultraviolet
VCO	-	Virgin Coconut Oil
µg	-	microgram
µm	-	Micrometre

cfu	-	C*olony-forming unit*
cm	-	Centimetre
g	-	Gram
h	-	*hour*
kg	-	Kilogram
mg	-	milligram
mL	-	Millilitre
mm	-	Millimetre
mV	-	Millivolt
pH	-	measure of the concentration of hydrogen ions in a solution
ppm	-	parts per million
rpm	-	round per minute
wt	-	Weight
$\%$	-	Percentage
n_1	-	total concentrations of ferulic acid in the VCO
n_2	-	concentrations of ferulic acid in encapsulated VCO
E	-	Electric field
ºC	-	degree Celsius
v	-	Velocity
ε	-	Permittivity of the electrolytic solution
η	-	Viscosity
ξ	-	Zeta potential
A	-	Surface area, cm^2
C	-	Concentration of ferulic acid from calibration graph, mg/L
D	-	Diffusion coefficient
Js	-	Flux at the steady state, ug/cm^2h
Kp	-	Permeability coefficient, cm/h
Pr	-	Permeation rate, ug/cm^2h
V	-	Total Volume of VCO-SLPs, mL
dF	-	Dilution factor
v	-	Volume, mL

CHAPTER I

INTRODUCTION

1.1 Research Background

Virgin coconut oil (VCO) is one of the nutraceutical ingredients that has been extensively used in tropical areas for health related purposes. It is also traditionally used to improve skin health and hair growth. Virgin coconut oil is the highest quality of coconut oil obtained from coconut fruit (Fife and Kabara, 2004). As the finest grade coconut oil, VCO shares similar chemical properties as coconut oil with some added benefit of being higher in phenolic content and antioxidant activity (Marina *et. al.,* 2009).

There are limited scientific based studies on the benefits of virgin coconut oil from cosmetic point of view. Cosmetic treatments refer to non-medical procedures to improve the appearance of skin and hair. Nowadays, there are many cosmeceutical products incorporated with the latest nanotechnology materials to enhance the performance of the products (Hommoss, 2008; Uner and Yener, 2007 and Manconi *et. al.,* 2006). Solid Lipid Particles (SLPs) is one of the nanocarrier techniques widely used in the cosmeceutical and pharmaceutical industries to enhance penetration and control the release of active ingredients to the targeted area (Mishra

et. al., 2011; Manconi *et. al.,* 2006). In this work, SLPs was studied to improve dermal delivery of VCO as moisturizing properties. SLPs incorporated with VCO can be a potential cosmetic product that targets skin dehydration issues.

The basic processes of keeping skin in good condition are through cleaning and moisturizing (Fluhr *et. al*. 2008; Draelos, 1995). Cleaning is necessary to remove dirt, skin secretion and microorganism, which otherwise would produce unpleasant odour and disease (Kownatzki, 2003; Larson *et. al.,* 2000; Rhein, 2007). Ultimate goal of cleaning is not just a clean skin, but a healthy skin.

Moisturizing of the skin aims to restore skin to its natural protective condition, resulting in healthy skin. Cleansers and moisturizers can be considered as cosmeceuticals if they can alter structure and function. Moisturizers are externally applied compounds comprising multiple components, including occlusive ingredient, emollients and humectants (Gao *et. al.,* 2008*).* Occlusive moisturizing ingredients are the oily substances that impair the evaporation of skin moisture by forming an epicutaneous greasy film that impedes water loss. By reducing evaporation, it will increase skin's hydration.

Nowadays, there are many moisturizers in the market that are formulated based on skin type. Basically the cosmetic manufacturers will add occlusive agents and humectants for restoration of natural moisturizing factors on the skin (Draelos, 2009). They fulfill a variety of functions by either acting directly on skin or being a cosmetically elegant vehicle for the delivery of specific active ingredients.

Based on the statistics from Euromonitor International (Datamonitor, 2011) worldwide skin care market remains the most important category in terms of values, comprising 23% of global beauty and personal care. Facial moisturizer shows the highest growth compared to other skin care. Figure 1.1 shows the future trend for global skin care market until 2014. From the graph, it shows that the future growth in

skin care will continue to be driven by anti-agers followed by facial moisturizers. It can be said that, facial moisturizer is still one of the major skin care product that will be chosen by the consumers.

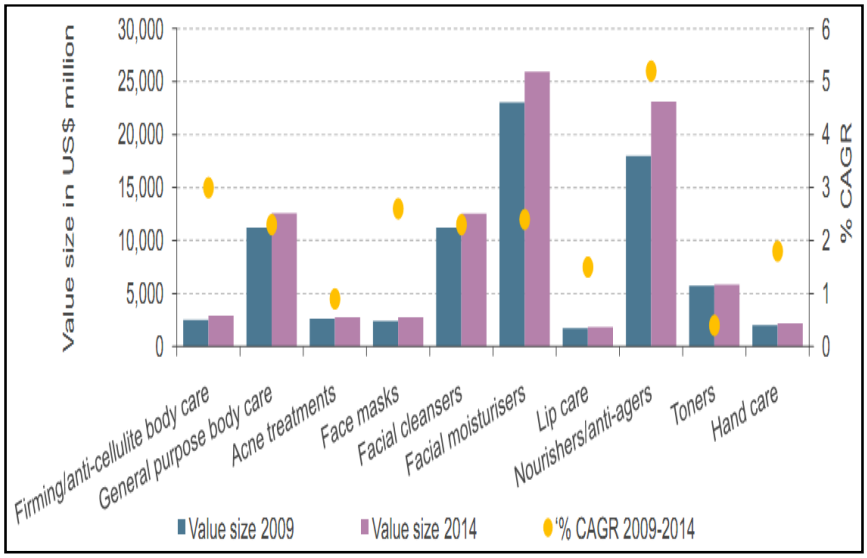

Figure 1.1 : Skin Care Performance by Category 2009-2014 (Datamonitor, 2011)

Due to that, this research was focused on the formulation of a moisturizer based on VCO loaded solid lipid particles. Virgin coconut oil was encapsulated in solid lipid particles to ensure better delivery into the skin. The efficacy of the VCO-SLPs moisturizing cream was evaluated *in vivo* based on skin moisture and elasticity throughout 28 days of application. Figure 1.2 shows finished product of hand and body moisturizer using VCO-SLPs commercialized by Phyto Biznet Sdn Bhd using the patented method by Mohamed Noor *et. al.* (2010).

Figure 1.2 : Hand & Body Lotion containing VCO-SLPs commercialized by Institute of Bioproduct Development, UTM (Brand : Wisderm Cosmetics, Mohamed Noor *et. al.,* 2010)

1.2 Problem Statement

Virgin coconut oil becomes popular since a few years back, due to its therapeutic value. Nowadays consumers are demanding edible oils that are natural and free from chemical treatment. VCO is also incorporated in cosmetic products such as skin moisturizers and hair care products. However, there is a limited number of research works on the performance of virgin coconut oil in topical cosmetic products. Work in this area is crucial as topical administration of bioactive compounds can result in poor absorption and limited bioavailability. More importantly, many of these compounds are chemically unstable.

This problem may be solved by developing a wide variety of delivery systems that not only result in significant improvements in efficacies of the administered bioactive compound but also allow for better control of the release rate and targeting of encapsulated compound. In addition, delivery system can improve

the physicochemical stability of bioactive compound by decreasing the reactivity of the encapsulated material in relation to the outside environment, and promote easier handling of the compounds by achieving uniform dispersion. In this work, solid lipid particles (SLPs) were chosen as the delivery vehicle of choice for the VCO. In order to study the potential of SLPs as a potential carrier of VCO, characterization of the VCO-SLPs was done. Particle size, zeta potential, entrapment efficiency and penetration study were measured as an as an indicator of product quality, stability and efficacy.

1.3 Objective

The objective of this study was to investigate a carrier for VCO that would improve its dermal delivery. Solid lipid particles were studied as the possible carrier to improve the performance and efficiency of VCO to the skin.

1.4 Scope of Study

In order to achieve the objectives, four scopes of work have been covered in this research as listed below:-

(i) Determination of the appropriate formula for VCO-SLPs formulation.

(ii) Investigation of the effect of ultrasonication processing parameters on the particle size of VCO-SLPs formulation.

(iii) Characterization of VCO-SLPs:

   a. Determination of the particle size using Mastersizers 2000S

   b. Measurement of zeta potential using Nano Zetasizer Z

c. Monitoring the surface morphology using Transmission Electrons Microscope
d. Determination of the entrapment efficiency using Sephadex G50 and ferulic acid as a marker
e. Evaluation of transdermal penetration of VCO-SLPs in rat skin

(iv) Determination of the performance of a moisturizing lotion containing VCO-SLPs.

1.5 Significance of the Study

This study will help in the understanding of the effect of particle size of VCO-SLPs and skin moisturization effects. The understanding of the solid lipid particles formulation is useful in designing a better delivery system for better dermal delivery. This study also can minimize the gap in the scientific based study on VCO based cosmeceuticals.

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