UNIVERSITI PUTRA MALAYSIA

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By

NG SOOK HAN

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfillment of the Requirement for the Degree of Doctoral of Philosophy

August 2012

DEDICATED TO:

My beloved family: Papa & Mama, sisters,

brother, Muffin, Danny and my Lord

for the understanding, encouragement and unconditional love

and support throughout the course of this work.

I love you.

Abstract of the thesis presented to the Senate of the Universiti Putra Malaysia in the fulfillment of the requirement for the degree of Doctor of Philosophy

DESIGN AND DEVELOPMENT OF PALM OIL ESTER-BASED NANOCOSMECEUTICALS

By

NG SOOK HAN

August 2012

Chairman : Professor Mahiran Basri, PhD

Faculty : Science

Palm oil esters (POEs), esters derived from palm oil and oleyl alcohol have great potential in the cosmetic and pharmaceutical industries due to the excellent wetting behavior of the esters without the oily feel. Nonionic based emulsifiers such as polyoxyethylene sorbitan monostearate (Tween 60), polyoxyethylene sorbitan monooleate (Tween 80) and polyoxyethylene sorbitan trioleate (Tween 85) are widely used in the application of cosmetic products. These nonionic surfactants have excellent safety, mildness and effectiveness. Phase behaviors of palm oil esters were determined through the construction of ternary phase diagrams using nonionic surfactants.

The increase of Hydrophilic Lipophilic Balance (HLB) value of the surfactants gave larger homogeneous and isotropic region in ternary phase diagrams. Three types of nonionic surfactants were selected, namely, Tween 60, Tween 80 and Tween 85. Phase diagrams of POEs:Tocotrienol/T60/water, POEs: Tocotrienol/T80/water and POEs:Tocotrienol/T85/water systems were constructed at room temperature. The results showed that the POEs:Tocotrienol/T80/water system gave better performance than the other two individual surfactant systems. It was observed that the POEs:Tocotrienol/T80/water system exhibited better solubility of water to produce a larger isotropic region as compared to the other system.

Solubilisant gamma, a type of co-surfactant was added in the ternary phase diagram of POEs:Tocotrienol/T80/water system. The ratio of 1:0.5 of POEs + Tocotrienol:solubilisant gamma was selected in contribution for enlargement of the isotropic region. Furthermore, as the regions moved to high oil content compositions, more homogeneous regions were observed as compared to single surfactant. Binary surfactants showed better mixing between components and hence better stability.

Compositions from the ternary phase diagrams were selected as pre-formulated emulsions. The emulsions were then subjected to rotor-stator, followed by ultrasound cavitation to obtain nano-size emulsions. Nanoemulsions with 10%,

20% and 30% (w/w) oil phase concentration were chosen for further studies. The influence of oil and surfactant concentrations to the stability and rheological behavior of the palm oil esters stabilized with nonionic surfactant was evaluated. The stability of the nanoemulsions system was examined with respect to the mean droplet size and zeta potential for over 3 months. The increase in oil phase concentration from 10 to 30% (w/w) showed no distinct changes in the particle size. This indicated the nanoemulsions were stable regardless of the emulsifiers' types used.

The rheological property of nanoemulsions was investigated using oscillatory measurements and viscometry test. The droplet size of the nanoemulsions was found to decrease with the increase in the oil and surfactant concentrations which give effect on the viscosity and yield stress of the nanoemulsions. The flow curve of the emulsions exhibited shear thinning behavior and obeys the Power Law viscosity. The Power Law Index was found to be decreased when the oil, surfactant concentrations and acoustic amplitudes were increased due to the smaller droplet size and narrower size distribution.

The dynamic properties of the nanoemulsions were also affected by the oil and surfactant content which indicated stronger structural integrity and greater interdroplets interactions. The viscoelasticity of the nanoemulsions was enhanced by the increase in the oil and surfactant concentrations. The

nanoemulsions with higher oil phase concentration (30% (w/w)) showed greater elasticity which implied strong dynamic rigidity of the nanoemulsion. It was the most stable with longest shelf-life.

All the formulations were stable after undergoing thaw cycles test, storage at room temperature and 45°C for more than 4 months. The stable nanoemulsions also showed sedimentation rates at earth gravity of 5.2, 3.0 and 2.6 mm/month for 10%, 20% and 30% (w/w) oil phase, respectively. The TGA thermograms showed two major weight losses due to the evaporation of water content and destruction of oil phase. The palm oil esters nanoemulsions containing tocotrienol gave higher Trolox Equivalent Antioxidant Capacity (TEAC) values which implied higher antioxidant capability. Nanoemulsion with 10%, 20% and 30% (w/w) oil phase concentration showed an antimicrobial effect against selected microorganisms and fungal growth.

Abstrak tesis dikemukakan kepada Senat Universiti Putra Malaysia bagi memenuhi syarat untuk mendapatkan ijazah Doktor Falsafah

REKA BENTUK DAN PEMBANGUNAN NANOKOSMECEUTIKAL BERASASKAN MINYAK SAWIT ESTER

Oleh

NG SOOK HAN

Ogos 2012

Pengerusi : Profesor Mahiran Basri, PhD

Fakulti : Sains

Minyak sawit ester (POEs) adalah ester yang dihasilkan daripada minyak sawit dan oleyl alkohol yang mempunyai potensi tinggi dalam industri kosmetik and pharmasi kerana sifat basahan ester yang baik tanpa rasa berminyak. Pengemulsi berasaskan tak-ionik seperti polioksietilen sorbitan monostearate (Tween 60), polioksietilen sorbitan monooleate (Tween 80) dan polioksietilen sorbitan trioleate (Tween 85) telah digunakan dengan meluas di dalam barangan kosmetik. Surfaktan tak-ionik ini mempunyai tahap keselamatan, kelembutan dan keberkesanan yang tinggi. Sifat fasa minyak sawit ester telah

ditentukan melalui pembinaan rajah tiga fasa menggunakan surfaktan tak-ionik.

Peningkatan nilai keseimbangan sifat suka air dan minyak (HLB) surfaktan memberikan fasa homogen dan isotropik yang lebih luas di dalam rajah tiga fasa. Tiga jenis surfaktan tak-ionik telah dipilih, polioksietilen sorbitan monostearate (Tween 60), polioksietilen sorbitan monooleate (Tween 80) dan polioksietilen sorbitan trioleate (Tween 85). Gambarajah fasa bagi sistem POEs:Tocotrienol/T60/air, POEs:Tocotrienol/T80/air dan POEs:Tocotrienol/T85/air telah dibina pada suhu bilik. Keputusan menunjukkan bahawa sistem POEs:Tocotrienol/T80/air telah memberikan hasil yang lebih baik jika dibandingkan dengan dua sistem individu surfaktan yang lain. Pemerhatian menunjukkan bahawa sistem POEs:Tocotrienol/T80/air memberikan kadar keterlarutan di dalam air yang tinggi dan menghasilkan fasa isotropik yang besar jika dibandingkan dengan sistem yang lain.

Solubilasi gamma, sejenis ko-surfaktan telah ditambah ke dalam sistem tiga fasa POEs: Tocotrienol/T80/air. POEs + Tocotrienol:solubilasi gamma dengan nisbah 1:0.5 telah dipilih untuk memperbesarkan kawasan isotropik. Tambahan pula, peningkatan komposisi kandungan minyak menghasilkan fasa homogen yang besar jika dibandingkan dengan sistem yang menggunakan surfaktan

tunggal. Surfaktan binari telah menunjukkan percampuran yang baik antara komponen dan dengan itu meningkatkan kestabilan.

Komposisi daripada gambarajah fasa telah dipilih sebagai pre-formulasi emulsi. Emulsi didedahkan kepada mesin pengemulsi, diikuti dengan mesin ultrasonik untuk menghasilkan emulsi bersaiz nano. Nanoemulsi dengan kepekatan 10%, 20% dan 30% (w/w) kandungan minyak sawit ester telah dipilih untuk dikaji. Pengaruh kepekatan minyak dan surfaktan terhadap kestabilan dan sifat rheologi minyak sawit ester yang distabilkan dengan surfaktan tak-ionik telah dikaji. Penilaian terhadap kestabilan sistem nanoemulsi telah dijalankan melalui saiz titisan dan keupayaan zeta dalam tempoh melebihi 3 bulan. Peningkatan komposisi kandungan minyak daripada 10 hingga 30% (w/w) menunjukkan tiada perubahan terhadap saiz titisan dalam tempoh masa 3 bulan. Ini menunjukkan nanoemulsi memberikan kestabilan terhadap surfaktan yang digunakan.

Ciri rheologi nanoemulsi telah dikaji dengan menggunakan teknik rincihan secara berayun dan ujian viskometrik. Saiz titisan nanoemulsi didapati menurun apabila kepekatan kandungan minyak dan surfaktan yang digunakan meningkat. Ini memberi kesan pada kelikatan dan tegasan alah nanoemulsi tersebut. Lengkungan aliran bagi nanoemulsi tersebut mempamerkan sifat penipisan secara rincihan dan mematuhi kelikatan Power Law. Indek Power

Law didapati menurun apabila kandungan minyak, kepekatan surfaktan dan amplitud akustik meningkat disebabkan oleh saiz titisan yang lebih kecil dan taburan saiz titisan nanoemulsi yang lebih sempit.

Sifat dinamik bagi nanoemulsi juga dipengaruhi oleh kandungan minyak dan surfaktan yang menunjukkan kekuatan integriti struktur dan interaksi antara titisan nanoemulsi yang lebih besar. Sifat viskoelastik bagi nanoemulsi dapat dipertingkat dengan meningkatkan kepekatan minyak dan surfaktan. Nanoemulsi dengan kepekatan fasa minyak yang tertinggi (30% (w/w)) memberikan sifat keanjalan yang lebih besar dan menunjukkan kekuatan ketegaran dinamik nanoemulsi. Ini merupakan emulsi yang paling stabil dengan tempoh penyimpanan yang terpanjang.

Kesemua formulasi adalah stabil pada suhu bilik, 45°C dan selepas menjalani ujian kitaran mencair melebihi 4 bulan. Nanoemulsi yang stabil juga menunjukkan kadar pemendapan pada graviti bumi iaitu 5.2, 3.0 dan 2.6 mm/bulan untuk 10%, 20% dan 30% (w/w) kandungan minyak masing-masing. Gambarajah haba TGA menunjukkan dua pengewapan berlaku iaitu pengewapan air dan penguraian fasa minyak. Nanoemulsi minyak sawit ester yang mengandungi tocotrienol memberikan nilai Trolox Equivalent Antioxidant Capacity (TEAC) yang tinggi dan ini menunjukkan keupayaan sebagai antioksida yang tinggi. Nanoemulsi yang mengandungi 10%, 20% dan

30% (w/w) kepekatan fasa minyak menunjukkan kesan antimikrobial terhadap pertumbuhan mikroorganisma dan kulat terpilih.

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I certify that a Thesis Examination Committee has met on **3rd August 2012** to conduct the final examination of Ng Sook Han on her thesis entitle "**Design and Development of Palm Oil Ester-Based Nanocosmeceuticals**" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The committee recommends that the student be awarded the Doctor of Philosophy Degree.

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Date: 27 August 2012

This thesis was submitted to the Senate of Universiti Putra Malaysia has been accepted as fulfillment of the requirements for the degree of **Doctor of Philosophy**. The members of Supervisory Committee were as follows:

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Date:

DECLARATION

I declare that the thesis is my original work except for quotations and citations, which have been duly acknowledged. I also declare that it has not been previously, and is not concurrently submitted for any other degree at Universiti Putra Malaysia or other institutions.

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(NG SOOK HAN)

Date: 3 August 2012

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