

STABILITY AND EFFICIENCY OF KACIP  
FATIMAH-CHITOSAN NANOPARTICLES AS A  
DELIVERY SYSTEM IN FACIAL CLEANSING  
APPLICATION

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STABILITY AND EFFICIENCY OF KACIP FATIMAH-CHITOSAN  
NANOPARTICLES AS A DELIVERY SYSTEM IN FACIAL CLEANSING  
FORMULATION

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A thesis submitted in fulfillment of the  
requirements for the award of the degree of  
Master of Engineering (Bioprocess)

Faculty of Chemical Engineering  
Universiti Teknologi Malaysia

JUNE 2014

*Dedicated to my beloved husband, RM Syibli Fakh.*

## ACKNOWLEDGEMENTS

Alhamdulillah, I'm very thankful to Allah s.w.t. for the source of strength and inspiration. My most sincere gratitude to my supervisor Associate Professor Dr Azila Abd Aziz for her continuous guidance and support through all stages of this research works.

I would like to acknowledge Universiti Teknologi Malaysia (UTM) for funding this project through the provided Research University Grant. My special thanks to Institute of Bioproduct Development (IBD) for providing facilities in carrying out this project and also all staff members involved in helping out with this project. I would also like to thank Dr Che Wan Zanariah Che Wan Ngah from USIM, Mr Mohamad Mohd Salleh from Ibnu Sina Institute, UTM and also Mr Albert Lim from DKSH for their help in this study.

I specifically would like to thank my fellow labmates, Nur Zatul Iradah Bt Ruslan, Syalwati Asnawi, Norhayati Mohamad Noor, Nurul Bashirah Bt Yusof and Siti Maria Bt Abdul Ghani for their tremendous support.

Finally, I wish to thank my biggest supporter, my husband and also my other family members for their encouragement, support and love through my ups and downs during my Masters journey.

## ABSTRACT

Kacip Fatimah is a potential anti-aging active ingredient in cosmetics. A delivery system is essential to deliver the active ingredient through the skin but the challenges were how to deliver the active ingredients in wash-off products. Negatively charged skin surface leads to development of cationic vesicle as the delivery system. The objective was to develop Kacip Fatimah-Chitosan nanoparticle as a stable and effective delivery system in the facial cleansing formulation. This naturally cationic delivery system was prepared by tripolyphosphate (TPP) crosslinking (ionic gelation method) with chitosan's concentration of 1.5 mg/ml and TPP's concentration of 0.7 mg/ml, with ratio of chitosan to TPP as 7:1. Particles were successfully formed by ultrasonication at 40% amplitude for 3 minutes. Low molecular weight (LMW) chitosan was the best choice for further deacetylation process based on its size at 122.1 nm compared to higher chitosan's molecular weights with sizes below 100 nm. Deacetylation process was done to obtain 90% DD (degree of deacetylation) nanoparticles. Zeta potential results showed stable nanoparticles for both LMW and 90% nanoparticles but 90% DD nanoparticles showed better size distribution with PDI (polydispersity index) value of 0.432. Encapsulation efficiency (EE%) of Kacip Fatimah by 90% DD nanoparticles was higher than LMW nanoparticles with values of 74.37% and 33.95%, respectively. 90% DD nanoparticles deposited more actives ( $1.83 \mu\text{g}/\text{cm}^2$ ) on skin after washing, as compared to LMW nanoparticles which only deposited  $0.67 \mu\text{g}/\text{cm}^2$  active ingredient. These results showed that chitosan nanoparticle can be a potential carrier for Kacip Fatimah in facial cleansing formulation with better stability using deaceatylated chitosan.

## ABSTRAK

Kacip Fatimah ialah bahan berpotensi sebagai anti-penuaan dalam kosmetik. Sistem penyampaian adalah penting untuk menyampaikan bahan aktif ke kulit namun cabarannya adalah untuk menyampaikan bahan aktif di dalam produk pembersihan diri. Permukaan kulit yang bercas negatif telah membawa kepada pembentukan sistem penyampaian yang bercas positif. Objektif kajian ini adalah untuk menghasilkan Kacip Fatimah-Nano partikel kitosan sebagai sistem penyampaian yang stabil dan efektif dalam produk pembersihan diri. Sistem penyampaian yang bersifat kationik secara semulajadi ini dihasilkan melalui pemautesilangan dengan tripolifosfat (TPP) (kaedah ionik gel) dengan kepekatan kitosan 1.5 mg/ml dan kepekatan TPP 0.7 mg/ml dengan nisbah kitosan ke TPP 7:1. Partikel berjaya dihasilkan melalui ultrasonikasi pada amplitud 40% selama 3 minit. Kitosan yang berjirim molekul rendah (LMW) telah dipilih untuk proses deasetilasi berdasarkan saiznya pada 122.1 nm jika dibandingkan dengan kitosan berjirim molekul lebih tinggi. Deasetilasi kitosan telah dilakukan untuk menghasilkan 90% DD (darjah deasetilasi) nano partikel. Potensi zeta menunjukkan nano partikel yang stabil bagi kedua-dua partikel LMW dan 90% DD tetapi 90% DD nanopartikel menunjukkan taburan saiz yang lebih baik dengan nilai indeks polidispersiti 0.432. Kecekapan pengkapsulan (EE%) Kacip Fatimah oleh 90% nano partikel adalah lebih tinggi daripada LMW nano partikel dengan masing-masing bernilai 74.37% dan 33.95%. 90% DD nano partikel menyampaikan lebih banyak bahan aktif ke kulit selepas pembasuhan ( $1.83 \mu\text{g}/\text{cm}^2$ ) berbanding LMW nano partikel ( $0.67 \mu\text{g}/\text{cm}^2$ ). Keputusan ini menunjukkan bahawa kitosan berpotensi menjadi sistem penyampaian untuk Kacip Fatimah dalam produk pembersihan diri dengan kestabilan yang lebih baik menggunakan deasetilasi kitosan

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**LIST OF ABBREVIATIONS**

AHA	-	Alpha hydroxy acids
CNP	-	Chitosan Nanoparticles
DD	-	Degree of deacetylation
DLS	-	Dynamic light scattering
EE	-	Encapsulation efficiency
FTIR	-	Fourier Transform Infrared Spectroscopy
GlcNAc	-	N-acetyl glucosamine
HMW	-	High molecular weight
HPLC	-	High performance liquid chromatography
IR	-	Infrared
LD	-	Laser diffraction
LCMS	-	Liquid chromatography-mass spectroscopy
LMW	-	Low molecular weight
MMW	-	Medium molecular weight
NaOH	-	Sodium hydroxide
NMR	-	Nuclear magnetic resonance
NLC	-	Nanostructured lipid carriers
PDI	-	Polydispersity index
ROS	-	Reactive oxygen species
SLN	-	Solid lipid nanoparticles
TEM	-	Transmission electron microscope
TPP	-	Triphosphate
UV-Vis	-	Ultraviolet-visible
WHO	-	World health organization
ZCP	-	Zero crossing point

1DUVS - First derivate UV Spectroscopy



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## CHAPTER 1

### INTRODUCTION

#### 1.1 Background of Study

Kacip Fatimah or *Labisia Pumila* is a traditional herbal medicine which has been used by many generations of Malay women to facilitate childbirth and as post-partum medicine. They are also available commercially as health supplements which claimed to prevent and treat illnesses mainly related to women's hormones stability. Many researches have been done to identify bioactives or phytochemicals in *Labisia Pumila* that contributed to their pharmacological activities (Chua *et al*, 2011; Norhaiza *et al*, 2009; Karimi and Jaafar, 2011; Nadia *et al*, 2012; Nik Hussain and Abdul Kadir, 2013). Their antioxidants are believed to play a crucial role in protecting against several diseases and delaying the aging process. From a cosmetic point of view, studies have demonstrated the ability of *Labisia Pumila* to specifically protect skin against photoaging (Choi *et al*, 2009) and increase collagen synthesis (Mukhrish *et al*, 2012) based on their high antioxidant activities (Norhaiza *et al*, 2009). These reports suggest that Kacip Fatimah or *Labisia Pumila* has the potential as an anti-aging cosmetic ingredient.

However, there are no studies yet on Kacip Fatimah's incorporation in cosmetics formulation and its efficacy for skin. For many years, a cosmetic vehicle or a delivery system is used in delivering specific components or active ingredients to the skin for better performance (Magdassi, 1996). A stable and effective encapsulation by a delivery system is essential for the active ingredients to be preserved during formulation and targeted to specific cells of the skin for their benefits delivery (Ammala, 2013). Polymeric nanoparticles have long been studied for their ability as an effective drug delivery system in pharmaceutical industries. Recently, researchers have also explored their use in cosmetics application and were studied in this work (Guterres *et al*, 2007).

Cosmetic products that are normally used on a daily basis by consumers include lotions, make-up, facial moisturizers and facial cleansers. Skin cleansing is the most important application as it removes dirt, sebum and microorganism for cleaner and healthier skin. In this study, focus was done more on facial cleansing which is more exposed to the environment and is the most frequently used when compared to hair conditioner and eye shadow (Loretz *et al*, 2008). Facial cleansing products segment has grown over the years as the products are no longer only used for pure cleansing but also for imparting functional skin benefits. Active ingredients such as vitamins, salicylic acid and others are currently being incorporated in facial cleansing products for better performance.

Surfactants make up the highest amount of most cleansing products' ingredients and are primarily responsible for removing oily residues and dirt on the skin. Unfortunately, most of the time, cleansing action removes active ingredients that are included in the cleanser. Numerous improvements and advancements have been done on the delivery of active ingredients in cleansers to address the challenges in delivering active ingredients in wash-off personal care products.

One promising technology is using positively charged vesicles to deliver the active ingredients. The concept of electrostatic interaction with negatively charged

substrates has always been used in hair conditioning formulation. Among cationic polymers normally used in hair conditioners are Polyquaternium 4, Polyquaternium 7 and Polyquaternium 10 (Hossel *et al*, 2000). The deposition efficiency of these polymers onto hair is reported to be influenced by several factors such as charge level, molecular weight (Gruber *et al*, 2001) and types of surfactants (Faucher and Goddard, 1976).

These cationic polymers have also found wide acceptance in skin care products. Cationic polymers provide skin protection properties and improve skin's smoothness due to its moisturizing effect. Unlike hair, skin is a living organ that constantly replaces its outermost layer. Therefore, its conditioning effect is different from hair. This 'conditioning effect' too can be manipulated to provide anti-aging benefits through the use of appropriate active ingredients. Many of these purposes are achieved through binding of cationic charge to anionic skin under normal or acidic pH levels. Depending on the nature of the material, the use of cationic polymers in skincare products can result in improvement in skin's barrier function (Gruber, 1999), enhancement of the deposition of active ingredients (Bierganns, 2011) or improvement in skin feel (Gruber, 1999).

This idea has been applied by companies such as Air Products, Amerchol and Aqua Scientific Corporation in their technology where cationic polymers are used for delivering or depositing active ingredients on skin. Air Products patented Deposilk<sup>™</sup> Q1 Polymer (Air Products and Chemicals Inc, 2012) for the use in depositing active ingredients in high water, high oil and high alcohol formulations while Aqua Scientific Corporation patented Wash-On<sup>™</sup> (Traynor *et al*, 2006) a delivery system which enables sunscreens to remain on skin even after thorough cleansing. This technology can be found in products such as Freeze 24-7 Ice Shield Facial Cleanser. Amerchol Corporation, a subsidiary of The Dow Chemical Company, patented SoftCAT<sup>™</sup> SK conditioning polymers (Amerchol Corporation, 2005) to keep skin moisturized while focusing on enhanced emollient deposition efficiency. These technologies used different types of polymers, mostly synthetic polymers, different designs and different methods in incorporating the active ingredients.

Among available cationic polymers, chitosan, a natural, non toxic, bioadhesive, biocompatible, and biodegradable polymer has the potential to be used as vesicle to encapsulate active ingredients. It has been widely used in pharmaceutical, cosmetics, food and other industries as a functional biopolymer (Kumar, 2000). The uniqueness of chitosan is that it possesses both nonionic hydrophobic functionality as well as a hydrophilic cationic charge. It can interact with anionic groups found in skin through its cationic glucosamine groups (Cattaneo, 2005) and the interaction promotes its bioadhesive ability (Guo *et al*, 2003). Chitosan degrades in the body through the action of chitosanase and lysozyme unlike most synthetic polymers, which makes it safe for use in cosmetics (Pangburn *et al*, 1982). Several factors that affect the positive charge and the effectiveness of chitosan include molecular weight, degree of deacetylation and pH.

Chitosan nanoparticles are chosen for several reasons. They are stable, easier to prepare, able to control release of active agents and have low toxicity (Agnihotri *et al*, 2004). It has been extensively developed and explored for pharmaceutical applications but researches (Leonida *et al*, 2011; Yoksan *et al*, 2009; Kim *et al*, 2006; Leelapornpisid *et al*, 2010) has proven that chitosan nanoparticles can also benefits in cosmetics application. Characterizations of Kacip Fatimah-Charged Chitosan Nanoparticles that need to be studied to ensure a stable and effective delivery system include particle size, zeta potential, morphology, encapsulation efficiency and skin deposition study.

## **1.2 Problem Statement**

Chitosan nanoparticle has been used as a delivery system in many areas, but never been studied in cleansing products. Its cationic nature plays a major role in making sure the encapsulated active ingredients deposited on anionic skin through electrostatic interaction. Several factors including molecular weight, degree of deacetylation and pH could affect its surface charge, stability and efficiency. Highly deacetylated chitosan has more protonated amine groups which could mean better interaction with anionic material hence increasing its efficiency.

The efficiency of chitosan nanoparticle as a charged delivery system also depends on the its compatibility with the product where it is being incorporated. A special surfactant system should be used in the facial cleansing formulation to avoid precipitation, unstable mixture as well as decrease on its skin deposition.

## **1.3 Objective**

To investigate stability and efficiency of Kacip Fatimah-Charged Chitosan nanoparticles as a delivery system in facial cleansing application.

## 1.4 Scopes of Study

In order to achieve the objective, this study has been divided into Four scopes which are:

- i. Screening of Kacip Fatimah-Chitosan Nanoparticles Formula Determination (Effect of chitosan's concentration, chitosan's molecular weight, ratio and ultrasonication time and amplitude)
- ii. Deacetylation of Chitosan and Degree of Deacetylation (DD %) Determination
- iii. Characterization of Kacip Fatimah-Chitosan Nanoparticles (Particle size, zeta potential, morphology and encapsulation efficiency (EE %))
- iv. Skin Deposition Study of Kacip Fatimah-Chitosan Nanoparticles (Amount of active ingredient deposited on skin after washing)

## 1.5 Significance of Study

This study helps in understanding the use of natural polymer chitosan as charged polymeric nanoparticles in developing an efficient cationic delivery system for active ingredients delivery in facial cleansing formulation. This study also contributes to a new knowledge in providing a cleanser range of personal care products incorporating an anti-aging ingredient, Kacip Fatimah as there is no research works carried out in this area yet.

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