

OPTIMIZATION, STABILITY AND CHARACTERIZATION OF FACE SERUM
FORMULATION

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To my beloved mother and father

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ABSTRACT

Nowadays, the demand for skin care products which can give instant beauty effect is increasing rapidly. This has urged some companies to take short cut by incorporating hazardous chemicals into skin care products, consequently caused adverse skin effect over time. Instead, incorporation of face serum into daily skin care routine can give noticeable difference within four weeks. Face serum is a highly concentrated emulsion which consists of small molecules that allow better penetration into the skin thus deliver instant noticeable results. Nevertheless, the stability of face serum formulation needs to be maintained to ensure its effectiveness to the skin. The goal of this study was to determine the optimum and stable face serum formulation with regards to its viscosity and pH value with favourable rheology and sensory characteristics. The formulated face serum was prepared using emulsifiers, thickeners, alpha-mangostin and basic components for skin such as ceramide, amino acids and others. The concentration of emulsifiers and thickeners was optimized using D-optimal mixture design. The independent variables were thickeners (carbopol ultrez 20 and xanthan gum) and emulsifiers (glyceryl stearate and PEG 40 hydrogenated castor oil), while the dependent variables were the viscosity and pH value of the face serum formulations. The study continues in the stability testing concerning on centrifugation, freeze thaw, accelerated stability study and microbiological study. Rheology study was conducted to determine the flow behavior of the face serum. Lastly, 40 respondents was involved in a sensory evaluation test in order to pool public acceptance towards the characteristic of the commercial and formulated face serums. From the study, it was found that the optimum formulation of face serum formulation consists of 0.9% of carbopol ultrez 20, 0.3% of xanthan gum, 0.46% of PEG 40 hydrogenated castor oil and 0.34% of glyceryl stearate. The optimum viscosity and pH value was found to be 4082.65 ± 6.65 cP and 4.56 ± 0.26 , respectively. Coefficient of determination (R^2) indicated a good fit between the predicted values and the experimental data points. The R^2 for viscosity and pH value were found to be 0.9559 and 0.9893, respectively. The stability studies revealed that the optimum formulation exhibits good stability throughout the 90 days of stability testing period as there were no significant change in its viscosity and pH value. Besides, the optimum formulation passed the microbiology test. The optimum formulation shows pseudoplastic Bingham fluid rheology which is the preferred flow behaviour for cosmetic emulsion. Results from the sensory evaluation test revealed that the formulated face serum was able to mimic the characteristics of the commercial face serum since the ANOVA of all attributes showed no significance value. D-optimal mixture design was successful in determining the optimal face serum formulation which is stable with preferred viscosity, pH value, rheology and sensory profile.

ABSTRAK

Sekarang ini, permintaan produk penjagaan kulit yang dapat memberikan kesan kecantikan dalam jangka masa pendek kian meningkat. Ini mendorong sesetengah syarikat mengambil jalan mudah dengan menerapkan bahan kimia merbahaya ke dalam produk penjagaan kulit, yang menyebabkan kesan buruk pada kulit dalam jangkamasa panjang. Sebaliknya, penerapan serum wajah ke dalam rutin penjagaan wajah mampu memberikan kesan drastik dalam masa empat minggu. Serum wajah merupakan emulsi pekat yang terdiri daripada molekul kecil yang mudah menyerap ke dalam kulit dan memberikan kesan jangkamasa pendek. Walaubagaimanapun, kestabilan formulasi serum wajah perlu dikekalkan demi menjamin keberkesannya pada kulit. Kajian ini bertujuan menghasilkan formulasi serum wajah yang stabil dan optimum bersandar pada kelikatan dan pH dengan ciri-ciri reologi dan deria yang dikehendaki. Serum wajah dihasilkan dengan menggabungkan pengemulsi, pemekat, alfa-mangostina dan bahan asas kulit seperti seramid, asid amino dan lain-lain. Kepekatan pengemulsi dan pemekat dioptimumkan menggunakan perisian reka bentuk campuran D-optimal. Pembolehkan tak bersandar adalah pemekat (carbopol ultrez 20 dan gam xanthan) dan pengemulsi (gliseril stearat dan PEG 40 minyak kastor terhidrogenasi), manakala pemboleh ubah bersandar ialah kepekatan dan pH formulasi serum wajah. Seterusnya, kajian kestabilan merangkumi pengemparan, kestabilan beku-cair, kestabilan pecutan dan kajian mikrobiologi. Kajian reologi juga dijalankan bagi mengenalpasti kelikatan aliran serum wajah. Akhir sekali, seramai 40 orang responden mengikuti kajian deria bertujuan mengetahui penerimaan orang ramai terhadap ciri-ciri serum wajah yang dihasilkan berbanding jenama komersil. Melalui kajian ini, didapati bahawa formulasi optimum serum wajah dapat dihasilkan dengan 0.9% carbopol ultrez 20, 0.3% gam xanthan, 0.46% PEG 40 minyak kastor terhidrogenasi dan 0.34% gliseril stearat. Kepekatan dan pH optimum masing-masing adalah 4082.65 ± 6.65 cP dan 4.56 ± 0.26 . Pekali (R^2) menyatakan padanan baik antara nilai jangkaan dan nilai eksperimen. R^2 kelikatan dan pH masing-masing ialah 0.9559 dan 0.9893. Kajian kestabilan sepanjang 90 hari membuktikan formulasi optimum memiliki kestabilan yang baik, terbukti dengan tiada perubahan yang signifikan pada nilai kelikatan dan pH. Tambahan pula, formulasi optimum lulus ujian mikrobiologi. Formulasi optimum menunjukkan reologi bendalir Bingham pseudoplastik yang merupakan ciri aliran yang sesuai bagi kosmetik jenis emulsi. Keputusan dari kajian deria mendapati bahawa formulasi serum wajah yang dibuat adalah mirip kepada serum wajah komersil memandangkan ANOVA menunjukkan nilai perbezaan tidak signifikan. Perisian reka bentuk campuran D-optimal telah berjaya menghasilkan formulasi serum wajah optimum yang stabil yang juga memiliki kadar kelikatan, nilai pH, reologi dan nilai deria yang dikehendaki.

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LIST OF ABBREVIATIONS

(α -MSH)-induced	-	(alpha-melanocyte stimulating hormone)-induced
α -mangostin	-	Alpha-mangostin
ALS	-	Ammonium lauryl sulfate
ANOVA	-	Analysis of Variance
CU20	-	Carbopol ultrez 20
CAGR	-	Compound annual growth rate
EDTA	-	Ethylene diamine tetraacetic acid
GS	-	Glyceryl stearate
HLB	-	Hydrophilic-lipophilic balance
IOM	-	Institute of Medicine
O/W	-	Oil in water
OFAT	-	One factor at a time
PEG40	-	PEG 40 hydrogenated castor oil
PEG	-	Polyethylene glycol
SLS	-	Sodium lauryl sulfate
SPF	-	Sun protection filter
UV	-	Ultraviolet
USD	-	United States Dollar
VRBD	-	Violet red bile dextrose
W/O	-	Water in oil
XG	-	Xanthan gum
XLD	-	Xylose lysine deoxycholate

LIST OF SYMBOLS

cm	-	Centimeter
cP	-	Centipoise
pH	-	Concentration of Hydrogen ion
k	-	Consistency index
°C	-	Degree celcius
n	-	Flow index
g	-	Gram
H ⁺	-	Hydrogen ion
μg	-	Microgram
ml	-	Milliliter
%	-	Percentage
rpm	-	Rotation per minute
s	-	Second
$\dot{\gamma}$	-	Shear rate
τ	-	Shear Stress
τ_s	-	Yield stress

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CHAPTER 1

INTRODUCTION

1.1 Research Background

Public awareness on having beautiful and flawless skin has made skin care a compulsory routine for every individual including man. Statistics showed that by 2024, the global skin care market is estimated to be 180 billion USD (Statistica, 2018). Following a proper skin care routine will not only maintain skin health, but it may improve skin structure and skin function (Ganceviciene *et al.*, 2012). A basic skin care routine includes several products which are cleanser, toner, treatment mask, eye cream, face serum, moisturiser, sunscreen and night cream (Neil, 2012; Keefe *et al.*, 2004).

In the context of achieving beautiful skin, customers are more attracted to the products that promise instant results. This facilitates by the incorporation of hazardous chemicals such as hydroquinone and mercury. The hazardous ingredients are bleaching agents that bleach the melanin on the skin surface (Katsambas and Stratigos, 2001). This in turn caused major side effect includes skin irritation, chemical burns, skin exogenous ochronosis, contact dermatitis, cancer (leucomelanoderma) and even mutagenicity (FDA, 2017; Dadzie and Petit, 2009).

On the other hand, numerous studies on plant derived active ingredients (Hassan *et al.*, 2015; Gupta and Jain, 2011; Huang *et al.*, 2011) had been conducted in order to provide safe beauty solution for cosmetic products. In addition, a skin care formulation must be able to deliver the powerful agent into the skin to fulfil the intended objective. Face serum is the answer to deliver the precious active ingredient into the skin thus eliminates the use of hazardous chemicals in giving instant results.

According to Sasidharan *et al.*, (2014), face serum is a highly concentrated emulsion which available in water based and oil based. Serums or defined as concentrates, contain approximately ten times more of biologically active substances than creams, therefore allows better skin problems treatment. Incorporating a few drops of face serum with daily skin care routine will deliver noticeable results within a month or less (Herman-Axel, 2014; Sasidharan *et al.*, 2014). This is because face serums are made of very small molecules that help it to penetrate deep into the skin quickly (Sasidharan *et al.*, 2014). Serum is packed with a bunch of beneficiary active components and nutrients (Herman-Axel, 2014) such as antioxidants, ceramides, amino acids and others. This explains why face serum always being the most costly item in a skin care set (Herman-Axel, 2014).

In formulating a face serum, the physical properties and stability are the main characteristics in determining its quality. A face serum formulation is basically an emulsion consists of two immiscible liquids. In order to prevent emulsion instabilities, thickener and emulsifier are introduced to the system. Emulsifier will balance the system by minimising the interfacial tension between the two immiscible liquids and at the same time stabilises the dispersion phase from coalescence. Contributing to the system, thickener also plays an important role as rheology modifier and provides flexibility to the flow characteristic of the emulsion (Moravkova and Filip, 2014).

Besides stability, another problem to tackle in face serum formulation is pH value. If the pH value of the skin is changed, the skin's natural microbiology and function will be interrupted. This in turn causes numerous skin problems including acne, skin flakiness, excessive sebum secretion and other serious conditions (Schreml *et al.*, 2014). According to Schreml *et al.*, (2014), the natural skin microflora is intact on the skin with pH value ranging from 4 to 4.5, while pH value ranging from 8 to 9 eliminates the skin natural microflora (Schreml *et al.*, 2014). Formulating a face serum with suitable pH range can help in improving the skin barrier function.

Formulating a face serum or any other formulation can be challenging. This is because the traditional 'One Factor at a Time' (OFAT) method was highly time consuming and may result in unnecessary experiments that consume costs (Mostefa *et al.*, 2006). OFAT was done by changing one factor at a time while keeping the other factor as constant. On the contrary, optimization using Design Expert software could save time, costs and labour. D-optimal design is suitable to be used in formulating cosmetic formulations (Mostefa *et al.*, 2006; Djuris *et al.*, 2014; Suhaimi *et al.*, 2017) thus it is applied in this study.

Next, intricate customers' preferences always come into consideration in formulating a cosmetic formula. Customers are the most important judge that could determine the marketability of the product (Masson, 2011). In regards to this matter, sensory evaluation has become a useful tool in estimating customers' expectation on the texture of a cosmetic formula. Coupling sensory test with rheological study always give better prediction and understanding of how the product behave in the production plant and the end customer (Lukic *et al.*, 2013).

Therefore, the present work is aimed to produce efficient and stable face serum by optimising the thickeners and emulsifiers using D-optimal mixture design. This is done in order to fulfill customer preferences.

1.2 Problem Statement

The high demand of instant beauty products had urged some companies to incorporate hazardous chemicals into skin care products. This in turn caused adverse skin effect over time. Instead, incorporation of face serum into daily skin care routine can give noticeable difference within four weeks (Sasidharan *et al.*, 2014; Herman-Axel, 2014). To date, there are very few researches done on face serum.

In formulating a face serum, the mixing of water phase and oil phase is crucial in order to create a stable system over an extended period or longer product shelf life. Naturally, the oil and water system is thermodynamically unstable. Incorporation of emulsifiers into the system can minimize the interfacial difference between the water and oil phases thus mix the system. In addition, incorporation of thickener in a formulation can increase the stability of the formulation. Another factor to be considered is the pH value. The pH value of the skin care product should be able to keep the skin natural micro flora intact. This is important as neutral and alkaline pH value of a skin care product can destroys the skin barrier function.

Other than that, the subjective preferences of consumers in choosing their preferred face serum always become an issue for the product formulator. Therefore, sensory evaluation plays an important role to determine the customer acceptance towards the face serum formulation. Thus, the effect of thickeners and emulsifiers was studied and optimized in formulating a stable face serum with the best viscosity, rheology and pH value which can fulfill customer preferences.

1.3 Objective of Research

The main objective of this study is to determine the optimum and stable face serum.

The specific objectives of this study are:

1. To optimise the thickeners and emulsifiers of face serum formulation with regard to the viscosity and pH value.
2. To determine the most stable face serum formulation in term of its physicochemical stability study and microbiological study.
3. To characterise the face serum formulation in term of its flow behavior and sensory profile.

1.4 Scope of Study

The scopes of this study are:

1. Thickeners and emulsifiers of the face serum formulation were varied while other ingredients were made constant.
2. In the preliminary part, the thickeners used were carbopol ultrez 20, xanthan gum and hydroxyethyl cellulose, while the emulsifiers used were soy lecithin, glyceryl stearate and PEG 40 hydrogenated castor oil. The responses were phase separation, viscosity and pH value.
3. Optimization of the emulsifiers (PEG hydrogenated castor oil and glyceryl stearate) and the thickeners (carbopol ultrez 20 and xanthan gum) of the face serum formulation with regards to its viscosity and pH value was done using D-Optimal Mixture Design in Design Expert software.

4. Evaluation of the physicochemical stability of the face serum was made using three methods stated in COLIPA Standard (Marx, 2004) which are centrifugation (3000rpm for 30 minutes), accelerated stability study (4°C, 25°C and 45°C for three months respectively) and freeze thaw (-10°C, 25°C and 45°C for three cycles) with regards to its phase separation, viscosity and pH value.
5. The microbiological study was conducted using tryptic soy agar (total plate count), saboroud agar (total yeast, mould and *Candida albicans*), baird parker agar (*Staphylococcus aureus*), mac conkey agar (*Escherichia coli*), cetrimide agar (*Pseudomonas sp*), Xylose Lysine Deoxycholate (XLD) (*Salmonella sp*) agar and Violet Red Bile Dextrose (VRBD) agar (*Enterobacteria sp*) based on the standard method of topical cosmetic preparation in British Pharmacopoeia 2015.
6. Determination of the flow behavior of the formulated and commercial face serum formulations was done using the aid of Hershel Bulkley model.
7. Sensory profile was determine by sensory evaluation of the formulated and commercial face serum formulations with regards to its texture, absorption, moisture and after feel characteristics. It was done on 40 participants and analysed using SPSS software.

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