UNIVERSITI PUTRA MALAYSIA

OPTIMIZATION STUDY ON ANTIOXIDANT IN FRUIT EXTRACT OF Phaleria macrocarpa (SCHEFF.) BOERL IN MALAYSIA AND EVALUATION ON ITS FUNCTIONAL COSMETIC

KHURUL AIN BINTI MOHAMED MAHZIR

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By

KHURUL AIN BINTI MOHAMED MAHZIR

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January 2018

Chairman : Assoc. Prof. Siti Salwa Binti Abd Gani, PhD
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Phaleria macrocarpa (Scheff.) Boerl belong to Thymelaeceae family and widely known as 'Crown of God', 'Mahkota Dewa' and 'Pau'. It is a native plant from the Papua Island, Indonesia and grows in tropical areas. It had been reported *P.macrocarpa* have traditional medicine and bioactive activities such as anti-tumor, anti-hyperglycemia, anti-inflammation, anti-diarrhoel, anti-oxidant, anti-viral, anti-bacterial, anti-fungal and vasodilator effect. However, there is still lacking in investigation of antioxidants by using Response Surface Methodology (RSM).

Therefore,in this study to determine the antioxidants properties such as [2,2-diphenly-1-picrylhydrazyl (DPPH) free radical scavenging activity, total phenolic content (TPC), total flavonoid content (TFC) and ferric ion reducing power assay (FRAP) of *P.macrocarpa* fruits by using Response Surface Methodology, Central Composite Design (CCD) was applied to determine the maximum percentages yield by focusing on three independent variables which include extraction temperature (53.18-80°C), extraction time (66.30-133.64 minutes) and solvent ethanol :water ratio (63.18-96.82%v/v) with twenty experiments was carried out. The extraction was carried out manually by using reflux set apparatus and filter out the solvent manually. The optimal conditions for the antioxidants extraction were found to be extraction temperature (63.60 ºC), extraction time (66.36 minutes) and solvent of ethanol:water ratio (74.36 %v/v) with the highest percentage yield of DPPH, TPC, TFC and FRAP were 87.23%, 268.03&, 3.22% and 7.49%.

Therefore, the yield of antioxidants activities obtained experimentally was close to the predicted values and suitability of the model employed in RSM to optimizing the extraction condition. In a conclusion, RSM was a good statistical tool with empower evaluation of the effects of certain process variables and their interaction of response variables in a short time, less cost and less number of required experiments.

Abstrak tesis yang dikemukan kepada Senat Universiti Putra Malaysia
sebagai memenuhi keperluan untuk ijazah Master Sains

PENGOPTIMUMAN ANTIOKSIDAN DALAM EKSTRAK BUAH *Phaleria macrocarpa* (SCHEFF.) BOERL DI MALAYSIA DAN KEGUNAANNYA SEBAGAI KOSMETIK

Oleh

KHURUL AIN BINTI MOHAMED MAHZIR

Januari 2018

Pengerusi : Prof. Madya Siti Salwa Binti Abd Gani, PhD
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Phaleria macrocarpa (Scheff.) Boerl tergolong dalam keluarga Thymelaeceae dan dikenali sebagai 'Crown of God', 'Mahkota Dewa' dan 'Pau'. Ia merupakan tumbuhan asli dari Pulau Papua, Indonesia dan tumbuh di kawasan tropika. Ia telah dilaporkan *P.macrocarpa* mempunyai perubatan tradisional dan aktiviti bioaktif sepertianti-tumor, anti-hiperglisemia, anti-keradangan, anti-diarrhoel, anti-oksida, anti-virus, anti-bakteria, anti-kulat dan kesan vasodilator. Walaubagaimanapun, masih terdapat kekurangan dalam kajian antioksidan dengan menggunakan Kaedah Ransangan Permukaan (RSM).

Oleh itu, dalam kajian ini untuk menentukan kelebihan aktiviti antioksidan seperti memerangkap radikal bebas [2,2-diphenly-1-picrylhydrazyl (DPPH)], jumlah kandungan fenolik (TPC), jumlah kandungan flavonoid (TFC) dan ion ferik mengurangkan kuasa (FRAP) pada buah *P.macrocarpa* dengan menggunakan kaedah ransangan permukaan. Reka Bentuk Komposit Pusat (CCD) telah digunakan untuk menentukan peratusan hasil maksimum dengan memberi tumpuan kepada tiga pembolehubah bebas yang termasuk suhu pengekstrakan (53.18-80 ºC), masa pengekstrakan (66.30-133.64 minit) dan pelarut etanol:air nisbah (63.18-96.82 %v/v) dengan dua puluh eksperimen telah dijalankan. Pengekstrakan ini dijalankan dengan menggunakan alat refluks set dan menapis pelarut secara manual.Kesuaian yang optimum untuk pengekstrakan antioksidan yang didapati pada suhu pengekstrakan (63.60º C), masa pengekstrakan (66.36 minit) dan pelarut etanol:air nisbah (74.36 %v/v) dengan hasil peratusan tertinggi DPPH, TPC, TFC dan FRAP adalah 87.23%, 268.03%, 3.22% dan 7.49%.

Oleh itu, hasil daripada aktiviti antioksidan yang diperolehi melalui eksperimen adalah hampir kepada nilai-nilai yang diramalkan dan model yang digunakan dalam RSM sesuai untuk mengoptimumkan keadaan pengekstrakan. Kesimpulannnya, RSM adalah alat statistik yang baik dalam memberi kuasa penilaian kesan pembolehubah proses tertentu dan interaksi mereka pembolehubah tindak balas dalam masa yang singkat, kurang kos dan kurang eksperimen diperlukan.

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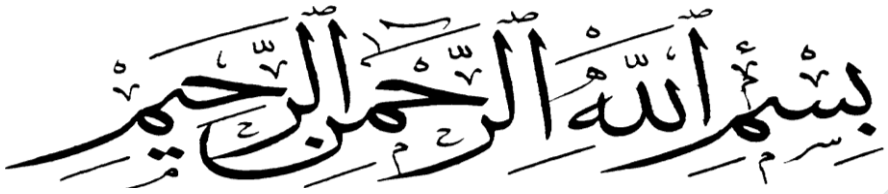

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I certify that a Thesis Examination Committee has met on 17 January 2018 to conduct the final examination of Khurul Ain binti Mohamed Mahzir on her thesis entitled "Optimization Study on Antioxidant in Fruit Extract of *Phaleria macrocarpa* (Scheff.) Boerl in Malaysia and Evaluation on its Functional Cosmetic" 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 Master of Science.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

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LIST OF ABBREVIATIONS

$AlCl_3.6H_2O$	Aluminium Chloride
ANOVA	Analysis of Variance
AP	Adequate Precision
BBD	Box-Behnken Design
CCC	Circumscribed
CCD	Central Composite Design
CC	Central Side
CCI	Inscribed
CF	Correction Factor
CV	Coefficient Variance
DCPIP	Metaphosphoric acid
	2,6dichlorophenolindophen
DNA	Deoxyribonucleic Acid
DPPH	1,1-diphenyl-1-picryl-hydrazyl
EE	Erythemal Effect Spectrum
FRAP	Ferric Ion Reducing Power Assay
FTIR	Fourier Transform Infrared Spectroscopy
Fe^{2+}	Ferrous Ion
Fe^{3+}	Ferric Ion
$FeCl_3.H_2O$	Ferric Chloride Solution
Fe $(TPTZ)^{2+}$	Blue Ferrous-Tripyridyltriazine
Fe $(TPTZ)^{3+}$	Yellow Ferric
GCMS	Gas Chromatography Mass Spectrometry
HBT	p-HydroxybenzaldehydeThiosemicarbazone
HCl	Hydrochloric Acid
I	Solar Intensity
L-DOPA	L-3,4-dihydroxyphenylalanine
MBT	p-methoxybenzaldehyde, thiosemicarbazone
MED	Minimal Erythema Dose
$NaHCO_3$	Sodium Carbonate
NIST	National Institute of Standard and Technology
OMC	Octylmethoxycinnamate

ROS	Reactive Oxygen Species
RSM	Response Surface Methodology
SPF	Sun Protection Factor
TAC	Total Anthocyanin Content
TFC	Total Flavonoid Content
TPC	Total Phenolic Content
TPTZ	2,3,5-triphenyl-1,3,4-triaza-2-azoniacyclopenta-1,4-diene chloride
UV	Ultraviolet

CHAPTER 1

INTRODUCTION

1.1 Background of the Study

Definition of *Halal* in Arabic word means lawful or permitted. In reference to food, it is the dietary standard, as prescribed in the Qur'an (the Muslim scripture). The opposite of halal is haram, which means unlawful or prohibited. Halal and haram are universal terms that apply to all facets of life. These terms are commonly used in relation to food products, meat products, cosmetics, personal care products, pharmaceuticals, food ingredients, and food contact materials. The reasons for prohibition are due to impurity and harmfulness. In terms of *Haram*, it is explicitly prohibited in the Qura'an, Sunnah and the consensus of the Muslim jurist (Ijma').

Halal products are very fast entering market within Europe and the United State. Europe is the world's largest producer of cosmetic products, followed by the United States and Japan. Out of the total projected global cosmetics sales of € 126 billion in 2007, the European market has the largest share of about 55 per cent. The halal cosmetic segment is growing 15% per years with the total world market for halal cosmetic is USD 5-14 billion at around 50% sales in the Middle East region (Hunter, 2011). As reported by Kassim (2010) the total global halal products market for cosmetic and personal care estimated at USD 13 billion. It can be indicate the huge margin of sales, give endless opportunity in exploring halal cosmetic. In the scope of halal cosmetics, the concept covers critical aspects of production such as halal ingredients and usage of permissible substances which must be manufactured, stored, packaged and delivered in conformity with Shari requirements. Interestingly, halal cosmetics has also gained momentum amongst modern consumers who are eco-ethical conscious and are willing to pay a premium for organic, natural and earthy cosmetics products to suit their modern lifestyle. The halal label on cosmetics and beauty products appeal to consumers seeking integrity and authenticity in their cosmetic and personal care products. In terms of cosmetic product, there is *Mashbuh*, Arabic definition to doubtful or suspected things whether halal or haram status of a particular ingredient, one should avoid consuming or using the product. The example considered *mashbuh* are gelatin, enzyme, emulsifier and glycerol or glycerin which mostly used as production of soap, toothpaste, shampoo, facemask and others.

Other than that, the uses of alcohol in cosmetic and food from side of Islamic view, the alcohol which extracted from grapes or dates it is not permissible. However, if it is from anything else besides dates and grapes and it does not intoxicate directly or through a mixture, then it is permissible. In some ASEAN countries such as Malaysia, Indonesia and Thailand, the percentages of alcohol content permissible is at 1% whilst Singapore state the level at 0.5% (Najiha et al. 2010). Besides that, in Brunei, United Kingdom and Canada, alcohol is not allowed to be present in Halal food product (Jamaludin et al. 2016). The guideline which is set at 1% in Malaysia was established based on a fatwa of Islamic scholars and research conducted on the

fermentation process of different substrates ranging from cereals, fruits and palm sugars (Vern et al. 2009). Others, benzyl alcohol which produced naturally by plants and commonly found in fruits, teas and variety of essential oil. It is used to kills bacteria in personal care formulations and does not cause intoxication therefore it is classed as Halal. Nowadays, in the processing of cosmetic products, the issues of ingredients that originate from animals, including haram sources cannot be escaped. Therefore, halal cosmetic used the definition of halal with addition of preparation, processing, manufacturing and storing of halal cosmetic must be distinguished from haram things. It must be safe to use by consumer and free from harmful and adverse effect. The halal label on cosmetics and beauty products appeal to consumers seeking integrity and authenticity in their cosmetic and personal care products.

The terms of cosmetics can be defined as intended to be applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance without affecting the external body. The use of plant was the major sources and foundation to cosmetics, before discovering method of synthetic substances with same properties. Despite, people had discovered wide information regarding the benefit of plant over time through continuous contact with their natural environment since plants are substantial sources of natural antioxidants. The extract from plant has been used in cosmetic and medicine application. A several part from plant such as leaves, stem, fruit flowers, barks, buds and roots were used appropriately. In cosmetic, plant and plant extracts were used to give moisture, whitening, tanning, color cosmetics, sun block, free radical scavenging, antioxidant, washings, preservatives and thickening effects (Schürch et al. 2008). Even nowadays, the trends of cosmetic market are develops from natural resources of plant since it has a lot of benefits and uses. Many studies have been done on research for the different part of plant extracts to get the information as possible so that chemical profile can be achieved. This procedure is proven to be very valuable to the scientific community to determine the potentials and benefits of a plant extracts in cosmetic or medicine.

A long-term exposure to ultraviolet (UV) irradiation from sunlight has deleterious effects in human skin. The existence of excessive number of reactive oxygen species (ROS) cause to natural aging (Mukherjee et al. 2011), wrinkles, pigmentation, loss of skin tone, immune suppresion, erythema, sunburn, hyperplasia and DNA damage which lead to skin cancer (Mizrahi, 1997). Even though, skin has self-defense system to deal with ROS, however, overexposure to UV light lead to oxidative stress and damage premature aging. It is due to the influences of over exposure to UV light and imbalanced diet. Moreover, UV radiation depending on its wavelength, which divided into the three categories: short wavelengths UVC (200–280 nm), medium wavelengths UVB (280–320 nm) and long wavelengths UVA (320– 400 nm). UVC radiation is filtered out by the atmosphere before reaching earth. UVB radiation is incompletely filtered out by the ozone layer and responsible for the damage due to sunburn and pyrimidine dimers. While, UVA radiation reaches the deeper layers of the epidermis, dermis and irritate the premature ageing of the skin and responsible for the generation of free radicals (Mbanga et al. 2014).

Skin produces enzymes such as elastase and collagenase at normal skin condition with similar rate as aging process happened and age increased (Karim et al. 2014). Tyrosinase is an enzyme present in animal tissues which actively induced the production of melanin. The excessive amount productions lead to severe hyper-pigmentation. Anti-tyrosinase catalytic very effective to inhibit excess melanin production and reduce hyper-pigmentation. Hence, natural plant sources which contain high antioxidants are able to stop free radical reactions and prevent oxidative damage. It helps to prevent the initiation and propagation of oxidizing chain reaction involving unmanageable metabolic processes from ROS and free radical (Chanda & Nagani, 2010).

The importance of the antioxidant compounds, photo-protective, anti-tyrosinase, anti-collagenase molecules and several types of fruits have been found with tremendous properties. One of the plants known as, *Phaleria macrocarpa* (Scheff.) Boerl, that belong to Thymelaeceae family have the major bioactive components such as alkaloid, lignin, saponin, terpenoid and polyphenol (Azmir et al. 2014). The fruits, leaves and stems contain phenolic compound that showed antioxidant activity (Irianti et al. 2008; Soeksmanto et al. 2007). This plant normally can be found in Bandar Baru Bangi, Selangor; Kuantan, Pahang and Johor Bahru. Despite of wide distribution of this plant, the investigation of its possible antioxidant activities are still limited especially by using the application of Response Surface Methodology (RSM). The optimization for the extraction method for antioxidant activities of *P.macrocarpa* fruits extract by using central composite design (CCD) where the several circumstance effect the responses by varying them simultaneously and bring out a limited number of experiments (Hamsaveni et al. 2001). The optimization process not only increases the adequacy of technologist, but the quality of product in plant extract also assured.

1.2 Problem Statement

Halal issue is starting to get the place and attention in the market and it is very influencing in marketplace particularly in most Islamic countries. The sources of active ingredients for cosmetic products are sometimes doubtful to Muslim user. Some of these ingredients such as gylcerine, collagen, elastin and myristic acid are used in preventing wrinkles on the skin face (Murray, 2011). Moreover, in cosmetic substances, the products from animal sources may cause problems. For example, collagen and gelatine, which are used in cosmetic preparation, are important animal products. The main sources of animal products in preparing cosmetics are skin and bones. The production from skins basically involves an extraction process of several stages with increasing temperatures, filtration and concentration in a vacuum evaporator. The alternative way to improve cosmetic by using natural product from plant based. In term of active ingredient from plant, the plant extract for method of processing or extraction should be known. These contribute questionable in Islamic law basically, halal almost related to the way of slaughtering of animal for Muslim's consumption (Krishnan et al. 2017).

Other than that, plant based ingredients needed to be extracted from the plant by using the type of solvent used. Currently, some of the issued related to the halalness of cosmetic with the presence of alcohol. Alcohol-free products basically mean products that do not contain ethyl alcohol. It may contain other alcohols such as ethyl, stearyl, cetearyl, or lanolin, which are known as fatty alcohols. If ethyl alcohol is added to a product, it is normally denatured first, to prevent the ethyl alcohol in the cosmetic from being diverted illegally for use as an alcoholic beverage or cosmetic. In Malaysia, some of the cosmetic products in the market have no status and bring confusion to the Muslim consumers. Moreover, the optimization extraction by using method of Response Surface Methodology (RSM) on *P.macrocarpa* fruit extract in antioxidant activities are still lack of information. From the optimized of crude extract obtained in *P.macrocarpa* fruit, the characterization of cosmetic properties such as total carotenoid content, total anthocyanin content, total ascorbic acid content, anti-tyrosinase, anti-collagenase and anti-microbial activity lead to investigation since no wide research yet regarding on this respectively. Hence, most researchers used this tool to provide the highest yield production through an experimental design suggested by RSM (Raissi, 2009; Madan et al. 2002).

1.3 Objectives

The objectives of this research are to:

1. To optimize the antioxidant activity in fruit extracts of *P.macrocarpa* by using response surface methodology of central composite design.

2. To investigate the physicochemical characterization of fruit extract of *P.macrocarpa* by using fourier transform infrared spectroscopy (FTIR) and gas chromatography-mass spectrometry (GCMS).

3. To evaluate the functional cosmetic properties in-vitro photo-protective activity, total anthocyanin content, total carotenoid content, total ascorbic acid, and bioactive compounds of anti-tyrosinase and anti-collagenase.

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