HAIR GROWTH AND HAIR TANNING ACTIVITIES OF MANGOSTEEN PERICARP WATER EXTRACT ON HAIR DERMAL PAPILLA CELLS

TAN YING FANG

Universiti Teknologi Malaysia

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To my beloved grandmum.

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ABSTRACT

Hair graying represents the most common phenomena of human, and the number of men and women who suffer hair loss is increasing in accordance with changes in lifestyle and nutritional balance. Thus, it is important to develop new therapies to enhance hair growth activity as well as hair tanning. In this study, water extract of mangosteen pericarp was used to investigate its hair growth and tanning activities on hair dermal papilla cells. The mangosteen pericarp extract was found to contain 3.706 mg/ml protein, 0.519 mg/ml polysaccharide, 5.103 gallic acid equivalents mg/g total phenolic content and 1.503 quercetin equivalent mg/g total flavonoid content. Mangosteen pericarp extract showed high IC_{50} values in both 2,2-diphenyl-1-picrylhydrazyl and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) assays (4.142 mg/ml and 2.373 mg/ml, respectively). This indicated that mangosteen pericarp water extract has low antioxidant activity. The effect of mangosteen pericarp extract on the cellular mitochondrial activity, viability and cytotoxicity of hair dermal papilla cells were measured by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide and Sulforhodamine B assays. It was found that the highest concentration of the extract which did not affect the cell viability was 500 μg/ml. For hair growth promoting activity, the degree of hair dermal papilla cells proliferation increased with increasing concentration of extract. By treated the cells with 500 μg/ml of extract, cell proliferation significantly increased by 157.56%, compared to untreated control cells. The mangosteen pericarp extract was found to stimulate melanin synthesis and tyrosinase activity of dermal papilla cells in concentration-dependent manner, up to the highest concentration of 500 μg/ml. The melanin synthesis was more than four-fold as compared to the untreated control group, indicating that this extract could be one of the melanogenic-stimulating agents. This study also showed that mangosteen pericarp extract was more potent and better in comparison with known effective melanogenic agents such as, α-melanocyte stimulating hormone and forskolin in inducing the melanogenic effects of dermal papilla cells. The overall results showed that mangosteen pericarp extract can potentially be used as a safe ingredient for the development of hair growth and hair tanning product.

ABSTRAK

Rambut beruban merupakan satu fenomena yang biasa dalam manusia, sementara bilangan lelaki dan wanita yang mengalami keguguran rambut semakin meningkat selaras dengan perubahan gaya hidup dan keseimbangan nutrisi/zat. Oleh itu, adalah amat penting untuk membangunkan terapi baru bagi meningkatkan aktiviti pertumbuhan rambut serta penghitaman rambut. Dalam kajian ini, ekstrak air kulit manggis digunakan untuk mengkaji aktiviti pertumbuhan rambut dan penghitaman rambut pada sel-sel kulit papilla rambut. Ekstrak kulit manggis didapati mengandungi 3.706 mg/ml protein, 0.519 mg/ml polisakarida, 5.103 setara asid gallic mg/g jumlah kandungan fenolik dan 1.503 setara quercetin mg/g jumlah kandungan flavonoid. Ekstrak kulit manggis menunjukkan nilai IC_{50} yang tinggi dalam kedua-dua eksperimen 2,2-diphenyl-1-picrylhydrazyl dan 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) (4.142 mg/ml dan 2.373 mg/ml, masing-masing). Ini menunjukkan bahawa ekstrak kulit manggis berasaskan air mempunyai aktiviti antioksidan yang rendah. Kesan ekstrak kulit manggis ke atas aktiviti mitokondria sel, kebolehhidupan dan sitotoksisiti sel papilla kulit rambut dikaji menggunakan eksperimen 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide dan Sulforhodamine B. Kepekatan tertinggi ekstrak yang tidak menjejaskan kebolehhidupan sel adalah 500 μg/ml. Untuk aktiviti penggalakkan pertumbuhan rambut, tahap proliferasi kulit rambut sel papilla meningkat dengan peningkatan kepekatan ekstrak. Apabila dirawat dengan 500 μg/ml ekstrak, perkembangan sel meningkat sebanyak 157.56%, berbanding dengan sel-sel kawalan yang tidak dirawat. Ekstrak kulit manggis didapati dapat merangsang sintesis melanin dan aktiviti tyrosinase pada sel-sel kulit papilla bergantung kepada kepekatan, sehingga kepekatan tertinggi 500 μg/ml. Sintesis melatin didapati meningkat empat kali ganda lebih tinggi berbanding dengan sel-sel kawalan yang tidak dirawat. Keputusan keseluruhan menunjuk bahawa estrak kulit manggis boleh dijadikan sebagai alternatif bagi menggalakkan pertumbuhan rambut dan sebagai produk penghitaman rambut.

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LIST OF SYMBOLS

α	Alpha
β	Beta
˚C	Degree Celcius
γ	Gamma
%	Percentage

LIST OF ABBREVIATIONS

α-MSH	alpha-Melanocyte Stimulating Hormone
APC	Adenomatous Polyposis Coli
BSA	Bovine Serum Albumin
DMSO	Dimethyl Sulfoxide
DPPH	1,1-diphenyl-2-picrylhydrazyl
FBS	Fetal Bovine Serum
FDA	Food and Drug Administration
FK	Forskolin
GSK-3β	Glycogen Synthase Kinase-3β
g/L	Gram per liter
HPLC	High Performance Liquid Chromatography
HDPCs	Human Dermal Papilla Cells
IGF	Insulin-like Growth Factor
min	minutes
mg/mL	milligram per milliliter
mL	milliliter
mM	millimolar
MTT	3-(4,5-Dimethylthiazol-2-yl)-2,5-dipheynyl tetrazolium bromide
NaOH	Sodium Hydroxide
nm	nanometre
OD	Oxygen Demand
pH	Power of Hydrogen
SD	Standard Deviation
SRB	sulphorhodamine B
T_3	Triiodothronine

T_4	Levorotatory thyroxine
TLC	Thin Layer Chromatography
TCA	Triochloroacetic acids
µg/mL	microgram per milliliter
µL	microliter
VEGF	Vascular Endothelial Growth Factor
WST-1	4-[3-(4-Idophenyl)-2-(4-nitrophenyl)-2H-5-tetrazolio]-1,3-benzene disulfonate

CHAPTER 1

INTRODUCTION

1.1 Research Background

In recent years, Global Beauty Market, also known as Cosmetics and Toiletries or Personal Care Products has grown by 4.5% a year on average Compound Annual Growth Rate (CAGR), with annual growth rates ranging from around 3% to 5.5%. This market has shown both its ability to achieve stable and continuous growth as well as its capacity for resilience in unfavorable economic conditions (Lopaciuk and Loboda, 2013). The Global Beauty Market is usually divided into five main business segments: skincare, haircare, color (make-up), fragrances and toiletries. These segments are complementary and through their diversity they are able to satisfy all consumers' needs and expectations with regard to cosmetics (Lopaciuk and Loboda, 2013). The global hair care market is characterized by nearly 10,000 launches per year, has become the dynamic nature of the market. Thus, the hair care market is growing robustly in both in the developed and the emerging markets and it leads to the global economic improvement and the consequent rise in disposable income among consumers. Geographically, Asia Pacific is the second largest market for cosmetics after Europe, expected to reach $126.8 billion by 2020, registering a CAGR of 4.02%. The firm's analysts report Asia to be one of the most diverse and dynamic cosmetics markets in the world (Yeomans, 2015).

In the product category segment of the Asia-Pacific cosmetics market, skin and sun care, and hair care products are the most widely used product and hold a considerable percentage share (Kumar, 2015). Furthermore, demand for natural and organic cosmetic products is supplementing the growth of this market (Kumar, 2015). Those organic beauty products and natural cosmetics that manufactured in accordance with the fair-trade philosophy are becoming more and more visible in the global market. Consumer preferences towards the use of natural cosmetic products is increasing and forcing the manufacturers cosmetic and toiletries to change strategies according to their preferences (Lopaciuk and Loboda, 2013).

In a previous literature reported, it evidenced that graying hair may be contributed by massive oxidative stress via accumulation of hydrogen peroxide in the hair follicle. In this regard, previous studies by Hamid *et al*. (2012), which claimed the strong antioxidant activity and melanogenic effects of the mangosteen leaf extract has given an insight into the potential in development of gray hair prevention agent. In this study, the mangosteen leaf extract has stimulated the melanin production and tyrosinase activity on B16F1 melanoma cells in a dose-dependent manner and thus proposed that the extract can be used to treat disease of hypopigmentation and beneficial to the field of tanning cosmetic. However, there have been no reports specifically addressing the effects of the mangosteen pericarp extract on hair growth activity a hair tanning in hair dermal papilla cells. Furthermore, the use of chemicals and synthetic ingredients in hair growth and hair tanning product in the market has been reported associated with adverse consequences. Thus, it is of great importance to explore new natural ingredients for substitute the use of harmful chemicals in hair growth and hair tanning products.

Garcinia mangostana Linn., known as mangosteen, is a tropical fruit classified to the Guttiferae family (Zarena *et al*., 2011). The pericarp of mangosteen has a long history of medicinal use in both Chinese and Ayurvedic medicine (Shibata *et al.,* 2013). People have used this waste pericarp as a traditional medicine for the treatment of abdominal pain, diarrhea, dysentery; heal the wound infection, suppuration and chronic ulcer (Zhou *et al*., 2011), because it contains considerable

amounts of biologically active compounds that have been reported beneficial to human health, such as, xanthones which have relatively strong antifungal and antibacterial activities (Obolskiy *et al.,* 2009); tannins that assure astringency to discourage infestation by insects, fungi, plant viruses, bacteria and animal predation (Akao *et al*., 2008); anthocyanin like cyanidin-3-sophoroside which have high antioxidant properties (Chaovanalikit *et al*., 2012); and phenols which exhibited strong pH-dependent bacteriostatic and bactericidal effects against Gram-positive bacteria (Palakawong *et al*., 2013). This study was designed to investigate the effect of mangosteen pericarp extract on hair-growth promoting activity and hair tanning in hair dermal papilla cells.

1.2 Problem Statement

Hair loss is an emotionally distressing condition in humans and its major factors are genetic disorders (hypotrichosis), an increase in the induction of the telogen phase (telogen effluvium), genetic follicular miniaturization (androgenetic alopecia), an increase in telogenic depilation with detention of the follicle in early anagen (alopecia areata), and/or the elimination of the hair in anagen (anagenic effluvium) (Park *et al.,* 2012). Besides, hair graying, one of the most ordinary phenotype of human, is a common process of decreasing in the melanin content of hair follicles as individual aging. Other than the physiology of aging, there is also premature hair graying which the most commonly is from autosomal-dominant genetic inheritance or pathologic conditions (McDonough and Schwartz, 2012).

There are limited available treatment options for hair loss and hair graying and the aging impacts on the melanocyte system in hair follicle still an unknown. Furthermore, the use of chemicals and synthetic ingredients in hair growth and hair tanning product has been reported associated with adverse consequences. There are studies reported that hair products in market consists of many harmful chemicals, such as phthalates and parabens which associated with breast cancer; DEA

(Diethanolamine) and DEA compounds likes, cocamide DEA and lauramide DEA, and related chemicals likes MEA (Monoethanolamine), TEA (Triethanolamine) are hormone-disrupting chemicals that can react to form cancer-causing nitrosamines and research indicated a strong link to liver and kidney cancer; dibutyl phthalate (DBP) are toxic to reproduction and may interfere with hormone function; P-Phenylenediamine has potential to cause cancer and can be contaminated with heavy metals toxic to the brain; formaldehyde-releasing preservatives likes methenamine and quarternium-15 which causes cancer; siloxanes likes cyclomethicone and cyclotetrasiloxane can interfere with hormone function and damage the liver; and sodium lauryl sulfate and sodium laureth sulfate are one of the most toxic ingredients which exposures will causes eye damage, depression, diarrhea and many other ailments (Onge, 2012; Lipman, 2016). There are some natural ingredients used in hair treatment in market, such as jamaican castor oil, coconut oil, evening primrose oil, rosemary, aloe vera, lemongrass, horsetail and sage (Banks, 2014; Jackson, 2014). However, due to the lack of natural products, it is very important to develop new ingredients to enhance hair growth, to treat hair graying and to explore new natural ingredients for substitute the use of harmful chemicals in hair growth and hair tanning products. Previous studies showed that there is a strong melanogenesis activity on B16F1 melanoma cells using mangosteen leaf extract and it bring advantages to cure the disease of hypopigmentation and also tanning effect cosmetic field (Hamid *et al.,* 2012). Therefore, the use of the mangosteen pericarp water crude extract is believed can stimulate hair growth activity and hair tanning in hair dermal papilla cell.

1.3 Objective of Research

The objectives of the research were to investigate the hair growth and hair tanning activities of mangosteen pericarp extract on hair dermal papilla cells.

1.4 Scope of Research

The scopes of the research are:

i. Extraction of mangosteen pericarp by using turbo extraction.
ii. Investigate the primary and secondary metabolites contents of the mangosteen pericarp extract.
iii. Investigate the antioxidant activity of mangosteen pericarp extract by DPPH assay and ABTS assay.
iv. Investigate the viability and cytotoxicity effects of hair dermal papilla cells by using MTT assay and SRB assay.
v. Investigate the promoting hair growth activity by WST-1 assay on hair dermal papilla cells.
vi. Investigate the melanogenesis activity by measuring secreted melanin assay, intracellular melanin assay and intracellular tyrosinase activities of hair dermal papilla cells.

1.5 Hypothesis

The mangosteen pericarp water extract results in increment of cell proliferation and stimulate melanin synthesis which can promote hair growth and hair tanning activities on hair dermal papilla cells.

1.6 Significant of Study

This study was indicated that the mangosteen pericarp extract could be a new natural ingredient to substitute the use of harmful chemicals in the development of hair growth and hair tanning products. This has brought the advantage to cosmeceutical manufacturers who searching for new natural and safe plant based active ingredients, since the hair care and toiletries are the high demanding products in the cosmeceutical and pharmaceutical industries. Nowadays, cosmeceutical manufacturers are increasingly searching new products that was not harmful to the environment whilst their effectiveness remained comparable to the premium brand.

Other than that, the raw material used in this study was mangosteens, which are one of the local fruits in Malaysia which indirectly linked to the agriculture of the country. The agriculture's performance has brought the contribution to the country's economic development, since it is measured using information about harvests and the sale of raw materials, mainly crops and livestock. Furthermore, the increment of the demand of the mangosteen (raw materials) has generated the income to the local farmers, suppliers and industry and has contributed to impressive economic growth. In addition, this study also enhances the coordination effort among scientist, farmers, manufacturers, traders, and health care professionals and also regulatory authorities to drive the industry to a higher level of quality, safety and efficacy of native fruit products and thus economic return to the country. Thus, the most significant of this study can contribute to wealth creation, enhance quality of life and create a new industry.

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