UNIVERSITI PUTRA MALAYSIA

ISOLATION AND CHARACTERIZATION OF HYPOCHOLESTEROLEMIC BIOACTIVE AGENT EXTRACTED FROM Monascus purpureus FTC5391

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ISOLATION AND CHARACTERIZATION OF HYPOCHOLESTEROLEMIC BIOACTIVE AGENT EXTRACTED FROM *Monascus purpureus* FTC5391

By

ZAHRA AJDARI

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

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DEDICATION

Dedicated to my beloved husband and kids, family, friends and well wishes for their love, interest and encouragement

Abstract of thesis presented to the senate of Universiti Putra Malaysia
in fulfilment of the requirement for the degree of Doctor of Philosophy

ISOLATION AND CHARACTERIZATION OF HYPOCHOLESTEROLEMIC BIOACTIVE AGENT EXTRACTED FROM *Monascus purpureus* FTC5391

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Chairman: Professor Arbakariya B. Ariff, PhD

Faculty: Biotechnology and Biomolecular Sciences

One of the basic causes of mortality in developed countries is cardiovascular disease, especially coronary heart disease. Control of blood cholesterol level is important to avoid cardiovascular disease. In this study the bioactive compound(s) of *Monascus purpureus* FTC5391 with hypocholesterolemic potential was investigated.

In order to purify and identify the hypocholesterolemic bioactive agent of *M. purpureus* FTC5391 fermented product, cultivated via submerged fermentation in modified medium was sub-fractionated by solid phase extraction (SPE). The hypocholesterolemic active fraction in rats was selected for further purification by recycling preparative HPLC (RP-HPLC). The effective fraction significantly (*P*-value < 0.05) regulated the serum lipid-profile of hypercholesterolemic rats as compared with no treated control groups. This fraction increased the serum HDL-C (100%) and decreased the TC (42.6%), LDL-C (46%), TG (54.4%) levels as well as TC/HDL-C ratio (71.9%). Whereas, Atrovastatin, as a positive control, could regulate the rat

serum lipid profile by increasing the serum HDL-C (37.5%) and decreasing the serum TC, LDL-C, TG levels and TC/HDL-C ratio 45.15%, 42%, 54.3% and 61.4%, respectively. MS spectrum of the pure effective fraction and its comparison with spectra library suggested the cyclopropane-carboxylic acid 4-dodecanoeil ester as a novel hypocholesterolemic agent. The obvious superiority of this novel compound to regulate the lipid profile in comparison to the atrovastatin and its ability to decrease the liver damage indicator enzymes, revealed the golden perspective of this novel molecule as a potent future hypocholesterolemic drug.

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Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

PEMENCILAN DAN PENCIRIAN AGEN BIOAKTIF HIPOKOLESTEROLEMIK YANG DIEKSTRAK DARIPADA *Monascus purpureus* FTC5391

Oleh

ZAHRA AJDARI

Mac 2012

Pengerusi: Profesor Arbakariya B. Ariff, PhD

Fakulti: Bioteknologi dan Sains Biomolekul

Salah satu punca asas kematian dalam negara-negara membangun adalah penyakit kardiovaskular, terutamanya penyakit jantung koronari. Kawalan paras kolesterol dalam darah adalah penting untuk mengelakkan penyakit kardiovaskular. Dalam kajian ini sebatian bioaktif daripada *Monascus purpureus* FTC5391 dengan potensi hipokolesterolemik telah dikaji.

Dalam usaha untuk menulen dan mengenal pasti agen hipokolesterolemik bioaktif daripada produk fermentasi, *M. purpureus* FTC5391 dikultur melalui fermentasi fasa tenggelam dalam medium yang dimodifikasi dan dipecahkan melalui pengekstrakan fasa pepejal (SPE). Sebatian hipokolesterolemik aktif dalam tikus telah dipilih untuk penulenan selanjutnya dengan HPLC persediaan kitar semula (RP-HPLC). Sebatian yang efektif (P-nilai <0.05) mengawal serum profil-lipid daripda tikus hiperkolesterolemik dengan ketara berbanding dengan kumpulan kawalan yang tidak

dirawat. Sebatian ini meningkatkan serum HDL-C (100%) dan mengurangkan tahap TC (42.6%), LDL-C (46%), TG (54.4%) serta nisbah TC / HDL-C (71.9%). Manakala atrovastatin, sebagai kawalan positif, boleh mengawal serum profil-lipid tikus dengan meningkatkan serum HDL-C (37.5%) dan mengurangkan TC serum, LDL-C, tahap-tahap TG dan nisbah TC / HDL-C adalah 45,15%, 42%, 54.3% dan 61.4%, masing-masing. Spektrum MS sebatian tulen yang efektif dan perbandingannya dengan "spektra library" mencadangkan asid karboksilik siklopropana 4-dodecanoeil ester sebagai ejen hipokolesterolemik terunggul. Kelebihan yang jelas daripada kompaun terunggul ini untuk mengawal serum profil-lipid berbanding dengan atrovastatin dan keupayaan untuk mengurangkan penunjuk enzim kerosakan hati. Molekul novel ini mempunyai peluang keemasan sebagai dadah hipokolesterolemik yang mujarab untuk masa depan.

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I certify that a Thesis Examination Committee has met on 23 March 2012 to conduct the final examination of Zahra Ajdari on her thesis entitled "Isolation and Characterization of Hypocholesterolemic Bioactive Agent Extracted from *Monascus purpureus* FTC5391" in accordance with the Universities and University Collage 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.

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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 **Doctor of Philosophy**. The members of the Supervisory Committee were as follows:

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DECLARATION

I declare that the thesis is 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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ZAHRA AJDARI

Date: 23 March 2012

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