UNIVERSITI TEKNOLOGI MARA

EFFECTS OF PURE TOCOTRIENOLS ON THE STATUS OF ENDOTHELIAL ACTIVATION, INFLAMMATION, OXIDATIVE STRESS AND PLAQUE STABILITY IN THE PREVENTION OF EARLY AND ESTABLISHED EXPERIMENTAL ATHEROSCLEROSIS

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Thesis is submitted in fulfillment
of the requirements for the degree of
Master of Science

Faculty of Medicine

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CONFIRMATION BY PANEL OF EXAMINERS

I certify that a Panel of Examiners has met on 18th November 2015 to conduct the final examination of Nurmazni Binti Zulkafli on her Master of Science thesis entitled "Effects of Pure Tocotrienols on the status of endothelial activation, inflammation, oxidative stress and plaque stability in the prevention of early and established experimental atherosclerosis" in accordance with Universiti Teknologi MARA Act 1976 (Akta 173). The panel of Examiners recommends that the student be awarded the relevant degree. The panel of Examiners were as follows:

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AUTHOR'S DECLARATION

I declare that the work in the thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institutions or non-academic institution for any degree or qualification.

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ABSTRACT

Atherosclerosis is one of the leading causes of coronary artery disease (CAD). Studies on the cardioprotective activities of tocotrienols (T3) in the absence of alpha tocopherol (TCP) remain obscure. The aim of this study was to evaluate the effects of pure T3 supplementation on lipid lowering, tissue endothelial activation and inflammatory biomarkers, and oxidative stress in early and established atherosclerosis rabbit model. Fifteen New Zealand white rabbits were divided into two intervention groups: A1 [given 2 months normal diet (ND) and 2 weeks high cholesterol diet (HCD)] and A2 (given 2 months ND and 2 months HCD). Each group was further divided into three groups: T3-4mg/kg and T3-15mg/kg supplementation groups given pure T3 (delta90%-gamma10%) and placebo. Interventions were given throughout the study. Fasting serum lipids, plasma C-reactive protein and 8-isoprostanes were measured at baseline, 4, 8, 10, 12, 16 weeks. The aorta of the rabbits were evaluated for biomarkers of inflammation (CRP, IL-6, NFκB and TNF-α), endothelial activation (E-selectin, VCAM-1 and ICAM-1) and plaque stability (MMP-9, MMP-12 and SMA). In A1 groups, pure T3 significantly reduced total cholesterol, low density lipoprotein and tissue expression of E-selectin, VCAM-1, CRP, MMPs-9, MMPs-12 while in A2 groups, pure T3 significantly inhibited 8-isoprostanes and tissue expression of IL-6, SMA and MMPs-9 compared to placebo. Pure T3 exhibits anti-atherogenic by modulating lipid and pleiotropic properties in this study, implying its potential benefits in the prevention and progression of atherosclerosis.

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