



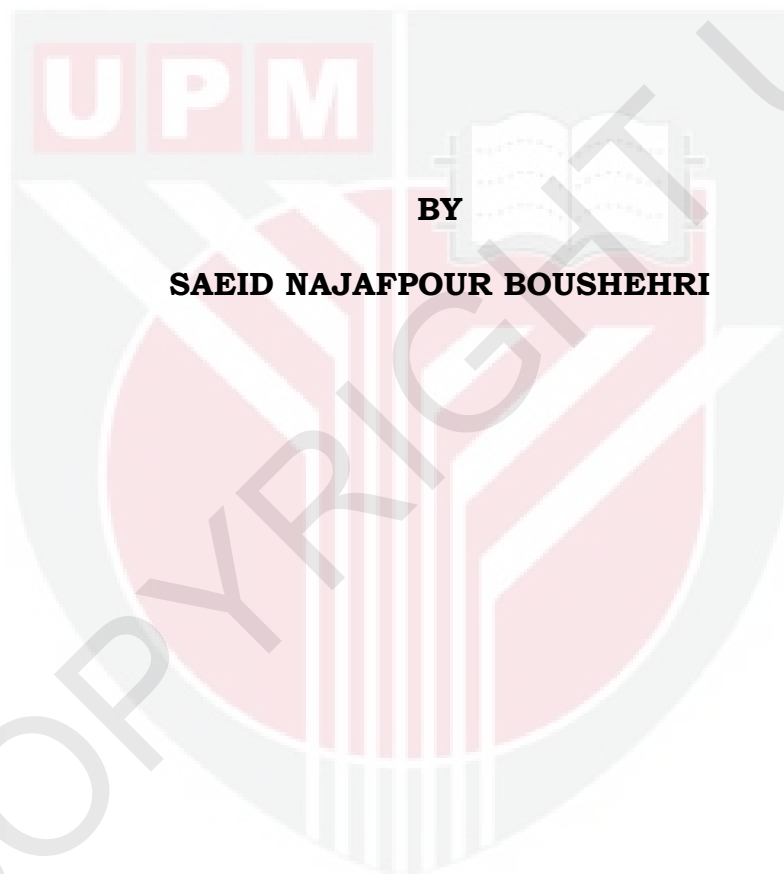
**UNIVERSITI PUTRA MALAYSIA**

**EFFECTS OF ANTIOXIDANT VITAMINS (C, E, BETA-CAROTENE)  
SUPPLEMENTATION ON CARDIOVASCULAR BIOMARKERS AMONG  
MALES WITH RISK FACTORS IN BOUSHEHR, IRAN**

**SAEID NAJAFPOUR BOUSHEHRI**

**FPSK(p) 2011 16**

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**BY**

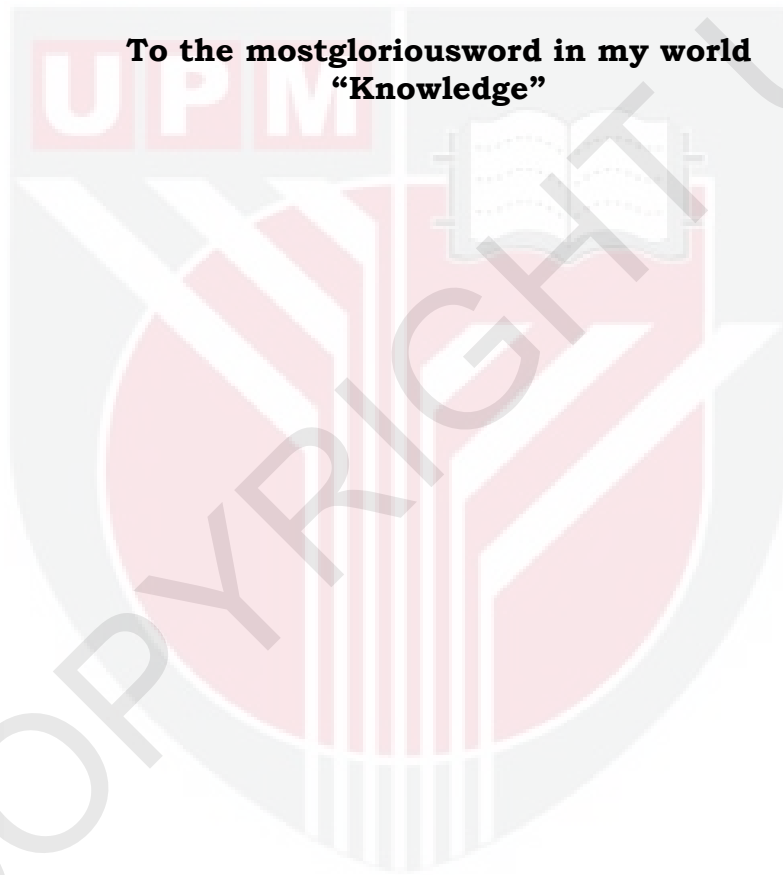
**SAEID NAJAFPOUR BOUSHEHRI**

**Thesis Submitted to the School of Graduate Studies, Universiti  
Putra Malaysia, in Fulfillment of the Requirement for the  
Degree of Doctor of Philosophy**

**August 2011**

## DEDICATION

**To the most glorious word in my world  
"Knowledge"**



Abstract of thesis to be presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirements for the Degree of Doctor of Philosophy

**EFFECTS OF ANTIOXIDANT VITAMINS (C, E, BETA-CAROTENE) SUPPLEMENTATION ON CARDIOVASCULAR BIOMARKERS AMONG MALES WITH RISK FACTORS IN BOUSHEHR, IRAN**

By

**SAEID NAJAFPOUR BOUSHEHRI**

**August 2011**

**Chairman: Rokiah Mohd Yusof, PhD**

**Faculty: Medicine and Health Sciences**

Iran, as an Eastern Mediterranean country, has accepted the western lifestyle with respect to nutrition habits, physical inactivity and smoking which contribute to higher prevalence of cardiovascular disease (CVD) risk factors among the Iranian community. In recent years (2006) CVD is the first cause of death in Iran with 167.7 deaths per 100,000 people, 23.4% wasted age (the years which person lives with disability) and 37% of all deaths were due to CVD. Two hundred (200) male subjects with age  $\geq 40$  years old were recruited in single-blinded, randomized intervention study at Persian Gulf Health Research Center, Bushehr University of Medical Sciences. The objective of this study was to determine

biomarkers risk of CVD, measured at baseline and subsequently after 12 weeks of supplementation with vitamin E (400 IU), C (500 mg), beta-carotene (15 mg), and combined (E, C, and beta-carotene) supplements and placebo, respectively. Socio-economic indices, dietary intake, anthropometry, biochemical indices, were collected. As for biochemical test studied include fasting blood sugar (FBS), lipid profile: total triglycerides (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), antioxidant vitamins (E, C, and beta-carotene) and inflammatory factors: high sensitive C-reactive protein (hs CRP), 8-iso-prostaglandin F<sub>2α</sub>, enzymatic oxidative defense: glutathione peroxidase (Gpx), superoxide dismutase (SOD), and also oxidized LDL (oxLDL), and total homocysteine (tHcy) were measured. The mean age of the subjects was 52.85±7.96 years old and the mean BMI was 27.56±4.26 kg/m<sup>2</sup>. In C group, dietary scores were for cereal 94.7, bread 93.1, beef 73.4. In E group, cereal had dietary score of 95.2, followed by bread 93.4. In beta-carotene group, cereal had dietary scores of 96.2, bread 90.8, dates 85.2. In combined group, dietary scores for cereal were 96.2, bread 94.2 and dates 85.9. In placebo group, rice received scores of 95.2, followed by bread 92.2. Among the subjects, 12.3 % had high fasting blood sugar (FBS) level and 80.1 % were normal level. Those subjects that had hypercholesterolemia and hypertriglyceridemia were 19.9 % and 41.4 % respectively. This

study also showed that 13.3 % of the total subjects had high level of LDL-C and 6.6 % with lower level of HDL-C. Result also indicated that 8-iso-PGF<sub>2</sub>α significantly decreased in groups E 17.62 % (*p*=.000), beta-carotene 17.56 % (*p*=.002), and combined 14.97 % (*p*=.014). For hs-CRP was significantly decreased in groups C 28.14 % (*p*=.036), E 23.27 % (*p*=.020), beta-carotene 27.93 (*p*=.021), and combined 23.69 (*p*=.0005). The oxidized LDL was significantly decreased in groups C 18.32 % (*p*=.005), E 23.86 % (*p*=.000), beta-carotene 17.31 % (*p*=.000), and combined 19.07 % (*p*=.000). However, SOD was found to have significantly increased in groups C 26.76 % (*p*=.0003), and combined 35.77% (*p*=.000). Whereas for Gpx, result also shown to have significantly increased in groups E 7.13 % (*p*=.003), and combined 5.34 % (*p*=.017) before and after the intervention. In conclusion, the findings from this study demonstrated that supplementation of antioxidant vitamins improved some of enzymatic antioxidant systems included SOD and Gpx, and decreased harmful biomarkers for cardiovascular diseases included hs-CRP, oxLDL, and 8-iso-PGF<sub>2</sub>α. People at risk for heart disease should be encouraged to use supplementation of antioxidant vitamins to reduce the occurrence of cardiovascular diseases.

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

**KESAN SUPLEMENTASI VITAMIN ANTIOKSIDAN (C, E, BETA-KAROTEN) KEATAS BIOMARKER BAGI CVD DALAM KALANGAN SUBJEK LELAKI BERISIKO DI BOUSHEHR, IRAN**

Oleh

**SAEID NAJAFPOUR BOUSHEHRI**

**Ogos 2011**

**Pengerusi: Dr. Rokiah Mohd Yusof, PhD.**

**Fakulti: Perubatan dan Sains Kesihatan**

Iran, adalah sebuah negara di Timur Mediterranean yang menerima gaya hidup barat dari segi amalan pengambilan makanan, fizikal yang tidak aktif dan merokok yang menyebabkan meningkatnya prevalen faktor risiko penyakit jantung vaskular (CVD) dalam kalangan populasi. Dalam masa terkini (2006) CVD merupakan penyebab utama kematian di Iran dengan 167.7 kematian per 100,000 populasi, dengan 23.4% merugikan umur (bilangan tahun seseorang hidup dengan ketidakupayaan) dan 37% daripada kematian disebabkan CVD (Ministry of Health, Iran

2006). Kajian ini bertujuan untuk menentukan kesan suplementasi vitamin antioksidan E, C, beta-karoten dan kombinasi (E, C, dan beta-karoten) keatas biomarker risiko CVD dalam kalangan subjek lelaki yang mempunyai faktor risiko CVD di Boushehr, Iran. Dua ratus (200) subjek lelaki yang berumur  $\geq 40$  tahun dan mempunyai indeks jisim tubuh (BMI)  $\geq 30$  Kg/m<sup>2</sup> telah terpilih dalam kajian intervensi rawak single-blinded ini. Objektif kajian adalah untuk menentukan paras biomarker risiko CVD, diukur pada paras asas dan selepas 12 minggu diberi suplementasi dengan vitamin E (400 IU), C (500 mg), beta-karoten (15 mg), dan kombinasi (E, C, dan beta-karoten) masing-masing. Parameter sekunder juga diukur pada paras asas dan selepas 12 minggu termasuklah petunjuk sosio-ekonomi, pengambilan diet, ukuran antropometri dan petunjuk biokimia, yang di ambil sekali sahaja pada paras asas. Ujian biokimia termasuklah paras gula berpuasa (FBS), profil lipid: jumlah trigliserid (TG), jumlah kolesterol (TC), lipoprotein kolesterol densiti rendah (LDL-C), lipoprotein kolesterol densiti tinggi (HDL-C), vitamin antioksidan: (E, C dan beta-karoten) dan faktor inflammasi: high sensitive C-reactive protein (hs CRP), 8-iso-prostaglandin F<sub>2</sub> $\alpha$ , enzymatic oxidative defense: glutathione peroksidase (Gpx), superoksida dismutase (SOD), dan juga LDL teroksid (oxLDL) dan jumlah homosisteine (tHcy) telah diukur. Min umur subjek adalah  $52.85 \pm 7.96$  tahun dan min BMI adalah  $27.56 \pm 4.26$  kg/m<sup>2</sup>. Bagi

pengambilan diet kumpulan C, bijirin mendapat skor kekerapan 94.7, roti (93.1), daging (73.4) dan ikan(73.9). Bagi kumpulan E, bijirin adalah yang paling kerap dimakan sebagai makanan rugi dengan skor kekerapan 95.2, diikuti dengan roti (93.4). Bagi kumpulan beta-karoten, bijirin mendapat skor kekerapan 96.2, roti (90.8), kurma (85.2), tomato (82.4), dan sayur-sayuran berwarna oren (80.9). Bagi kumpulan kombinasi, skor kekerapan bagi bijirin adalah 96.2, roti (94.2) dan kurma (85.9). Bagi kumpulan plasebo, nasi mendapat skor 95.2, diikuti oleh roti (92.2). Dalam kalangan subjek, 12.3 % mempunyai paras gula darah berpuasa yang tinggi (FBS) dan 80.1 % mempunyai paras yang normal. Subjek yang mengalami hiperkolesterolemia dan hipertrigliseridemia adalah sebanyak 19.9 % dan 41.4 % masing-masing. Kajian ini juga mendapati bahawa 13.3 % daripada jumlah subjek mempunyai paras LDL-C yang tinggi dan 6.6 % mempunyai paras HDL-C yang rendah. Keputusan juga menunjukkan bahawa 8-iso-PGF<sub>2α</sub> menurun secara signifikan dalam kumpulan E 17.62 % ( $p=.000$ ), beta-karoten 17.56 % ( $p=.002$ ), dan kombinasi 14.97 % ( $p=.014$ ). Bagi hs-CRP pula menurun secara signifikan dalam kumpulan C 28.14 % ( $p=.036$ ), E 23.27 % ( $p=.020$ ), beta-karoten 27.93 ( $p=.021$ ), dan kombinasi 23.69 ( $p=.0005$ ). LDL teroksid juga menurun secara signifikan dalam kumpulan C 18.32 % ( $p=.005$ ), E 23.86 % ( $p=.000$ ), beta-karoten 17.31 % ( $p=.000$ ), dan kombinasi 19.07 % ( $p=.000$ ).

Bagaimanapun, SOD didapati meningkat secara signifikan dalam kumpulan C 26.76 % ( $p=.0003$ ), dan kombinasi 35.77% ( $p=.000$ ). Keputusan juga menunjukkan bahawa Gpx, meningkat secara signifikan dalam kumpulan E 7.13 % ( $p=.003$ ), dan kombinasi 5.34 % ( $p=.017$ ) sebelum dan selepas intervensi. Selepas 12 minggu suplementasi, kumpulan kombinasi vitamin (E, C dan beta-karoten) dapat merendahkan paras 8-iso-PGF2 $\alpha$ , hs-CRP, oxLDL, secara signifikan dan meningkat SOD dan Gpx. Sebagai rumusan, suplementasi dengan vitamin antioksidan boleh menambahbaik sebahagian daripada sistem enzimatik antioksidan termasuk SOD dan Gpx, dan mengurangkan biomarker bahaya bagi penyakit kardiovaskular seperti hs-CRP, oxLDL, dan 8-iso-PGF2a. Oleh itu mereka yang berisiko bagi penyakit jantung perlu digalakkan mengambil suplementasi vitamin antioksidan bagi mengurangkan risiko penyakit kardiovaskular.

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## APPROVAL SHEET

I certify that an Examination Committee met on 25<sup>th</sup> August to conduct the final examination of Saeid Najafpour Boushehri on his thesis entitled “Effects of Antioxidant Vitamins (C, E, Beta-carotene) Supplementation on Cardiovascular Biomarkers Among Males with Risk Factors in Boushehr, IRAN” in accordance with 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 candidate be awarded the Degree of Doctor of Philosophy.

Members of the Examination Committee are as follows:

**Amin Ismail, PhD**

Associate Professor  
Faculty of Medicine and health Sciences  
Universiti Putra Malaysia  
(Chairman)

**Asmah Rahmat, PhD**

Professor  
Faculty of Medicine and health Sciences  
Universiti Putra Malaysia  
(Internal Examiner)

**Hejar binti Abd. Rahmat, M.D**

Associate Professor  
Faculty of Medicine and health Sciences  
Universiti Putra Malaysia  
(Internal Examiner)

**Donald K Layman, PhD**

Professor  
1729, Devonshire Drive Champaign  
Illinois 61821,  
Illinois U.S. A  
(External Examiner) \_\_\_\_\_

**NORITAH OMAR, PhD**

Associate Professor and  
Deputy Dean School of  
Graduate Studies  
Universiti Putra Malaysia  
Date:

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:

**Rokiah Mohd Yusof, PhD**

Associate Professor  
Faculty of Medicine and Health Sciences  
Universiti Putra Malaysia  
(Chairman)

**Mohd Nasir Mohd Taib, PhD**

Lecturer Faculty of Medicine and Health Sciences  
Universiti Putra Malaysia  
(Member)

**Zaitun Yassin, PhD**

Associate Professor  
Faculty of Medicine and Health Sciences  
Universiti Putra Malaysia  
(Member)

**Nizal Sarrafzadegan, MD**

Professor  
Isfahan Cardiovascular Research Center  
Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan,  
Iran  
(Member)

---

**HASANAH MOHD.GHAZALI, PhD**

Professor and Deputy Dean  
School of Graduate Studies  
Universiti Putra Malaysia

Date:

## **DECLARATION**

I declare that the thesis is my 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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**SAEID NAJAFPOUR BOUSHEHRI**

Date: 25 August 2011

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