Volume 6, No. 1 (Supplement)
June 2011
ISSN 1823-2140

The Official Journal of The Faculty of Medicine UKM

7th Malaysia Indonesia Brunei Medical Sciences Conference
"TOWARDS A HOLISTIC AND INTEGRATIVE APPROACH IN HEALTHCARE"

22nd - 24th July 2011
Equatorial Hotel, Bangi, Selangor, MALAYSIA

officiated by
Y.B Datuk Rosnah Hajj Abdul Rashid Shirlin
Deputy Minister of Health Malaysia

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MODULATION OF SENESCENCE ASSOCIATED GENES EXPRESSION IN HUMAN DIPLOID FIBROBLASTS BY TOCOTRIENOL-RICH FRACTION PREVENTS CELLULAR SENESCENCE

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Background:
Human diploid fibroblasts (HDFs) have a limited ability to divide when cultured in vitro and eventually enter a state of irreversible proliferation, termed replicative or cellular senescence. This study was conducted to evaluate the anti-aging effects of tocotrienol-rich fraction (TRF) by determining the expression of senescence associated genes in human diploid fibroblasts (HDFs).

Materials and Methods:
Primary HDFs were cultured into passage 4 (young cells), passage 15 (pre-senescence cells) and passage 30 (senescent cells) with and without TRF treatment. Expression of antioxidant associated genes (SOD1, SOD2, CAT, GPx-1, CCS-1, AOP-2), IGF-1/PI3K/Akt associated genes (FOXO3a), DNA damage (p16\(^\text{INK}\), p21\(^\text{WAF}\), p53) and cell proliferation genes (p38\(^\text{MAPK}\), AP-1) was quantitatively analyzed with real-time RT-PCR method.

Results:
Expression of p53 and p21\(^\text{WAF}\) was increased in senescent HDFs. Similar increase in gene expression was observed in senescent HDFs for AOP-2 and p38\(^\text{MAPK}\) with no change in FOXO3a and AP-1. Treatment with TRF has shown to modulate the expression of antioxidant associated genes, IGF-1/PI3K/Akt associated genes, DNA damage and cell proliferation genes.

Conclusion:
Our results confirmed that the expression of these genes was altered during cells senescent. Treatment with TRF however modulated these changes indicating the potential protective mechanism in delaying and preventing cellular aging.

Keywords:
Tocotrienol-rich fraction, senescence associated genes, cellular aging