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Food Consumption and Body Weight in Mice Treated with Palm Oil–Derived Tocotrienol Rich Fraction (TRF)

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Abstract: The effect of palm oil-derived tocotrienol rich fraction (TRF) treatment on body weight and food consumption in male ICR white mice was investigated in this study. Mice were randomly divided into 4 groups (n=10 for each group). The first group is designated as control group. The other three groups were given TRFby oral gavage at concentrations of 200, 500, and 1000 mg/kg respectively for 14 days. Mice were weighed twice weekly at the same hour, and food intake was recorded daily. The results showed that administration of TRF at different doses did not significantly affect body weight and food intake in mice.
Key Words: TRF – tocotrienol - mice – body weight.

Introduction

Tocotrienols are hydrophobic fat-soluble compound that belong to the vitamin E family and has been reported to possess a potent antioxidant activity[1]. The health benefits of tocotrienols had been described by various studies[2-4]. Vitamin E consists of two major homologous subgroups i.e. tocopherols (TP) and tocotrienols (T3). Both tocopherols and tocotrienols are structurally identical compounds in that they have a chromanol nucleus, which is the site for their potent antioxidant activities, however, they differ at the molecular tail section[5]. Tocopherols and tocotrienols are further subdivided into alpha (α), beta (β), gamma (γ) and delta (δ) tocopherols and alpha (α), beta (β), gamma (γ) and delta (δ) tocotrienols, depending on the numbering and location of methyl substitutions on the chromanol ring[6].

Tocotrienols are distributed throughout the body via the bloodstream and accumulate in many tissues such as adipose tissue, heart and skin. The absorption of vitamin E depends on lipid intake and the secretion of bile and esterases[7]. The excretion of bile, which is produced by the liver, generally depends on the level and type of dietary fat consumed, and reports have clearly identified that tocotrienol absorption is reduced in individuals who are fasting compared to individuals who are fully fed[8]. Palm oil had been shown to increase bile excretion and micelle formation, which enhanced the absorption of tocotrienols. This is partly due to the high fatty acid composition present in palm[9]. All isomers of vitamin E are metabolized by omega oxidation followed by beta oxidation. Omega oxidation is mediated by xenobiotic metabolizing enzymes, cytochrome P450(CYP450) enzymes, which are often regulated by their substrates themselves[10].

Vitamin E is widely distributed in natureand is found in many lipid-rich plant and vegetable oils. Tocopherols are present in corn, olive, peanut and sunflower seeds[11]. Tocotrienols can be found in rice bran, palm and annatto oil[12]. The ratio of tocopherols to tocotrienols in rice bran, palm and annatto oils are 50:50; 25:75 and 0.1:99.9 respectively[13]. A standardized palm oil tocotrienol-rich fraction (TRF) consists mainly of a

mixture of α, γ, δ-tocotrienols (68%) and α-tocopherols (32%) (Table 1), and can be obtained from palm oil after esterification and following distillation, crystallization, and chromatography[14].

Vitamin E had been reported to affect body weight in multiple studies conducted in mice[15-18]. However, no studies have been done to see the effect of different doses of palm TRF on body weight. Therefore, we undertook this study in order to observe the effect of different doses of palm TRF on body weight and food consumption in mice.

Table 1 Composition of the palm-derived TRF Gold Tri E 70

TRF composition	Concentration mg / g	Percentage %
α-tocotrienol	205.1	26.76 %
β-tocotrienol	32.9	4.29 %
γ-tocotrienol	249.8	32.60 %
δ-tocotrienol	119	15.53 %
α-tocopherol	159.5	20.81%

Source: Adapted from Lim et al. 2013 [20].

Material and Methods

Animals

Male *ICR*white mice (25–30 g) obtained from Universiti Kebangsaan Malaysia animal house, were used in this study.There were a total of 40 mice tested. All mice were individually housed in clean polypropylene cages ina well-ventilated room with 12 hour light-dark cycles. Animals were treated in compliance with Animal Ethics Committee of the Universiti Kebangsaan Malaysia (UKMAEC).

Body weight, fluid and food intake

Mice were weighed twice a week at the same hour, at the beginning and end of each week. All mice had access to water and pelleted chow diet (Gold Coin, Klang, Selangor, Malaysia)(Table 2). Food intake was recorded daily by weighing the food given and the foodremaining and correcting for the food spillage. Faecal weight and urinevolume were also measured.

Treatment of palm TRF in Mice

Mice were divided into four groups. In the first group (n = 10), which is the control group, mice were given distilled water (0.1 mL) by oral gavage. In the second group (n = 10), mice were administered a low dose of 200 mg/kg TRF (0.1 mL) by oral gavage. In the third group (n = 10),mice were administered a medium dose of 500 mg/kg TRF (0.1 mL) by oral gavage. In the fourth group (n = 10) mice were administered a high dose of 1000 mg/kg TRF (0.1 mL) by oral gavage. All treatments lasted for 14 days, and this duration represent sub-chronic administration in human.

Statistical Analysis

Statistical analysis was conducted using the SPSS software version 22. Results are expressed as mean ± SEM, and Student's t-test was used for statistical significance. The results were considered statistically significant when $P < 0.05$.

Table 2. Approximate composition of mice feed

Contents	Composition % w/w
Crude protein (min)	20.0
Crude fibre (max)	5.0
Crude fat (min)	2.5
Moisture (max)	13.0
Ash (max)	7.0
Calcium	0.7-1.4
Total phosphorous	0.6-1.2
Nitrogen-free extract	51.0

(By courtesy of Gold Coin, Port Klang, Selangor, Malaysia)

Results

Effect on body weight

The effects of different doses of palm TRF on body weight gain in mice are presented in Table 2.There was no statistically significant difference in mean body weight at the start and at the end of the experiment. All the mice in palm TRF 200, and palm TRF 500 groups gained weight (7.71 % and 4.57% increase, respectively), but the increase was not statistically significant as compared to controls. However, palm TRF treated group at dose of 1000 mg/kg exhibited decrease in weight gain (3.51% decrease), but it was also not significant as compared to control group (Fig. 1).

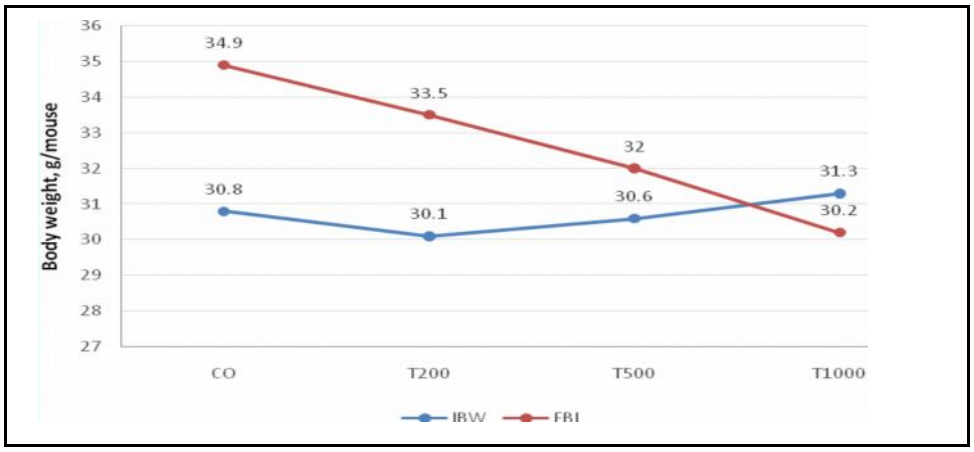

Fig 1. Changes in Body weight of mice exposed to TRF at different concentrations. Abbreviations: C, control group; T200, TRF at dose 200 mg/kg; T500, TRF at dose 500 mg/kg; T1000, TRF at dose 1000 mg/kg; IBW, initial body weight; FBI, final body weight.

Food Intake

Mean daily food intakes ranged from 1.4 ± 0.1 g/mouse to 6.0 ± 0.3 g/mouse. In most of the groups, food intake was continuously distributed and were close to the overall group mean (3.8 ± 0.1 g/mouse, n = 40).The daily food intake of mice supplemented with tocotrienol at different doses did not differ significantly from that of the control mice (Table 3).

Table 3. Body weight and food intake in control and experimental mice

Groups	Body weight			Food intake(g/bw/day)
	Initial (g)	Final (g)	% Change	
Control	30.80±0.9	34.90±1.0	+ 13.31%	4.46±0.5
T200	31.10±0.7	33.50±0.6	+ 7.71%	4.39±0.5
T500	30.60±0.8	32.00±1.1	+ 4.57%	3.80±0.5
T100	31.30±0.6	30.20±1.1	- 3.51%	3.05±0.5

Discussion

Food intake and body weight of male mice treated with different dose of TRF (200, 500, and 1000 mg/kg) were determined in this study. Our data showed gradual increase of body weight (7.71 % and 4.57% increase, respectively), except for 1000 mg/kg TRF treated group, which exhibited slight loss of body weight (-3.51%) but was still not statistically significant compared to controls. Furthermore, the daily food intake of mice supplemented with TRF at different doses did not differ significantly from that of the control mice.

Other studies had reported that vitamin E affected mice body weight. Administration of 500 µg/g DL-α-tocopherol acetate or a control diet containing 30 µg/g of vitamin E had been found to increase mice body weight significantly[15]. In another study, female mice supplemented with α-tocopherol acetate solubilized in 1 ml of ether and 1 ml of ethanol at a concentration of 4.4 mg/g also significantly affected food intake and body weight[16]. Supplementation of palm oil tocotrienol at a dose of 60 mg/kg to ovariectomized rats inhibited the increase in rat body weight that is usually observed after ovariectomy, however, the daily food intake of these rats did not differ significantly from that of the sham-operated group[17]. Moreover, Hsieh and Lin reported that MRL/lpr mice supplemented with all-rac-α-tocopherol acetate at concentrations of 250, 375, and 500 µg/g had no effect on feeding behaviour and body weight of mice[18]. Furthermore, the body weight was decreased in mice fed with all-rac-α-tocopherol at dose of 100 IU/kg per day[19].

In conclusion, the results of our study showed that administration of TRF at different doses did not significantly affect body weight and food intake in mice. Morphologically, all our TRF treated mice seemed as healthy as control mice. This suggests that TRF, even at higher doses (i.e 1000 mg/kg b.w.), was safe to be used and did not have negative implications on the health status of healthy mice. However, further studies needs to be done in order to investigate the impact of high doses of TRF on other health parameters.

Conflicts of Interests

The authors declare that they have no conflict of interests.

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References

1. Sylvester, P.W., Theriault, A. Role of tocotrienols in the prevention of cardiovascular disease and breast cancer. Curr. Top. Nutraceutical. Res.,2003, 1:121–136.
2. Clarke, M.W., Burnett, J.R., Croft, K.D. Vitamin E in human health and disease. Crit. Rev. Clin. Lab. Sci., 2008, 45:417–50.
3. Meydani, S.N., Han, S.N., Wu, D. Vitamin E and immune response in the aged: molecular mechanisms and clinical implications. Immunol. Rev., 2005, 205:269–84.
4. Mustacich, D.J., Bruno, R.S., Traber, M.G. Vitamin E. Vitam. Horm. 2007, 76:1–21.
5. Kannappan, R., Gupta, S.C., Kim, J.H., Aggarwal, B.B. Tocotrienols fight cancer by targeting multiple cell signaling pathways. Genes. Nutr., 2012, 7:43-52. 3.

6. Sen, C.K., Khanna, S., Rink, C., Roy, S. Tocotrienols: the emerging face of natural vitamin E. Vitam. Horm., 2007, 76:203–61.
7. Combs, G.F. The vitamins: Fundamental Aspects in Nutrition and Health, third edition, San Diego: Elsevier Academic Press., 2008, 64–65; 68.
8. Herrera, E., Barbas, C. Vitamin E: action, metabolism and perspectives. J. Physiol. Biochem., 2001, 57:43–56.
9. Sylvester, P.W., Kaddoumi, A., Nazzal, S., El Sayed, K.A. The value of tocotrienols in the prevention and treatment of cancer. J. Am. Coll. Nutr., 2010, 29:324S-333S.
10. Stocker, A. Molecular mechanisms of vitamin E transport. Ann. N. Y. Acad. Sci., 2004, 1031:44, 59.
11. Sen, C.K., Rink, C., Khanna, S. Palm Oil–Derived Natural Vitamin E a-Tocotrienol in Brain Health and Disease. J. Am. Coll. Nutr., 2010, 29:314S–323S.
12. Theriault, A., Chao, J.T., Wang, Q., Gapor, A., Adeli, K. Tocotrienol: a review of its therapeutic potential. Clin. Biochem., 1999, 32:309–19.
13. Aggarwal, B.B., Sundaram, C., Prasad, S., Kannappan, R. Tocotrienols, the vitamin E of the 21st century: its potential against cancer and other chronic diseases. Biochem, Pharmacol., 2010, 80(11):1613-31.
14. Sundram, K., and Gapor, A. Vitamin E from Palm Oil. Its Extraction and Nutritional Properties. Lipid. Technol., 1992, 4,137–141.
15. Lipman, R.D., Bronson, R.T., Wu, D., Smith, D.E., Prior, R. et al. Disease incidence and longevity are unaltered by dietary antioxidant supplementation initiated during middle age in C57BL/6 mice. Mechanisms of. Ageing and. Development.,1998, 103, 269–284.
16. Ledvina, M., Hodanova, M. The effect of simultaneous administration of tocopherol and sunflower oil on the lifespan of female mice. Experimental. Gerontology.,1980, 15, 67–71.
17. Muhammad, N., Luke, D.A., Shuid, A.N., Mohamed, N., Soelaiman, I.N. Tocotrienol supplementation in postmenopausal osteoporosis: evidence from a laboratory study. Clinics (Sao Paulo)., 2013, 68(10):1338-43.
18. Hsieh, C.C., Lin, B.F. Opposite effects of low and high dose supplementation of vitamin E on survival of MRL/lpr mice. Nutrition.,2005, 21, 940–948.
19. Yasunaga, T., Kato, H., Ohgaki, K., Inamoto, T., Hikasa, Y. Effect of vitamin E as an immunopotentiation agent for mice at optimal dosage and its toxicity at high dosage. J. Nutr.,1982, 112(6):1075-84.
20. Lim, J.J., Ngah, W.Z., Mouly, V., Abdul Karim, N. Reversal of myoblast aging by tocotrienol rich fraction posttreatment. Oxid. Med. Cell. Longev., 2013, 2013:978101.

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