

Chewable Tablets Containing Palm-based Vitamin E (Tocotrienol Rich Fraction, TRF) – A Preliminary Stability Study

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INTRODUCTION

Vitamin E (tocochromanols) comprises four tocopherol and four tocotrienol isomers, namely alpha (α), beta (β), gamma (γ) and delta (δ) (Brigelius-Flohé and Traber, 1999), and is an essential nutrient for the human body. Palm oil is one of the richest sources of vitamin E (800-1200 ppm) (Kushairi *et al.*, 2018). Palm-based vitamin E comprises of about 49%-53% γ -tocotrienol, 22%-34% α -tocotrienol, 6%-7% δ -toco-trienol, 14%-17% α -tocopherol and 3% α -tocomonoenol (Puah *et al.*, 2007). As it is very rich in tocotrienols, palm-based vitamin E is also known as the *tocotrienol rich fraction* (TRF). Palm-based vitamin E possesses unique and potent health-enhancing properties such as antioxidative (Cerecetto and López, 2007), cardioprotective (Heng *et al.*, 2013), neuroprotective (Sen *et al.*, 2000), anti-cancer and cancer-suppressing (Wong and Radhakrishnan, 2012), as well as neurological and brain development (Traber, 2014) effects. It has also been found to lower blood cholesterol levels (Qureshi *et al.*, 1995).

within the range of 50-360 mg day⁻¹ (Tan *et al.*, 1991) with an upper limit for safety at 1000 mg day⁻¹. A consistent intake of vitamin E is important for maintaining good health. Adequate levels of this essential micronutrient are especially critical for infants, the elderly, and women who are or may become pregnant. Vitamin E deficiency can cause poor transmission of nerve impulses, muscle weakness, and degeneration of the retina that leads to blindness. Severe vitamin E deficiency can be lethal, resulting in loss of life (Traber, 2014).

At present, supplements carrying RDA or a higher dosage of palm-based vitamin E are available in the form of soft gel capsules. Other forms of palm-based vitamin E supplements such as emulsions or oral tablets like chewable tablets are scarce in the market. Oral tablets have been manufactured for more than 150 years. An oral tablet is a compressed solid form containing a quantified amount or dosage of active ingredients to deliver certain therapeutic effects. In particular, the tablet is usually designed for ease of administration. A chewable tablet is an oral tablet that is required to be broken up and chewed before ingestion. Chewable tablets are intended to disintegrate

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The recommended dietary allowance (RDA) for vitamin E to maintain good health is about 15 mg day⁻¹ for people over the age of 14 years, and 20 mg day⁻¹ for lactating women (Traber, 2014). The more common dosages fall

smoothly in the mouth, with or without actual chewing, and they release a pleasant taste leaving no bitter or unpleasant aftertaste. The chewable tablet provides ease in drug administration, and is prescribed to those having difficulty in swallowing, especially children and the elderly. The chewable tablet also provides better bioavailability of the active ingredients through by-passing the disintegration process (Varma, 2016).

Malaysian Palm Oil Board (MPOB) has conducted a study on the formulation and storage quality of chewable tablets containing palm-based vitamin E. This paper reports on the stability of palm-based vitamin E in a chewable tablet formulation after one year of storage at ambient temperature. The physical properties of the palm-based vitamin E chewable tablets are also reported.

CHARACTERISTICS OF CHEWABLE TABLETS CONTAINING PALM-BASED VITAMIN E AFTER ONE YEAR OF STORAGE AT ROOM TEMPERATURE

The formulation of the chewable tablets is shown in *Table 1*. The tablets, each of which weighing 1000 mg, were produced using an automatic tableting machine, and were evaluated at selected intervals during storage.

Palm-based vitamin E powder used in the chewable tablet formulation contained 193.67 mg g⁻¹ vitamin E, which in turn comprised 77.74% tocotrienols (α -, β -, γ - and δ -tocotrienols) and 22.26% tocopherol (α -tocopherol) (*Table 2*). The most abundant tocotrienol isomers in the palm-based vitamin E were γ , α and δ .

Vitamin E retention in the palm-based vitamin E chewable

tablets after 1-year storage at ambient temperature was excellent at 92.6%, with the initial vitamin E content in the tablets being 18.94 mg g⁻¹ (*Table 3*). The high vitamin E retention in the chewable tablets was due to the use of powdered or encapsulated palm-based vitamin E in the formulation. Microencapsulation or nanoencapsulation is a method by which micro- or nano-droplets of bioactive components are surrounded by a coating to form microcapsules or nanocapsules. Encapsulation has been shown to protect bioactive components from

direct exposure to chemical and physical reactions, thus protecting the bioactive ingredients from degradation (Calvo *et al.*, 2011). Vitamin E deterioration during storage may arise from some extrinsic factors such as heat, light or air that could cause oxidation of the vitamin (Schauss *et al.*, 2012).

The palm-based vitamin E chewable tablets also possessed good physical stability in terms of tablet hardness, friability and disintegration time. The hardness of chewable tablets should be such that they can withstand the rigors

TABLE 1. FORMULATION OF PALM-BASED VITAMIN E CHEWABLE TABLETS

Ingredient	Amount (%)
Powdered palm-based vitamin E (containing 193.67 mg g ⁻¹ vitamin E)	10
Vitamin C	10
Binder (carbohydrate, cellulosic material)	51.3
Compressible carbohydrate	7.5
Sweetener	5.5
Fruit juice powder (flavouring)	15.0
Lubricant	0.4
Glidant	0.3

TABLE 2. CONTENTS OF TOCOTRIENOL AND TOCOPHEROL ISOMERS, AND TOTAL VITAMIN E IN POWDERED PALM-BASED VITAMIN E

Vitamin E isomers	Amount (mg g ⁻¹)
Tocotrienol isomers	
γ -tocotrienol	58.79 \pm 0.10
α -tocotrienol	55.75 \pm 0.09
δ -tocotrienol	31.41 \pm 0.02
β -tocotrienol	4.52 \pm 0.01
Tocopherol isomers	
α -tocopherol	43.19 \pm 0.34
β -tocopherol	n.d
γ -tocopherol	n.d
δ -tocopherol	n.d
Total vitamin E (tocotrienols + tocopherols)	193.67 \pm 0.53

Note: n.d. - not detected.

TABLE 3. VITAMIN E CONTENT OF CHEWABLE TABLETS AFTER 1-YEAR STORAGE AT AMBIENT TEMPERATURE

Storage period	Vitamin E content (mg g ⁻¹)
Day 1	18.94 ± 0.09 ^a
Day 30	18.62 ± 0.11 ^b
Day 90	18.45 ± 0.08 ^{bc}
Day 180	18.24 ± 0.15 ^c
Day 270	17.97 ± 0.14 ^c
Day 360	17.54 ± 0.17 ^d

Note: Means bearing different superscript letters are significantly different ($p < 0.05$).

of manufacturing, packaging, shipping and distribution, but remain chewable. It is recommended that the hardness of chewable tablets be kept low (*i.e.* <12 kp), so that the tablets can be safely chewed without damaging teeth or dentures, or causing other adverse effects associated with chewing these tablets (US Pharmacopeia, 2015). Friability is the tendency of a tablet to chip, crumble or break up on exposure to mechanical shocks and attrition during packaging, handling and shipping, and should be kept below 1%. Disintegration time of the chewable tablets in this study refers to the time required for the tablets to fully dissolve at 37°C, *i.e.* at human body temperature (in the event that the chewable tablet is being 'sucked' instead of being chewed while in the mouth). Slight increases in tablet hardness and disintegration time were noticed after one year of storage, but these values were still within the acceptable ranges, *i.e.*, <12 kp for hardness and 25-32 min for disintegration time. After 1-year storage at ambient temperature, tablet hardness increased from 5.64 kp (initial) to 7.79 kp, while disintegration time increased from 27 min (initial) to 31 min. There was no significant change in friability (<1%).

CONCLUSION

The stability of palm-based vitamin E when incorporated into chewable tablets is excellent, with retention of 92.6% after 1-year storage at ambient temperature. Chewable tablets which contain palm-based vitamin E also showed good physical stability (hardness, friability and disintegration time) after storage.

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