

# PALM OIL HEALTH AWARENESS CPD LUNCH TALK

@ KPJ AMPANG PUTERI SPECIALIST HOSPITAL



## Professor Emeritus Dr. Yuen Kah Hay

School of Pharmaceutical Sciences  
Universiti Sains Malaysia



# *Benefits of Palm Tocotrienols for the Aging Brain*

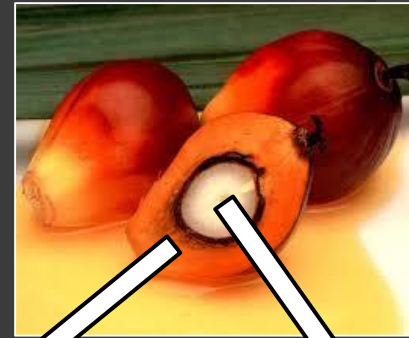
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11800, Penang  
Malaysia*



Malaysia is blessed with this marvelous crop

Oil Palm





Mesocarp

Kernel



Crude Palm oil

Palm Kernel oil

**Vitamin E  
Tocotrienols**

# Vitamin E Tocotrienols

- Crude palm oil is one of the richest sources of tocotrienols
- Extracted and commercialised by Malaysian companies and sold worldwide

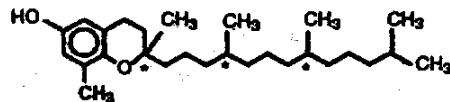
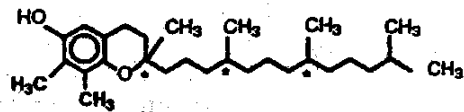
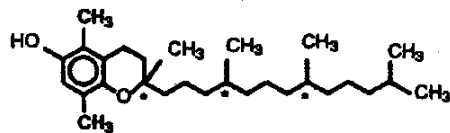
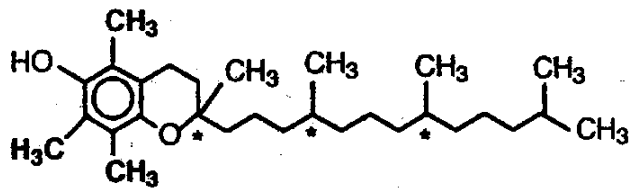


# Vitamin E consists of 8 isoforms

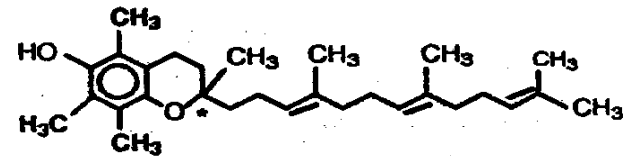
## 4 tocopherols

## 4 tocotrienols

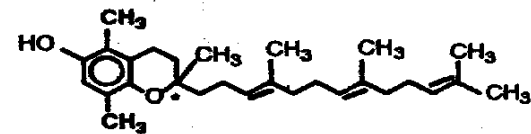
--- Chroman --- | --- Phytol --- |



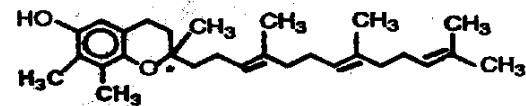
$\alpha$



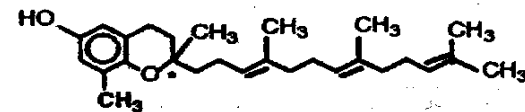
$\beta$



$\gamma$



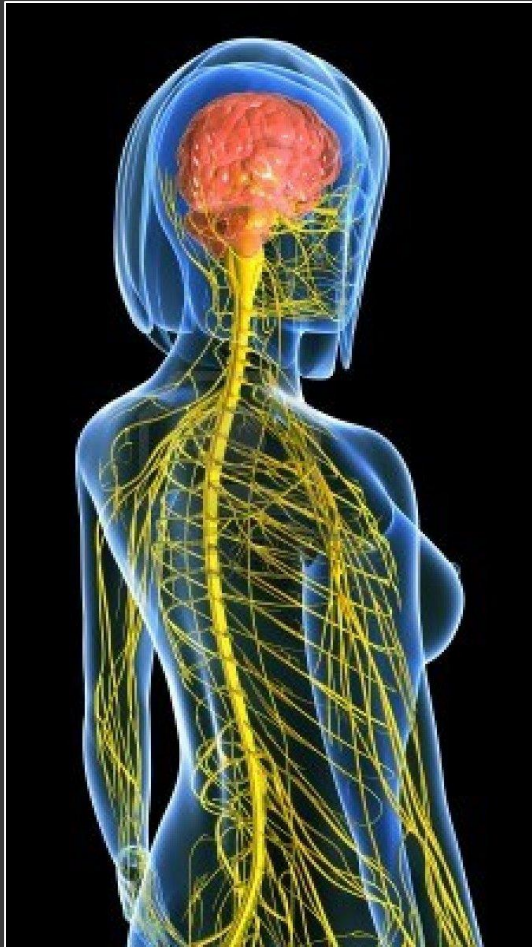
$\delta$



# Tocotrienols(T3) versus tocopherols

- Tocopherols discovered first, T3 some 25 years later
- Tocotrienols less found in nature
- Most research (>98%) in past focused on tocopherols
- Recent studies revealed that tocotrienols have some unique biological activities over the tocopherols
- **Focus of research on tocotrienols today**
  - neuroprotective
  - liver protective
  - kidney protective
  - radioprotective
  - anti-cancer properties

# Vitamin E in general



- Essential for normal functions and health of our nervous system
- Deficiency leads to muscle dystrophy and neurological deficits (ataxia and areflexia)
- **Tocotrienols also shown to possess neuroprotective activities**



## Early studies on neuroprotective properties

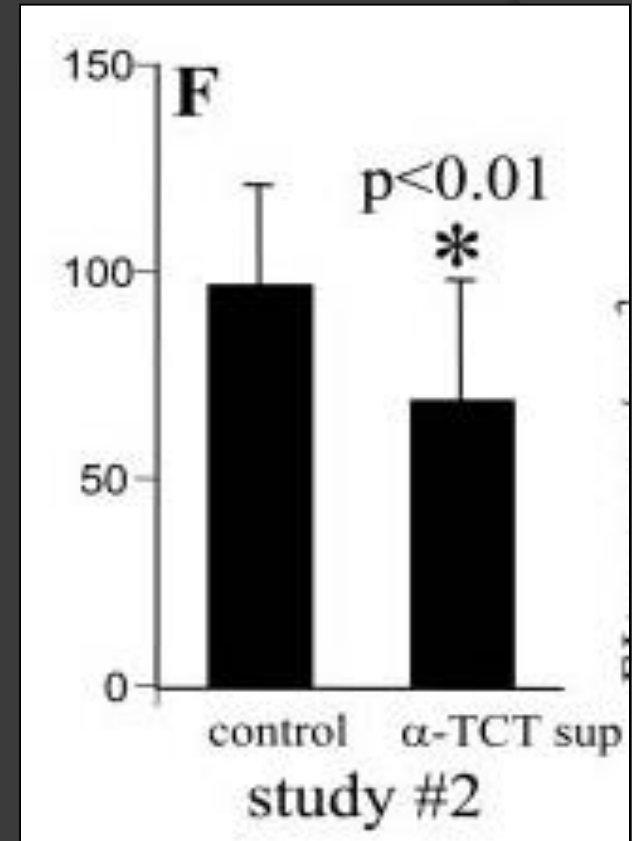
- ⦿ *α-tocotrienol* but **not *α-tocopherol*** at **nM** conc shown to protect neurons from degenerating when challenged with glutamate (*Sen et al, 2000*)
- ⦿ Through attenuating excitotoxic effects of glutamate by **modulating chemical signals** within the neuronal cells:
- ⦿ Via suppression of **C-src kinase** (*Sen et al 2000*) and **12-LOX** as well as inhibition of **phospholipase A2** activation during glutamate induced excitotoxicity (*Khanna et al 2003, 2010*)

## Later rodent study by *Khanna et al (2005)*



*Stroke induced in rats with and without T3 supplementation*

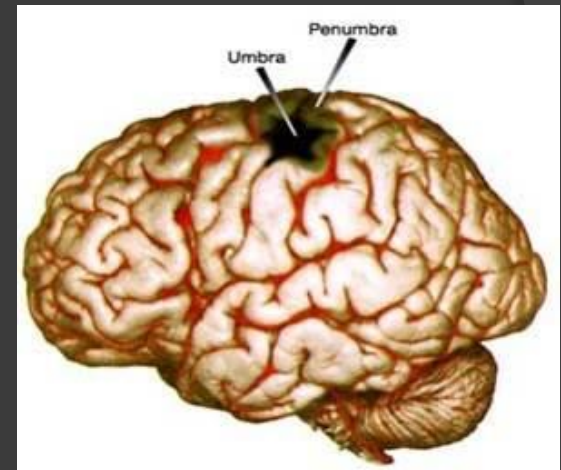
*Brain lesions of treated animals significantly smaller than matched controls after induction of stroke*



# Professor Koji Abe from Okayama, Japan

Recently published 2 papers in *Journal of Stroke and Cerebrovascular Diseases* in 2018

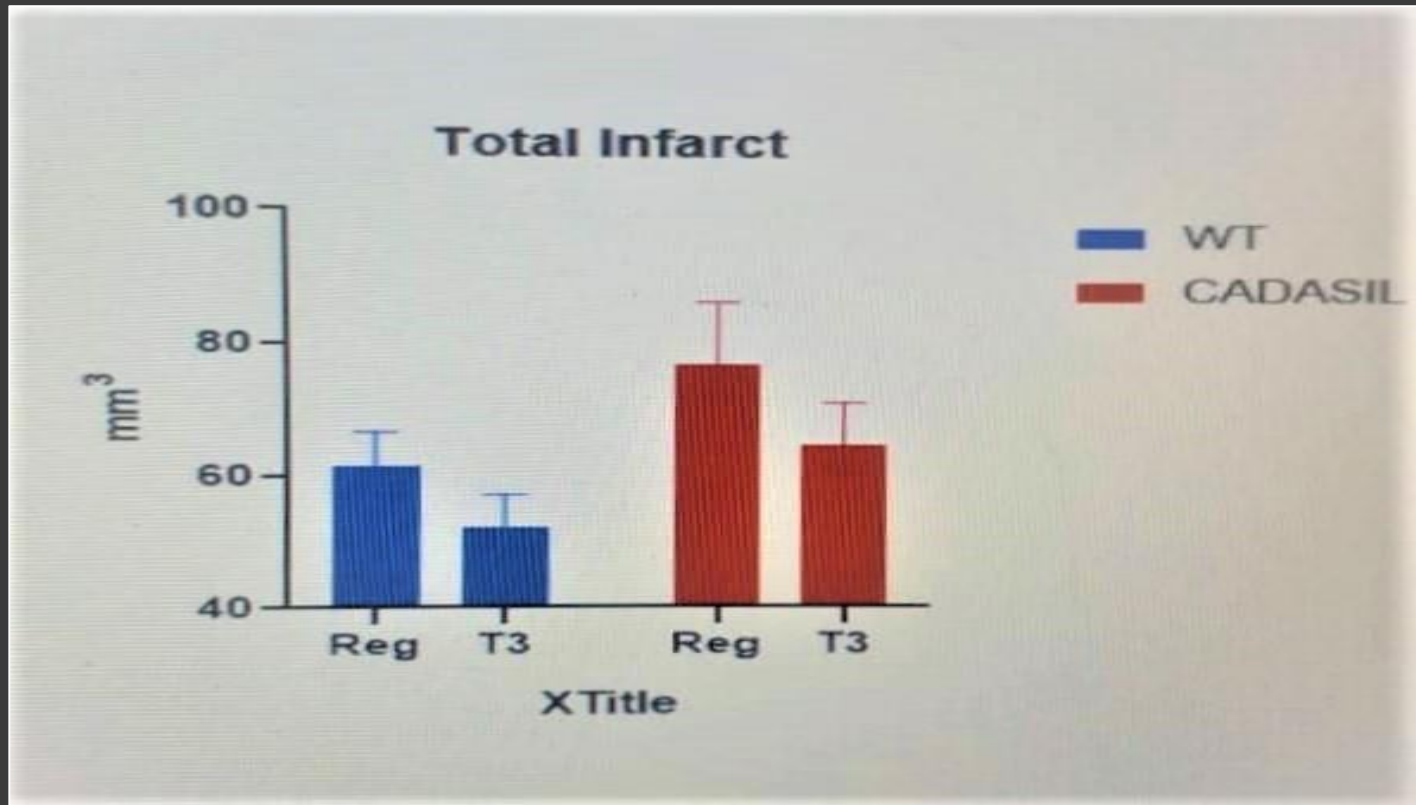
- Similar neuroprotective effects observed with the tocotrienols
- Reduced infarct volume in rats after induction of brain ischemia
- Decreased in inflammatory markers
- Reduced neurovascular unit dissociation
- **Concluded tocotrienols to be neuroprotective**



# Recent study from Harvard University, 2019

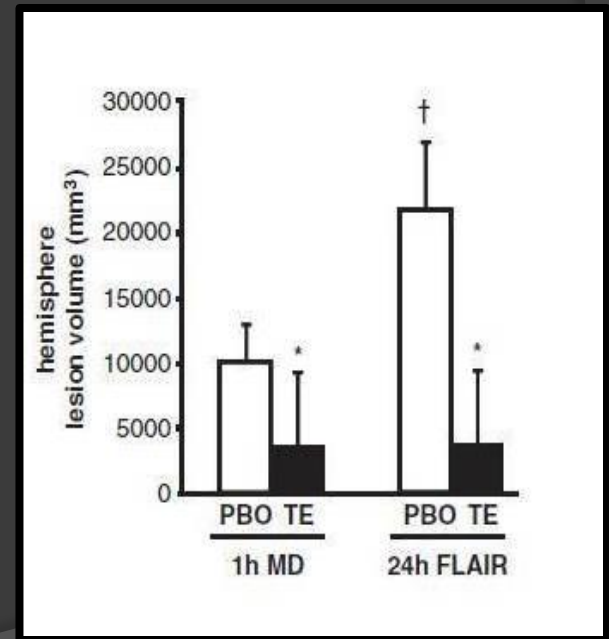
Similar results observed in **wild type** and **transgenic mice** model for **CADASIL** during induced brain ischemia,

**Volume of lesions shown to be smaller with T3 supplementation**



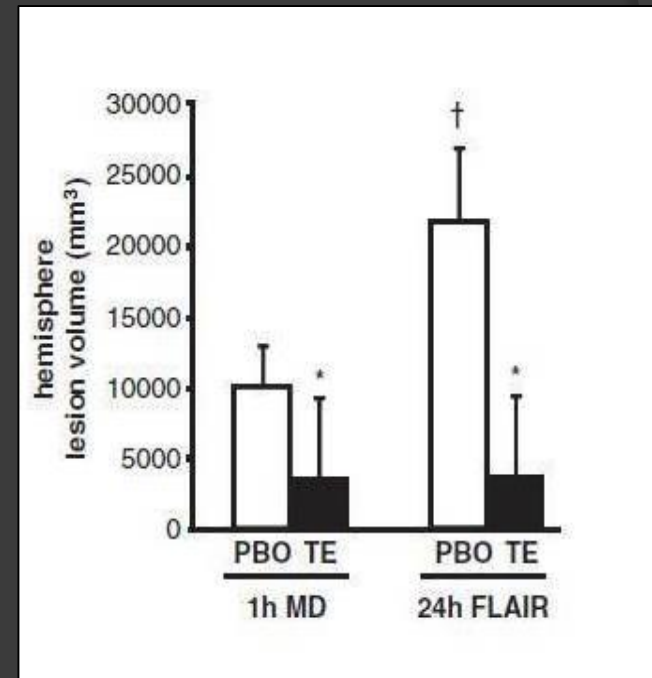
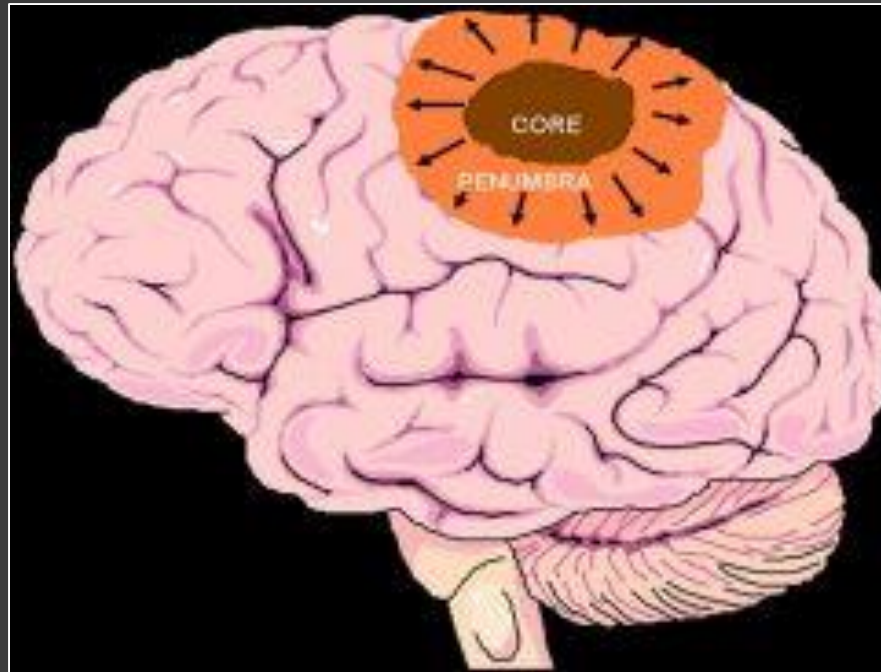
# Canine study by Rink et al (2011)

- Stroke induced in dogs with and without mixed T3 supplementation
- Again, lesion volume significantly smaller with mixed tocotrienol supplementation



# Another significant finding

- ⦿ Mixed T3 reported to increase blood flow to the affected zone
- ⦿ This can help reduce further injury of brain tissues and hence alter the clinical course and outcome of the stroke

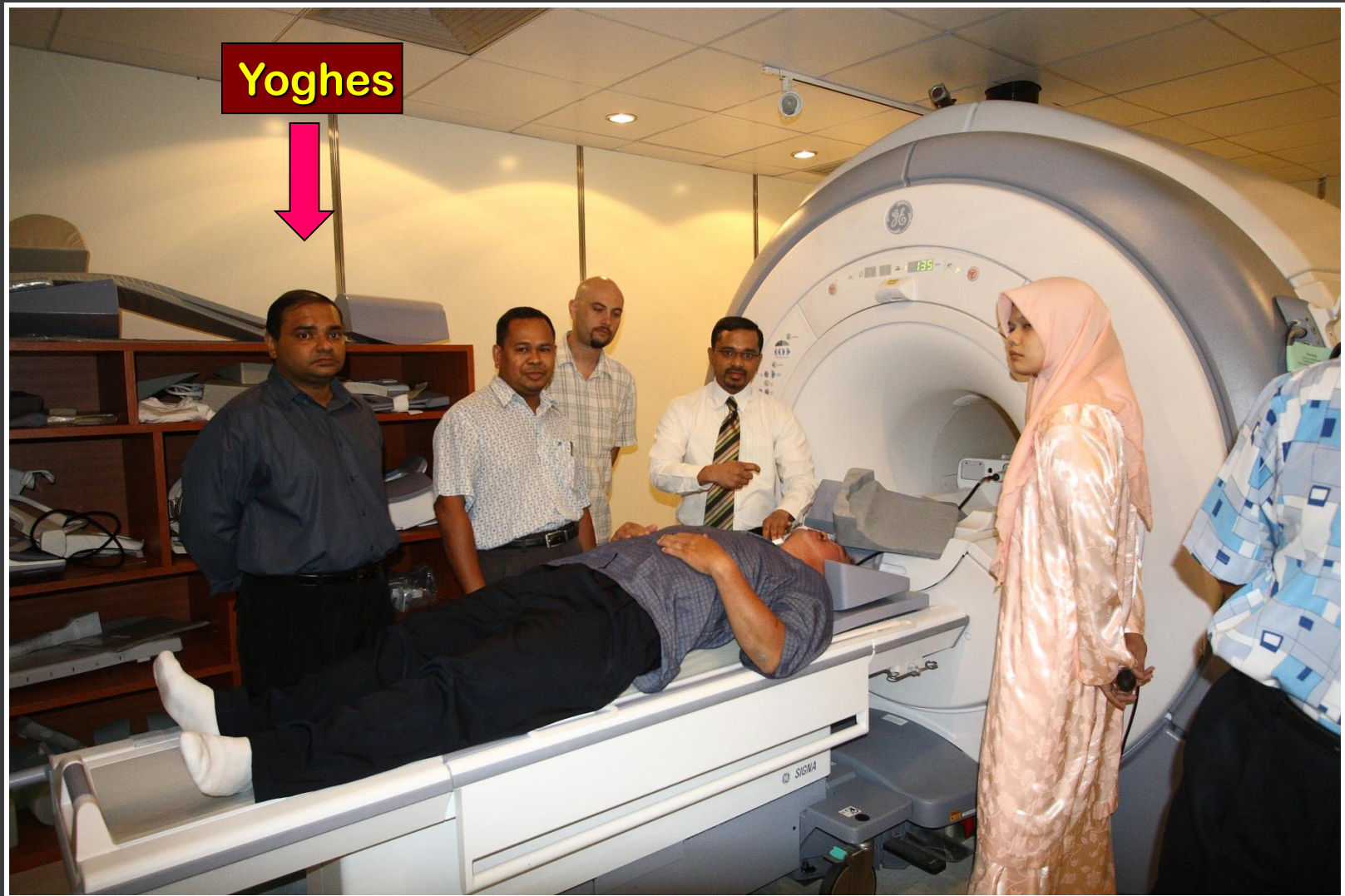


# Ultimate Proof is from Human Studies

- ① *We have conducted a study in human volunteers with White Matter Lesions (WMLs)*
- ② 121 subjects with **MRI-confirmed WMLs** were recruited and randomised to receive 200mg of mixed tocotrienols twice daily or placebo
- ③ MRI at baseline, repeated at 1 year and 2 years

**Study: double-blind placebo controlled**

# Imaging performed using our university MRI

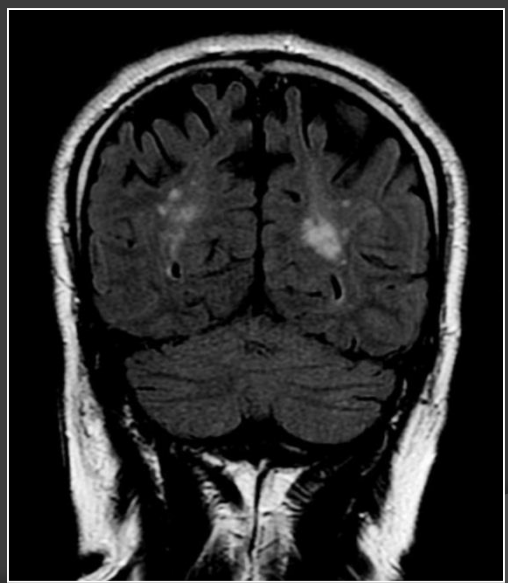
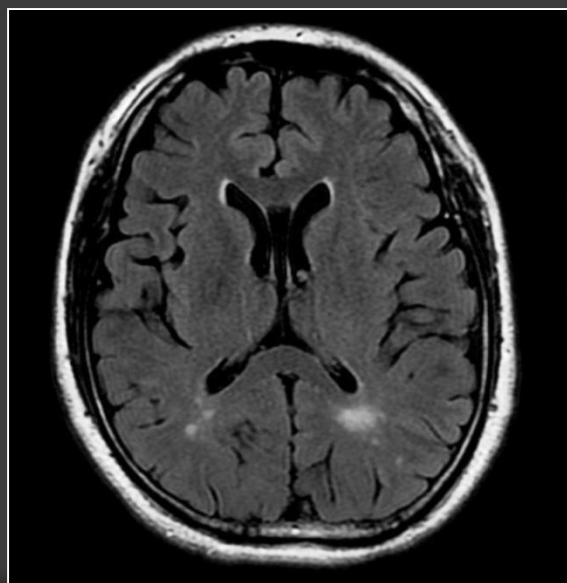
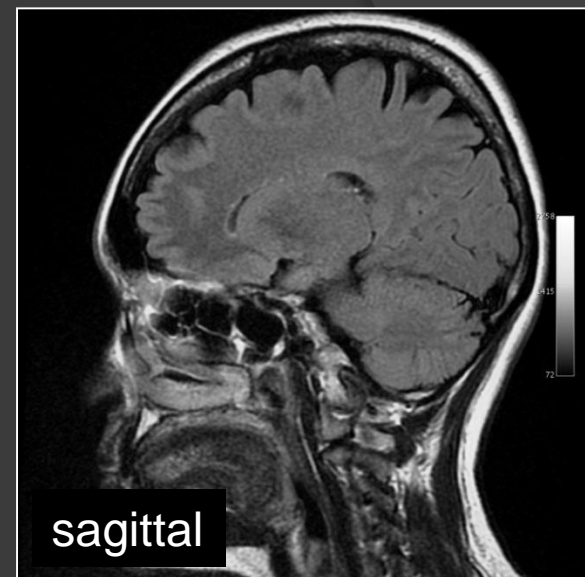
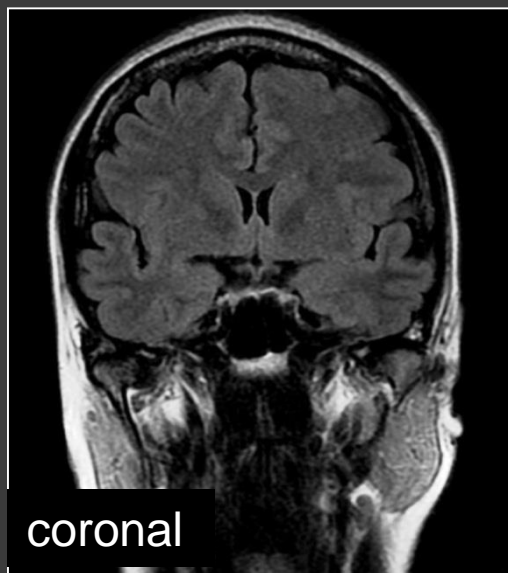
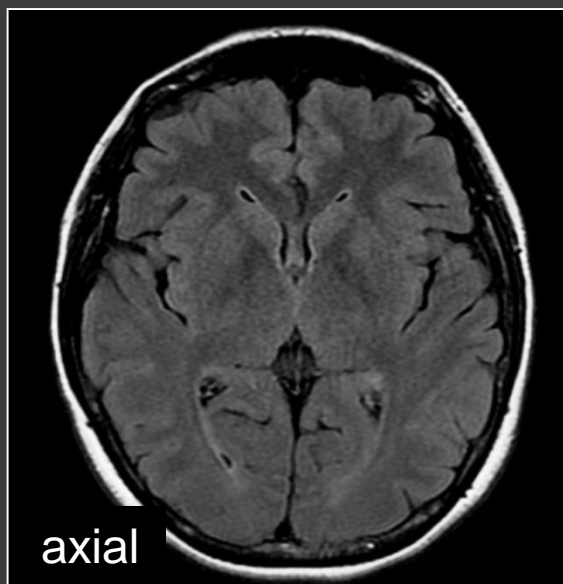




# What are White Matter Lesions (WMLs)?

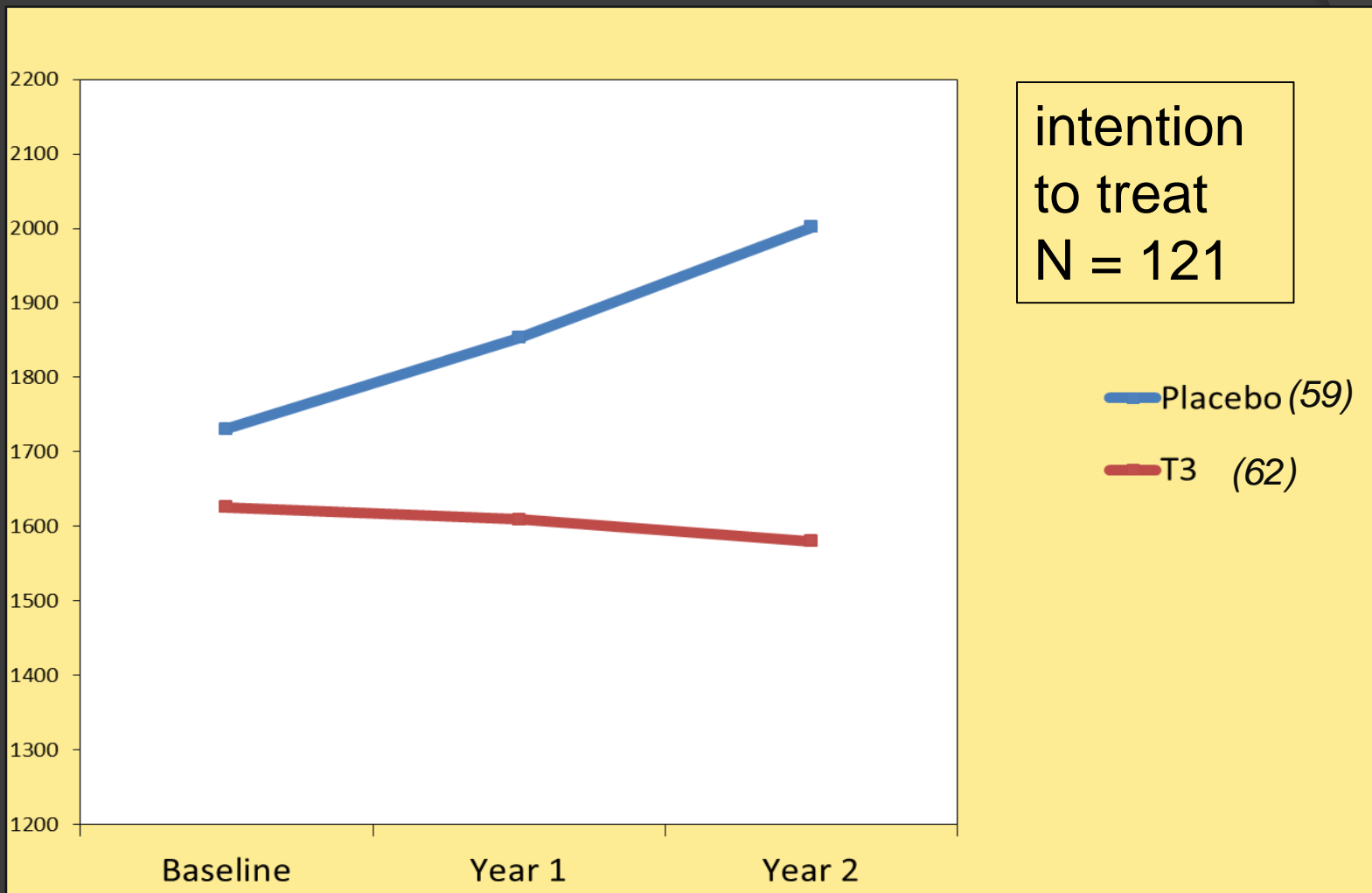
- ① *many older people have hyper-intensities (bright spots) in their brain MRI images, even with no apparent symptoms*
- ① *lesions formed from bundles of nerve fibers degenerating due to small blood vessel disease of the brain*
- ① *development increased with age and presence of CV risk factors (Schmidt et al 2002, Jeerakathil et al 2004, Murray et al 2005)*
- ① Deterioration of lesions/infarcts is **self progressive** (Veldink et al 1998, Whitman et al 2001, Schmidt et al 2002)

*Samples of MRI images (top=normal, bottom with WMLs)*

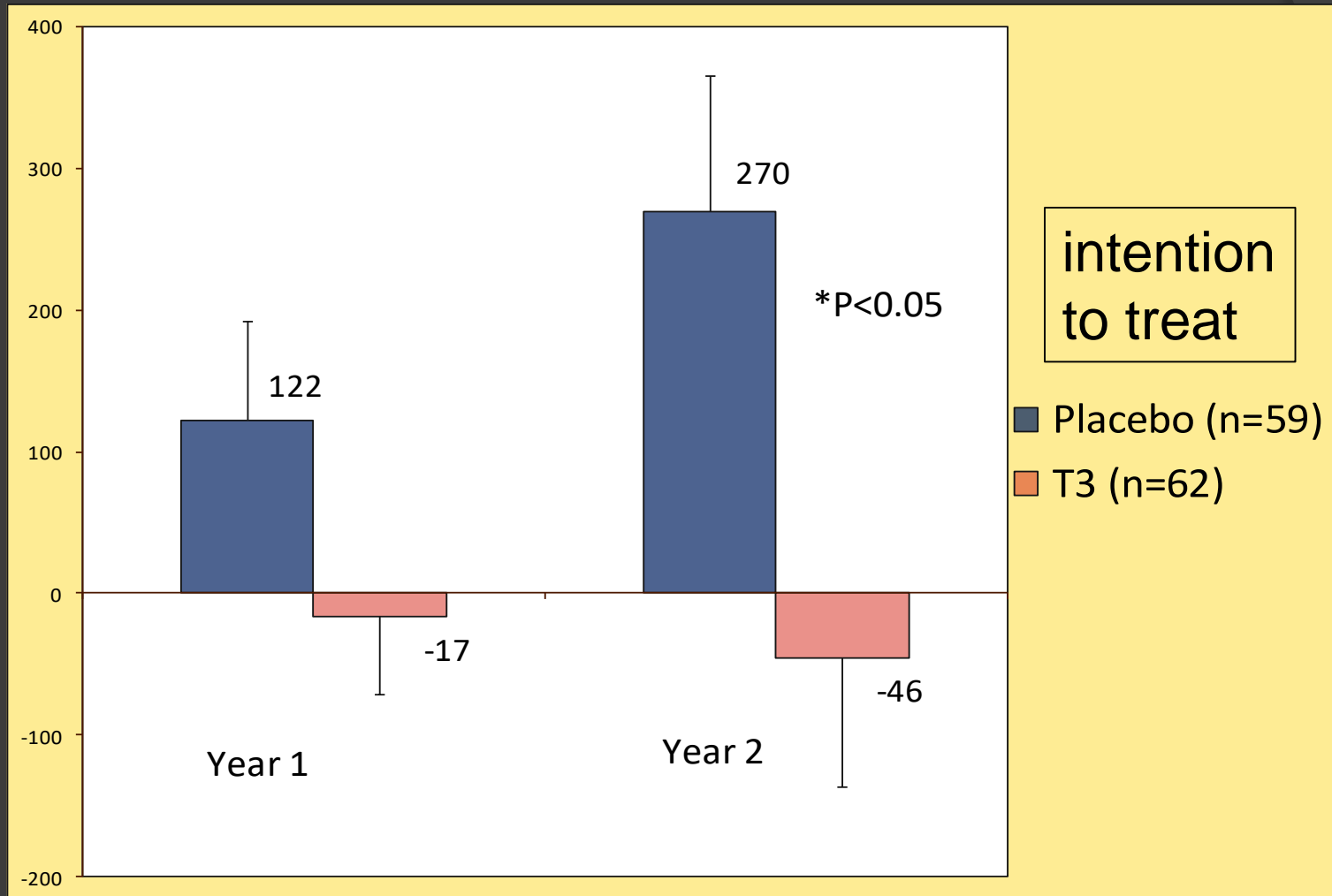


# Results

Mean volume of lesions(mm<sup>3</sup>) at baseline, Yr 1, Yr 2



# Change in mean volume of lesions



Average change in volume of lesions from baseline (mm<sup>3</sup>)

# Stroke

JOURNAL OF THE AMERICAN HEART ASSOCIATION



## **Clinical Investigation of the Protective Effects of Palm Vitamin E Tocotrienols on Brain White Matter**

**Yogheswaran Gopalan, Ibrahim Lutfi Shuaib, Enrico Magosso, Mukhtar Alam Ansari, Mohd Rizal Abu Bakar, Jia Woei Wong, Nurzalina Abdul Karim Khan, Wei Chuen Liong, Kalyana Sundram, Bee Hong Ng, Chinna Karuthan and Kah Hay Yuen**

*Stroke*. 2014;45:1422-1428; originally published online April 3, 2014;  
doi: 10.1161/STROKEAHA.113.004449

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# Many studies reported WMLs to be associated with

- cognitive decline and dementia (*Pantoni et al, 2007, Curr Opin Neurol., 20: 390-97*)
- cognitive impairment in Parkinson's Disease (*Perea et al, 2013, J AD and Parkinsonism*)
- progression of Alzheimer's Disease (*Prasad et al, 2011, Dement Geriatr Cogn Disord; 31:431-434*)

Progression of WMLs found to correlate with a decline in cognitive performance (*Schmidt et al, 2007, Stroke, 38: 2619-25*)

WMLs have become a predictor of cognitive decline and dementia including stroke and death (*Jokinen et al, 2005, J Neurol Neurosurg Psychiatry, 76:1229-33; Debette & Markus, 2010, BMJ, 341::c3666*)

# Mangialasche et al from Karolinska Institute

Published 3 papers: association of tocopherol and tocotrienol plasma levels with mental health of elderly folks

- Mangialasche et al, 2010, *J Alzheimer's Disease*; 20:1029-1037
- Mangialasche et al, 2012, *Neurobiology of Aging*; 33:2282- 2290
- Mangialasche et al, 2013, *Experimental Gerontology*,48(12):  
1428-14350

Elevated plasma levels of tocopherols and tocotrienols are associated with reduced risks of cognitive impairment and Alzheimer's Disease, but the odds are increased when the levels are low

# Tocotrienol improves learning and memory deficit of aged rats

Nozomi Kaneai,<sup>1</sup> Kazumi Sumitani,<sup>2</sup> Koji Fukui,<sup>2</sup> Taisuke Koike,<sup>3</sup> Hirokatsu Takatsu<sup>4</sup> and Shiro Urano<sup>1,\*</sup>

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*Journal of Clinical Biochemistry and Nutrition*

Animals given 3 types of diet:

- normal diet
- diet fortified with  $\alpha$ -tocopherol
- diet fortified with tocotrienols

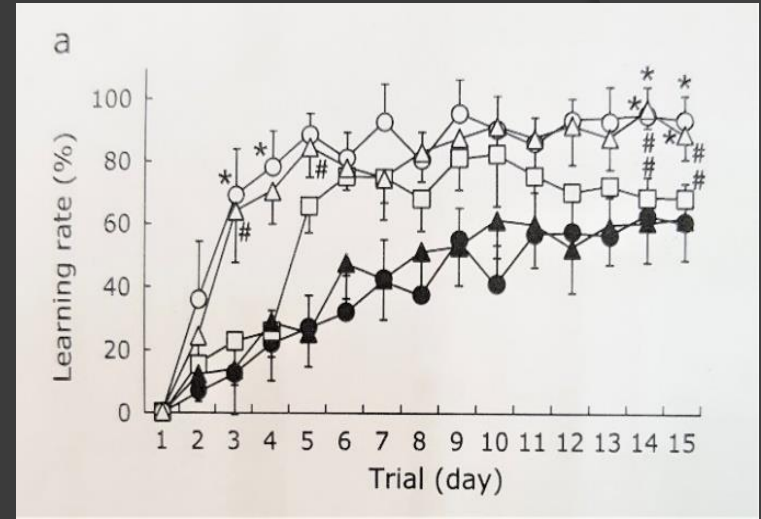


# Snapshot of the results

## Learning ability

### In Aged Rats

- Both  $\alpha$ -Toc and T3s enhanced learning ability
- But effect more significant with T3s

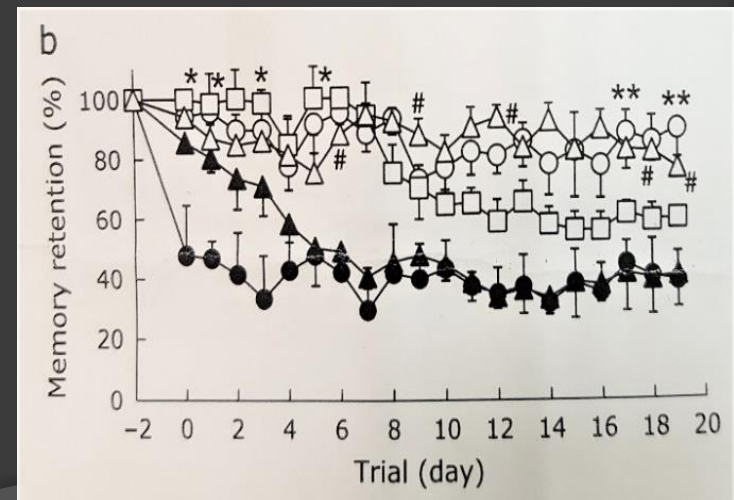


### In Young rats (subjected to oxidative stress)

- Decline in learning ability
- But was markedly enhanced with T3s

# Memory retention

- Declined in both **aged** and **young rats (subjected to oxidative stress)**
- Improved in **aged rats** by both  $\alpha$ -Toc and T3s
- But effect more sustained with T3s
- T3s also improved memory retention in **young rats (subjected to oxidative stress)**



# summary

Palm Vitamin E tocotrienols can play an important role in the **preventive management** of neurodegenerative disorders in the aging brain

- Stroke by reducing the tissue injury
- Attenuating or delaying development of dementia
- Protective against other neurodegenerative disorders

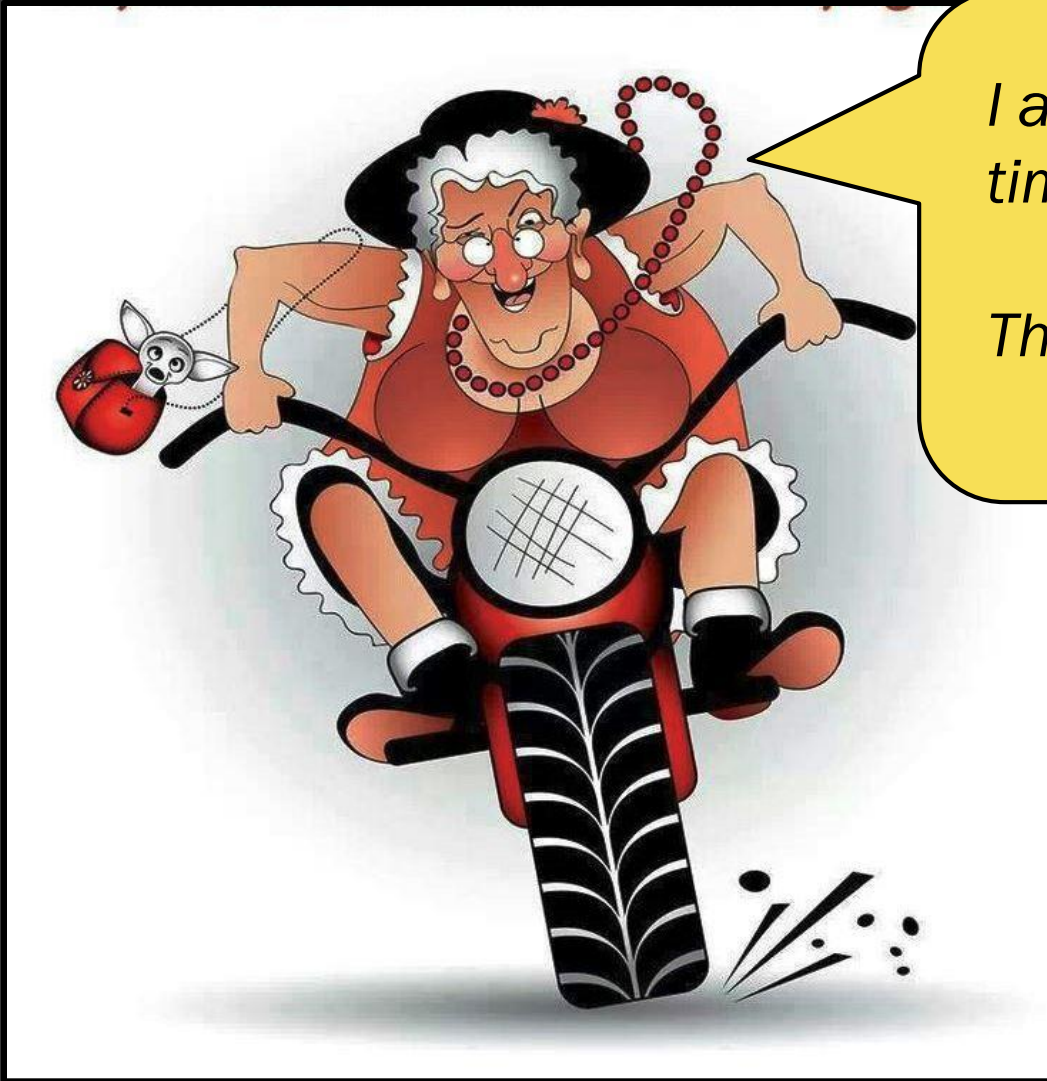
Tocotrienols are not drugs but natural vitamin E isoforms, and are safe to be taken as a long term neuroprotective supplement

# Some final words.....

*Lets pray, we will all grow old gracefully with our mental faculties intact, so that we can enjoy our golden years...*

*and not become a burden to our children, family and society.*

**Palm vitamin E tocotrienols may be the answer to our prayers...**



*I am having such fabulous  
time here.....*

*Thanks to Palm Tocotrienols*



*Thank You  
for your  
attention*

*Confucius*