



Biocomponents of Palm Oil: Tocotrienols and Carotenes and their Effects on Health

Dr Kanga Rani Selvaduray
Head of Nutrition Unit
Malaysian Palm Oil Board



M P O B



MINISTRY OF PLANTATION
INDUSTRIES AND COMMODITIES

Presentation Outline

Introduction

Types of Phytonutrients

Health Beneficial Effects

Take Home Messages

**Palm
Phytonutrients**

Palm Oil

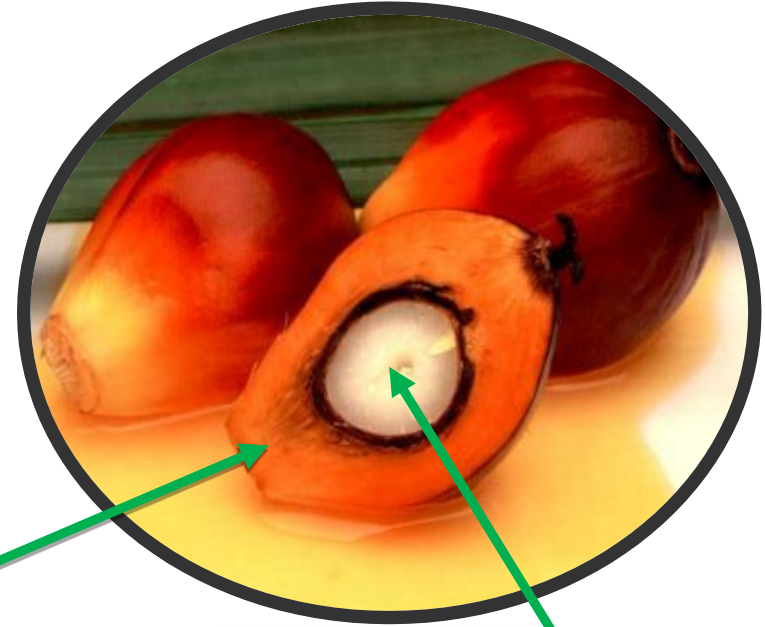
Oil Palm



Fresh Fruit Bunch (FFB)



Oil Palm Fruits



Mesocarp

Crude Palm Oil (CPO)

Kernel

Palm Kernel Oil (PKO)



Composition of crude palm oil



Component	Percentage
Triglycerides (TAG)	> 90
Diglycerides (DAG)	~ 2-7
Monoglycerides (MAG)	< 1
Free Fatty Acids (FFA)	~ 3-5
Phytonutrients	~ 1

- Tocopherols & tocotrienols
 - Carotenoids
 - Phytosterols
 - Squalene
 - Lecithin
- Co-enzyme Q10
- Polyphenols



Major phytonutrients in palm oil

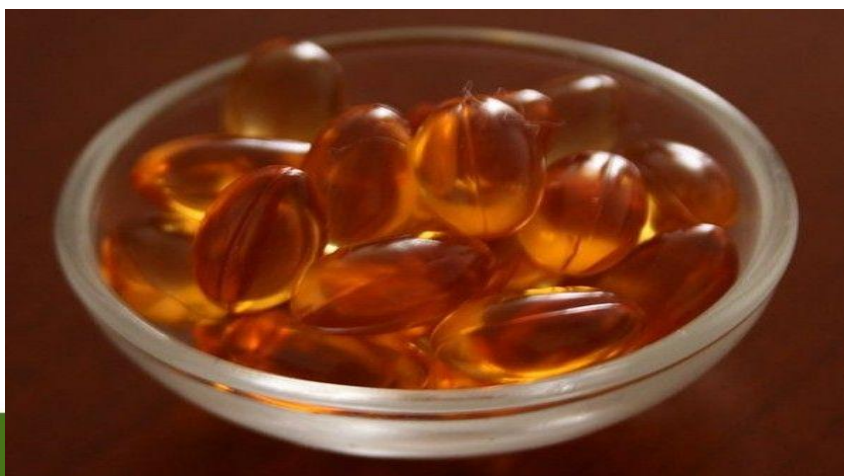
Phytonutrients	Concentration (ppm)
Vitamin E (tocotrienols, tocopherols)	600-1000
Carotenoids (α -carotene, β -carotene, lycopene, phytoene)	500-1000
Phytosterol (Sitosterol, stigmasterol, campesterol)	300-620
Squalene	250-800
Lecithin (Phospholipids)	20-100
Co-enzyme Q10 / Ubiquinones	10-80
Polyphenols (Phenolic acids, flavonoids)	40-70



PALM TOCOTRIENOLS

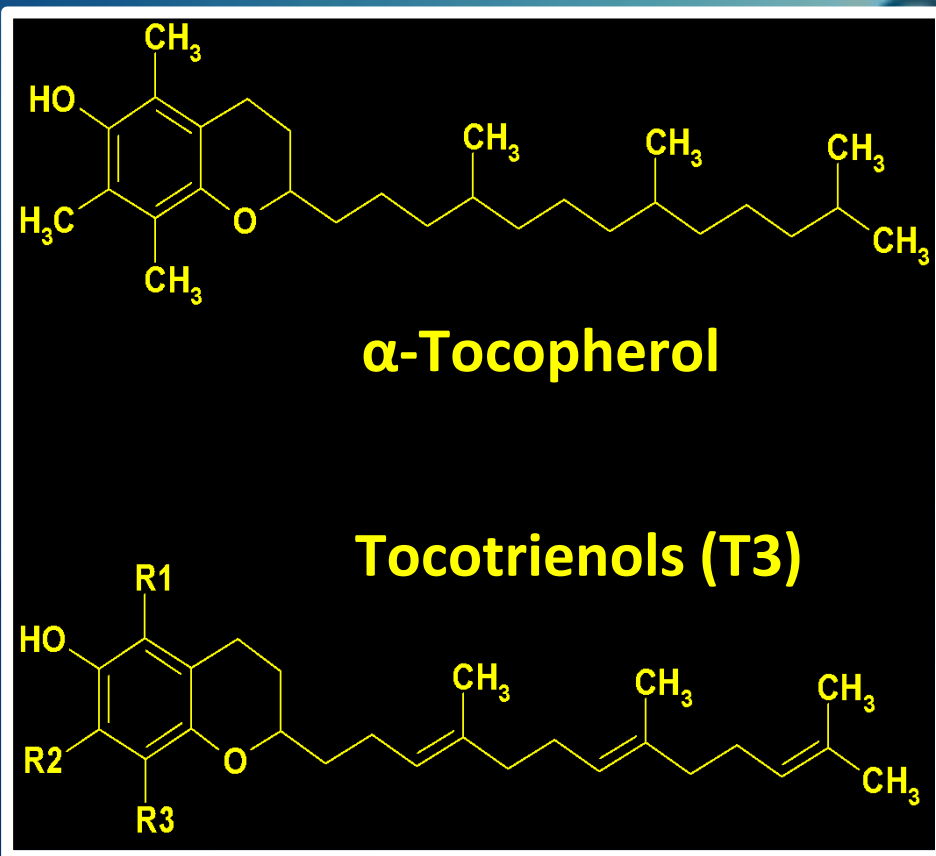


Palm Vitamin E



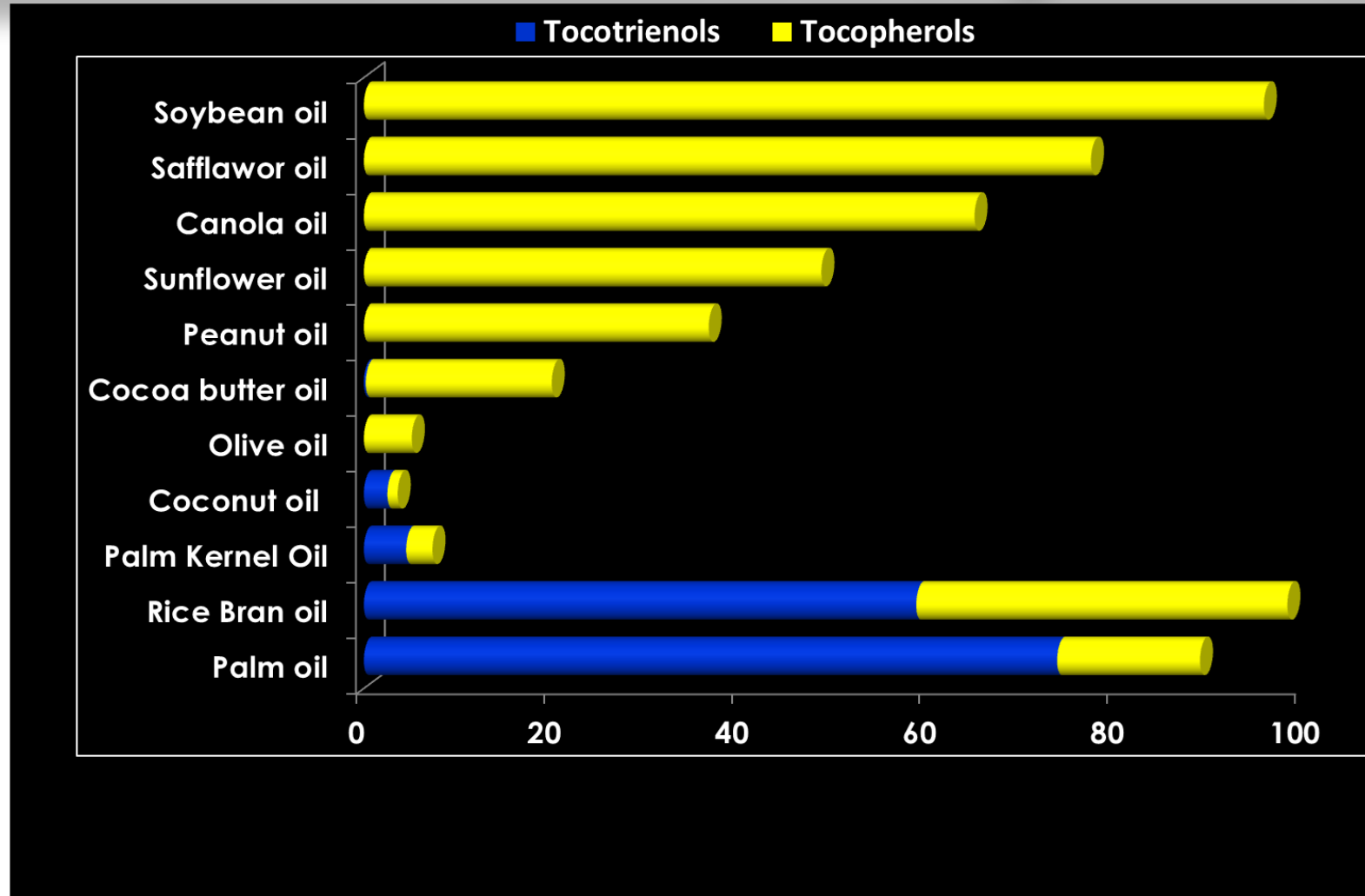
- ❖ Lipid-soluble vitamin E accounts for less than 1% of total palm oil content
- ❖ Vitamin E is important in preserving oil stability, shelf-life, contributing to the health benefit of dietary PO consumption
- ❖ Vitamin E in palm oil - 70 % tocotrienols (TRF) 30 % tocopherols

Vitamin E Isoforms



	R1	R2	R3
α -T3	CH ₃	CH ₃	CH ₃
γ -T3	H	CH ₃	CH ₃
δ -T3	H	H	CH ₃

Source of Vitamin E in Vegetable oils





OVERVIEW OF PALM TOCOTRIENOL RESEARCH

1981-1990

Animal studies on palm oil vitamin E and carcinogenesis

1991-2000

in vitro and Animal studies on cancer and other diseases using Tocotrienols

2001-2010

in vitro, Animal and human studies on mechanisms of tocotrienols, in diseases

2011-2020

Animal and human clinical studies on phyto-nutrients and various disease pathways, preliminary studies on Nano-T3; Regulation and recognition

2021-2030

Nano-T3 Pilot plant and bioavailability studies

Product development and Commercialisation

Human clinical studies – Application

NRVs (Nutrient reference values)

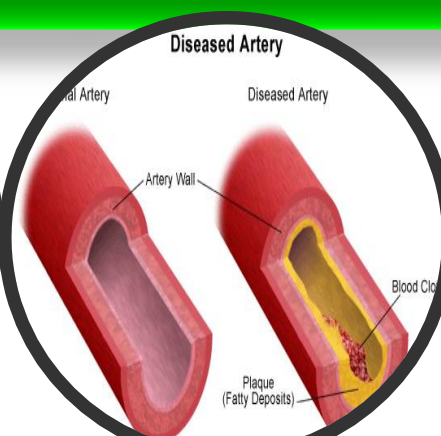
HEALTH BENEFITS OF VITAMIN E -TOCOTRIENOLS



Neuroprotection
(Sen et al., 1999)



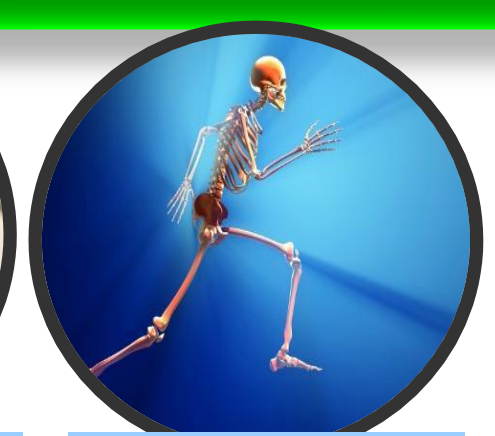
Radioprotection
(Singh et al., 2016)



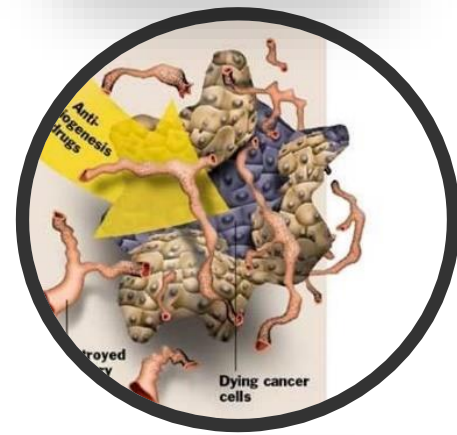
Cardiovascular prevention
(Das et al., 2008)



Antioxidant
(Theriault et al., 1999)



Bone protection
(Shen et al., 2017)



Cancer prevention
(Selvaduray et al., 2010)



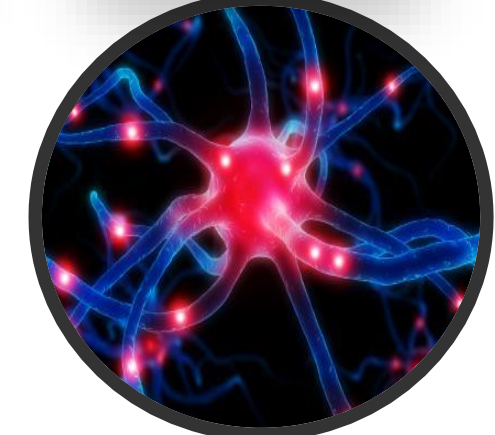
Immune booster
(Radhakrishnan et al., 2014)



Skin protection
(Yap, 2018)



Anti-inflammation
(Yam et al., 2009)



Hormone regulator
(Saito et al., 2003)

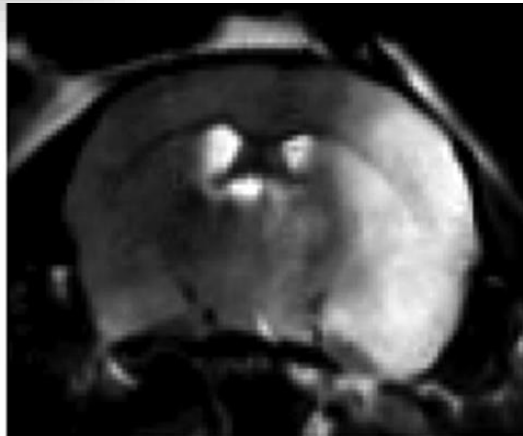
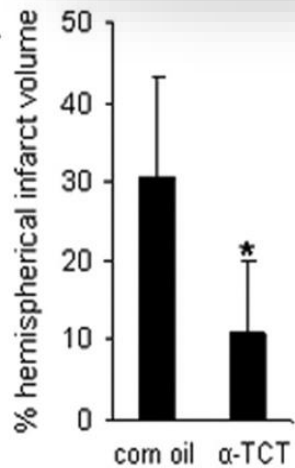
Tocotrienols & Neuroprotection



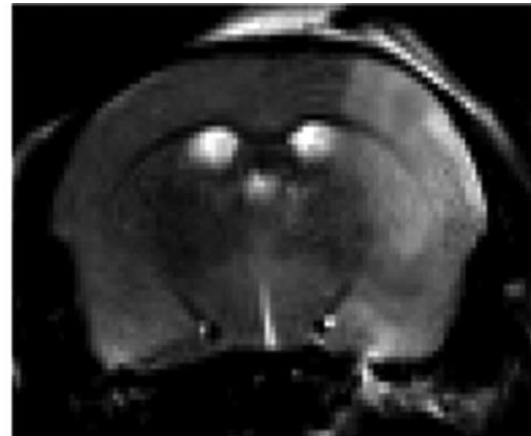
STROKE STUDIES

Prof. Chandan Sen

- Nanomolar of tocotrienol prevented glutamate induced damage neural cells.
- T3 improved cerebrovascular circulation and fiber connectivity after ischemic stroke
- T3 supplementation reduced occlusion-induced brain injury.



corn oil



α-TCT

Khanna et al., J. Neurochem. 2010

Rink et al., J Cereb Blood Flow Metab. 2011

Park et al., Stroke, 2011

Tocotrienols & Neuroprotection



NEUROPROTECTION

Prof. Yuen Kah Hay

- 2 years supplementation of T3 suppressed mean volume change in white matter lesion.
- 1 year supplementation of T3 reduced lancinating pain in diabetic patients with peripheral neuropathy.



*The Vitamin E in Neuroprotection Study (VENUS)
Investigators, JAMA Neurology. 2018*

Gopalan et al., Stroke. 2014

Tocotrienols & Neuroprotection



NEUROPROTECTION

Karolinska Institute, Sweden



- Higher tocotrienol levels in blood had lower risk of developing Alzheimer's disease.
- Higher gamma-tocotrienol levels in their blood had lower risk of developing cognitive impairment.

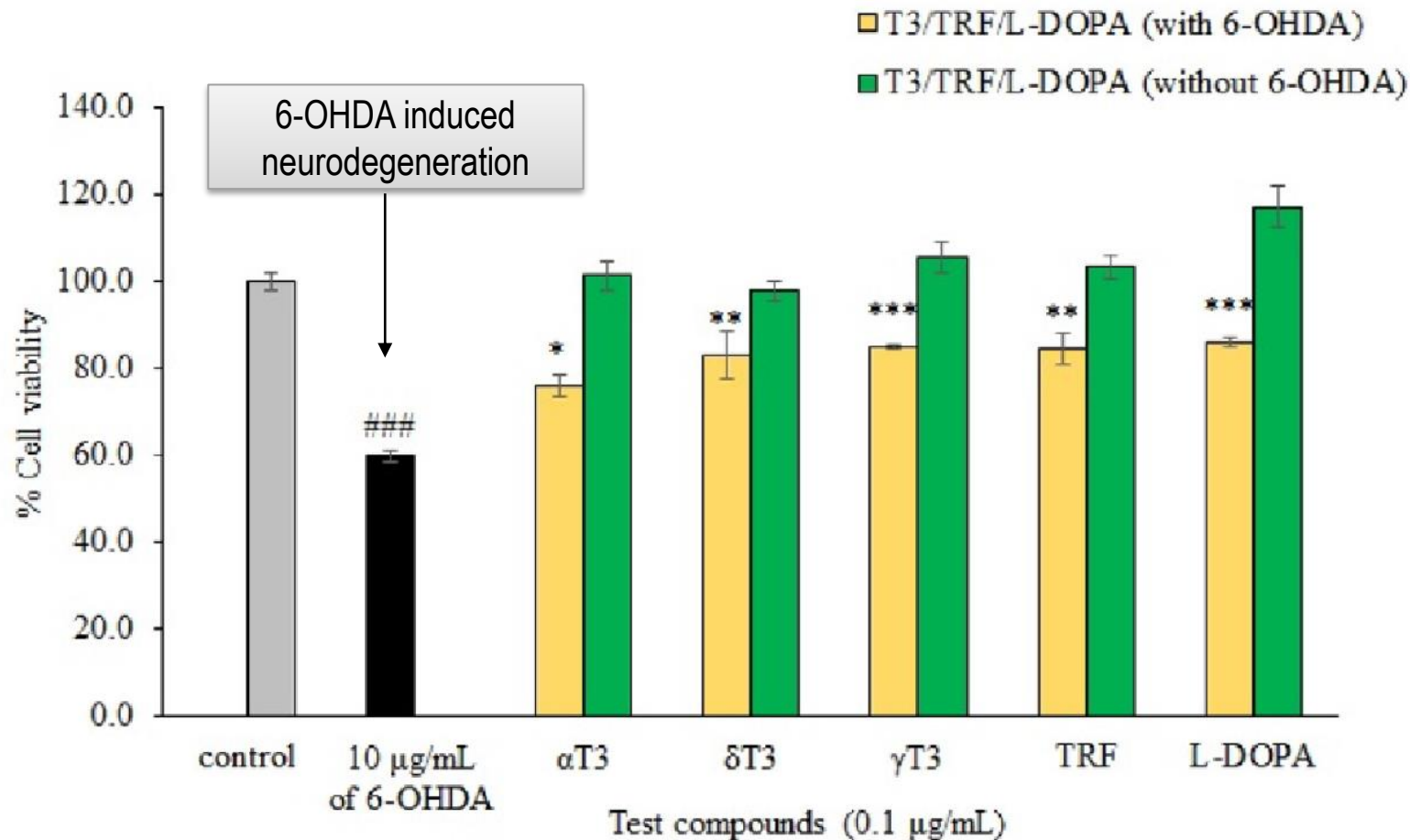
Mangialasche et al. 2010

Mangialasche et al. 2012

Mangialasche et al. 2013

Tocotrienols & Neuroprotection

Effect of tocotrienols on in-vitro model of Parkinson's disease

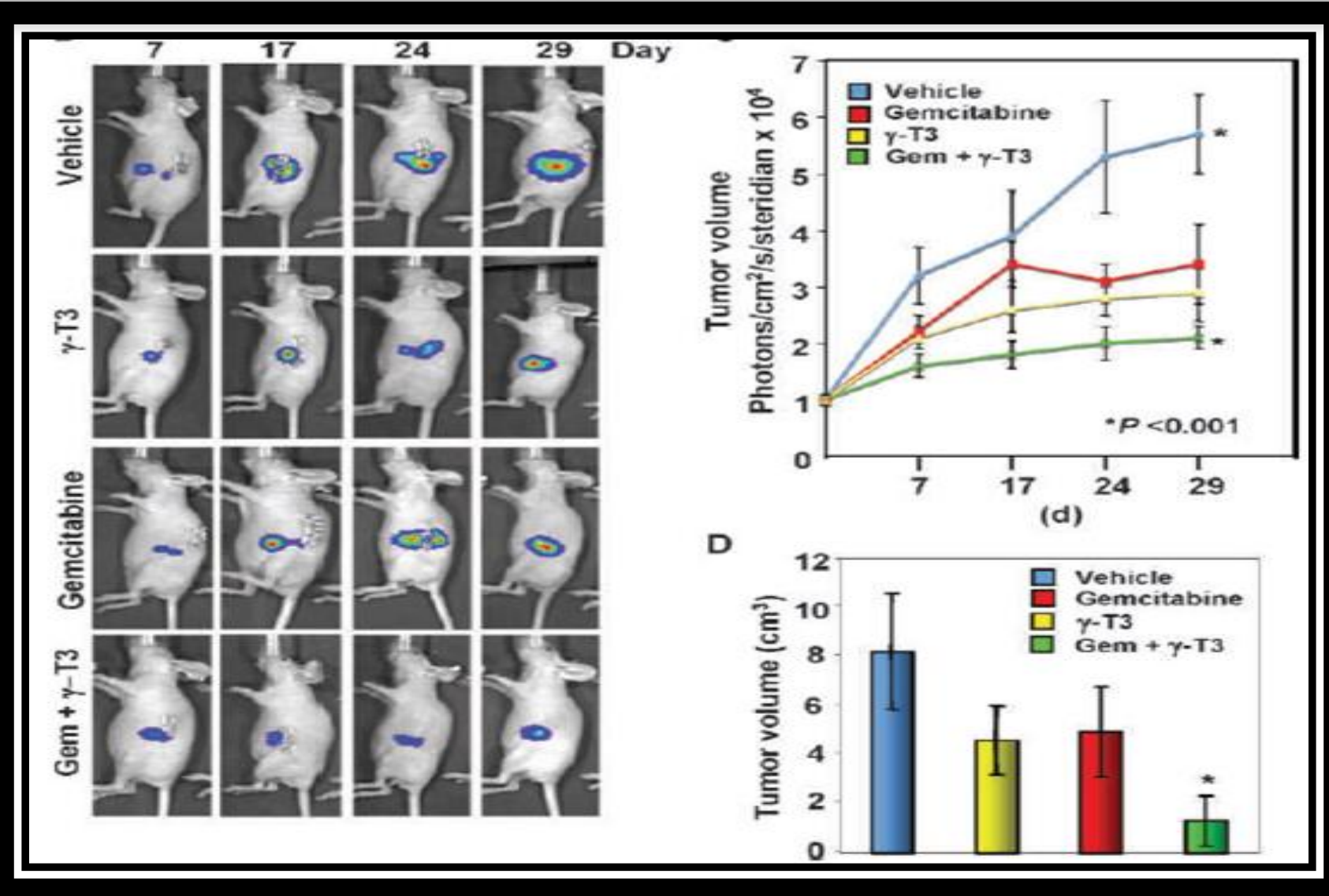


Pre-treatment of tocotrienols restored cell viability in differentiated SH-SY5Y neural cells.

Significant difference observed in cells pre-treated with tocotrienols compared to positive control (6-OHDA group).

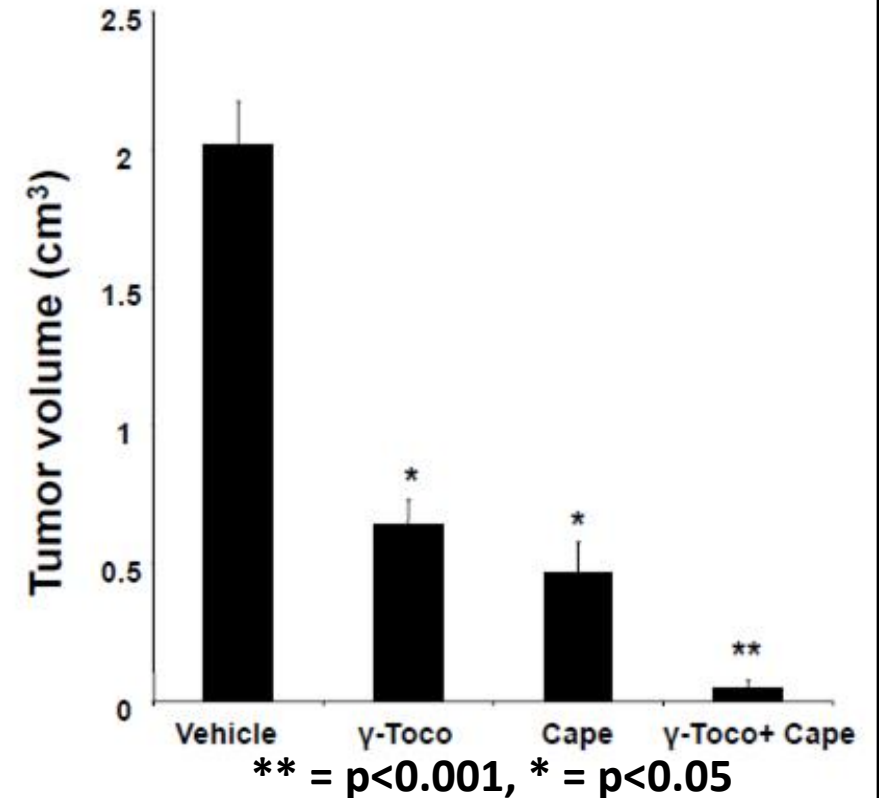
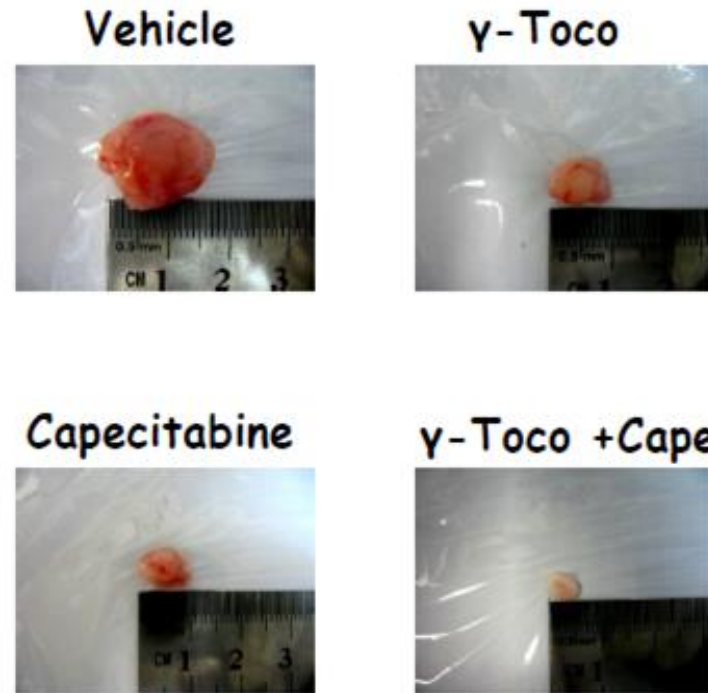
(Magalingam et al., 2022. Nutrition Research)

**Kunnumakkara
et al., 2010
Cancer Res.**



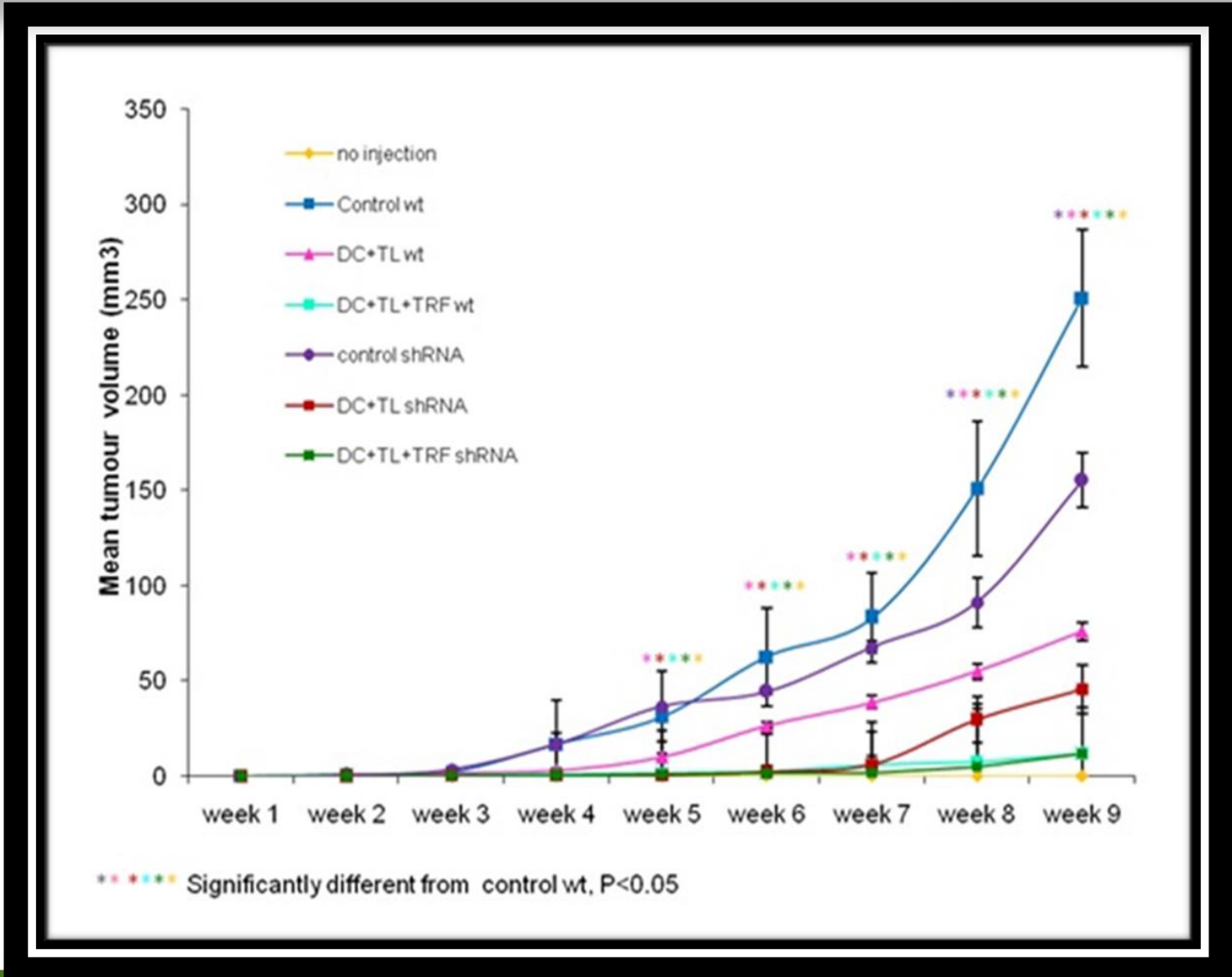
**Gautam Sethi,
2011**

γ -Tocotrienol potentiates the effects of capecitabine to inhibit the growth of gastric cancer in nude mice

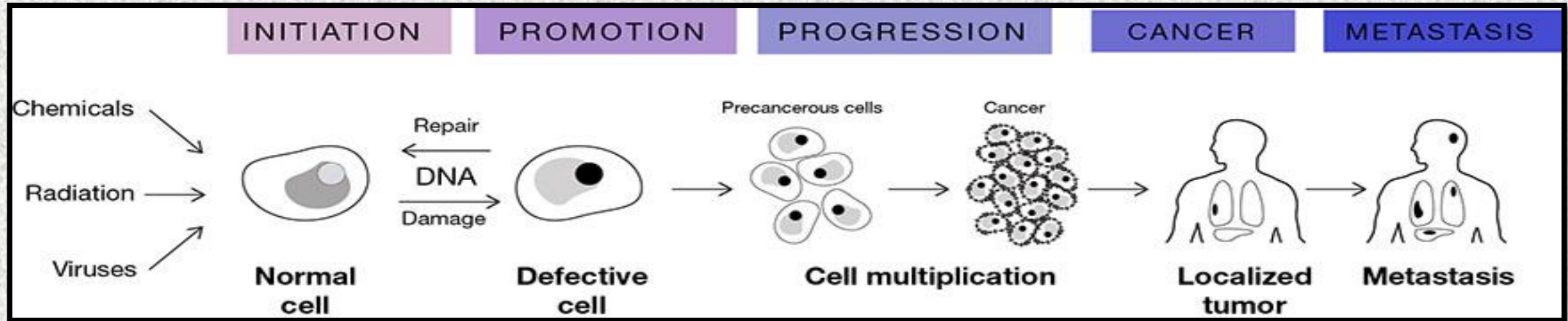


Abdul Hafid et al., 2021

Tocotrienols significantly inhibited and **reduced tumour volume** in mice injected with 4T-1 tumour cells



Stages of Cancer



Mechanism of Action by Tocotrienols

Anti-proliferative

Anti-angiogenic

Pro-apoptotic

Anti-inflammatory

Augment Immune response

Tocotrienols & Cancer

Multi-targeted

- Inflammatory cytokines**
IL-1, IL-6, IL-8, IL-12, PF-4, IFN- γ
- Enzymes**
12-LOX, COX-2, DNAPol λ , eNOS, GGT, GST, GSTP-1, HMGCR, hTERT, iNOS, MMP-2, MMP-9, NQO1, PLA2, telomerase
- Growth factors**
VEGF, HER2/neu, TGF- β
- Receptors**
DR, EGFR, ER- α , ER- β , ErbB-3R, VEGFR
- Adhesion molecules**
E-selectin, ICAM-1, VCAM-1
- Anti-apoptotic proteins**
Bcl-2, Bcl-xL, IAP-1, IAP-2, survivin, TRAF-1, XIAP, c-FLIP, Bfl-1/A1
- Protein Kinases**
CKD-2, CDK-4, CDK-6, IKK- α , IKK- β , Pdk-1, ERK1/2, GSK-3 β , PI3K, PKC, Src, JAK-1 & -2
- Transcriptional factors**
C/EBP- α , c-myc, NF- κ B, STAT-3, PPAR- γ , E2F, HIF-1 α , STAT-5
- Others**
Cyclin D1, Cyclin D3, Akt, Apo B, Cyclin E, Id-1, PGE-2, Raf-1, Ras, TX-B2

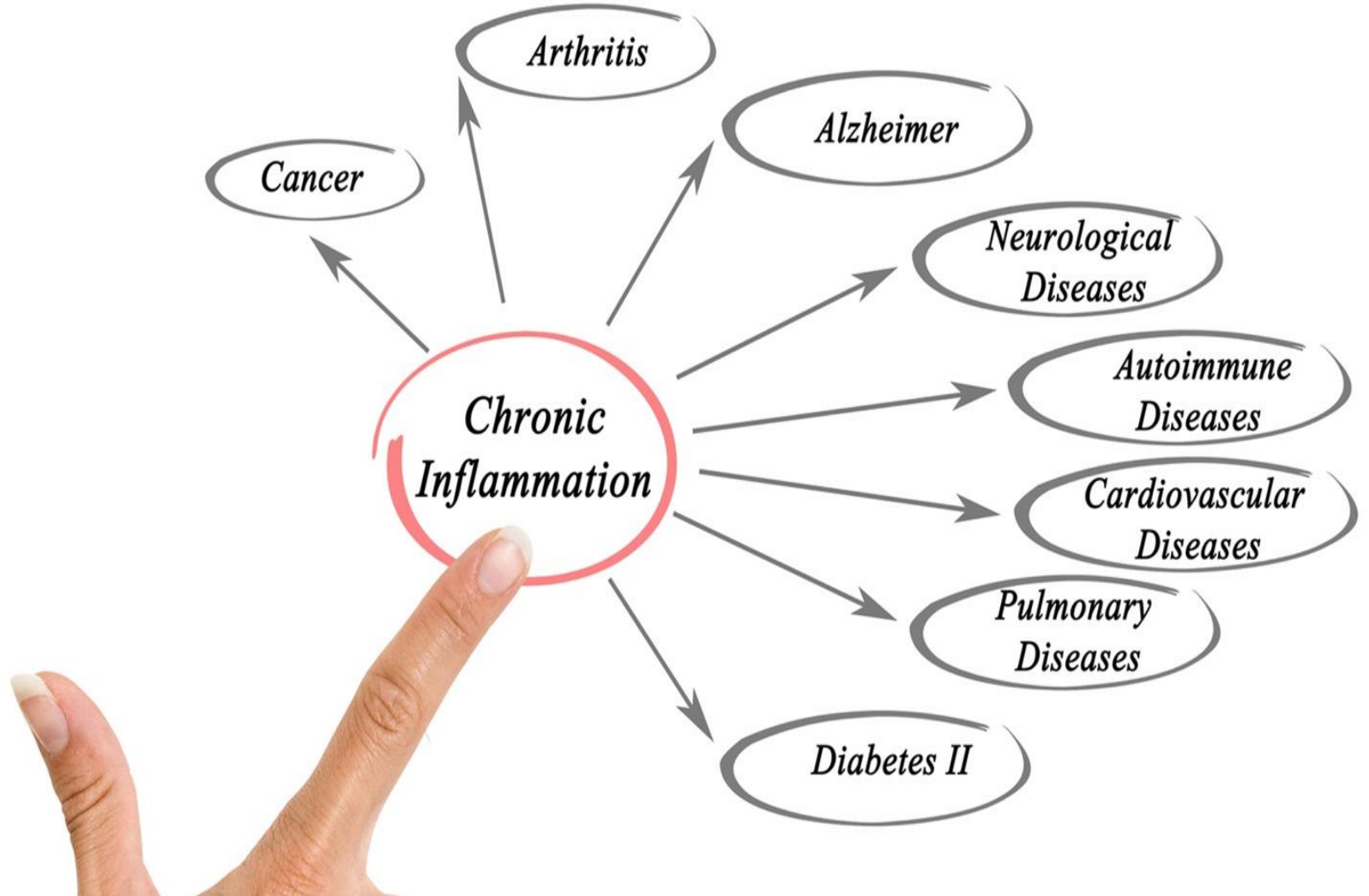
Mono-targeted

- COX-2 | Celecoxib
- EGFR | Erbitux
- NF- κ B | Velcade
- HER-2 | Herceptin
- ? Bcr-Abl | Gleevac
- VEGF | Avastin
- ? Tubulin | Paclitaxel
- ? Topoisomerase | Camptothecin



(Kannappan et al., 2011)

Tocotrienols & Inflammation





Review Paper on Palm Tocotrienols in Food Research International (June 2022)

Food Research International 156 (2022) 111175



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Food Research International

journal homepage: www.elsevier.com/locate/foodres



Review

Therapeutic potential of palm oil vitamin E-derived tocotrienols in inflammation and chronic diseases: Evidence from preclinical and clinical studies

Zaida Zainal^{a,*}, Huzwah Khaza'ai^b, Ammu Kutty Radhakrishnan^c, Sui Kiat Chang^d

^a Nutrition Unit, Product Development and Advisory Technical Services Department, Malaysian Palm Oil Board, No. 6, Persiaran Institusi, Bandar Baru Bangi 43000, Selangor, Malaysia

^b Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang 43400, Selangor, Malaysia

^c Jeffrey Cheah School of Medicine and Health Sciences, Monash University Malaysia, Jalan Lagoon Selatan, Bandar Sunway, 47500 Subang Jaya, Selangor, Malaysia

^d Department of Allied Health Sciences, Faculty of Science, Universiti Tunku Abdul Rahman, Kampar 31900, Perak, Malaysia

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 Tocotrienol
 Antioxidant activity
 Anti-inflammation
 Stroke

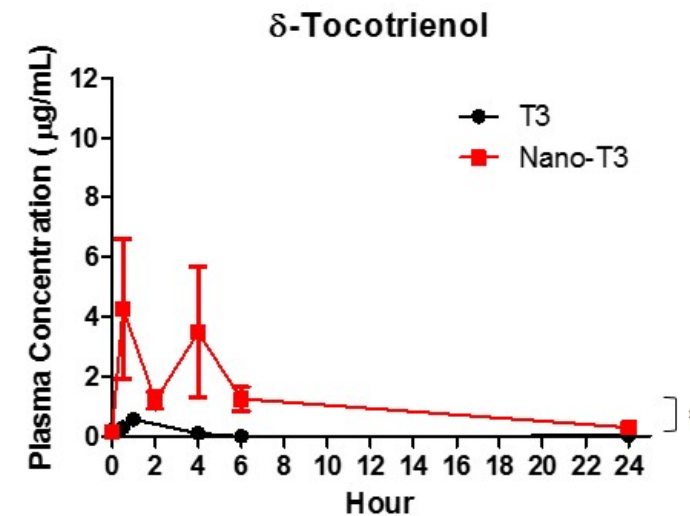
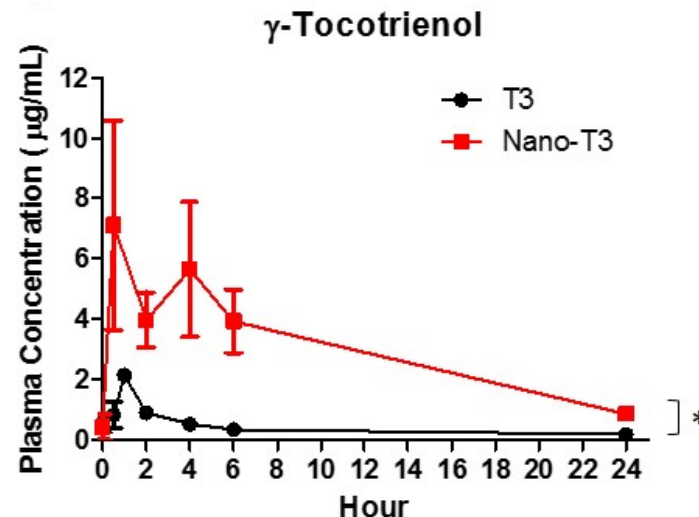
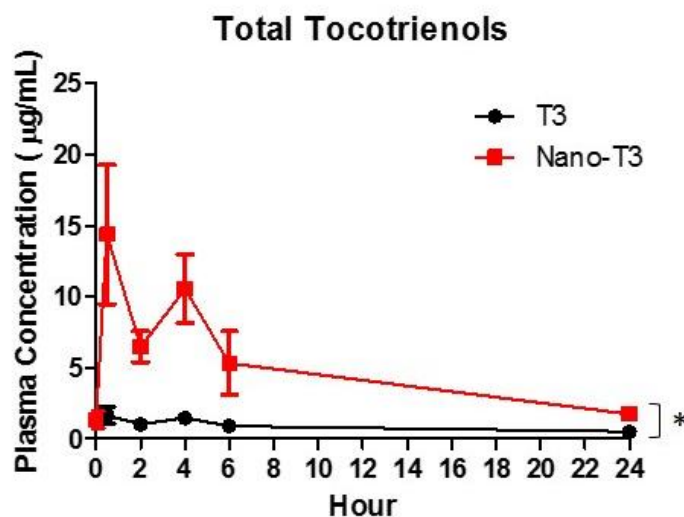
ABSTRACT

Palm oil is rich in tocotrienols (T3s), a type of vitamin E that has garnered considerable research interest as it exhibits anti-inflammatory as well as antioxidant characteristics that are comparable to or exceed those of tocopherols (Toc). Notably, T3 must be consumed as it cannot be produced by the human body. Here, we reviewed the anti-inflammatory activities of T3s in the prevention and treatment of various inflammatory disorders; focusing on recent preclinical and clinical studies. There is compelling data from experimental models and human studies that shows that T3 administration can inhibit the release of various inflammatory mediators that contribute to age-related disease by enhancing oxidative stress, reducing melanin production and skin damage.

Nano-Tocotrienols

Fu et al., AOCS. 2021

Enhanced Bioavailability



Stereoisomer		AUC ₀₋₂₄ (µg/ml*hour)	F (%)
α-tocotrienol	Test	51.97 ± 18.60	403
	Reference	12.90 ± 1.41	
γ-tocotrienol	Test	69.77 ± 9.48	829
	Reference	8.42 ± 3.26	
δ-tocotrienol	Test	26.66 ± 0.79	1374
	Reference	1.94 ± 1.08	

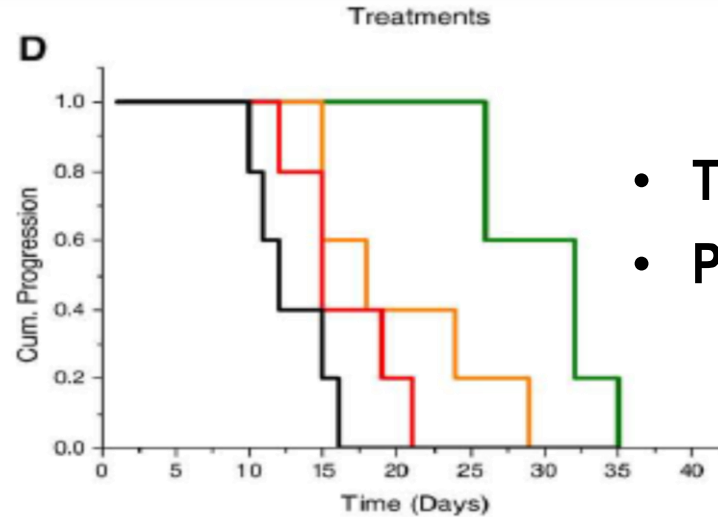
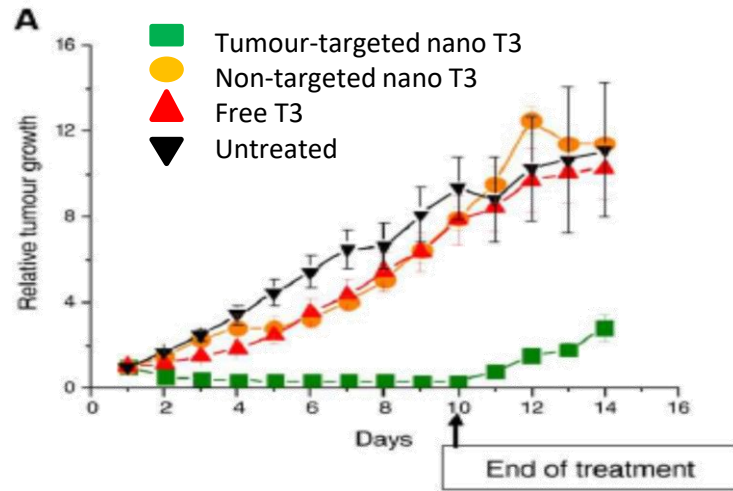
Relative bioavailability, *F*



1. Higher plasma concentration
2. Prolonged circulation time

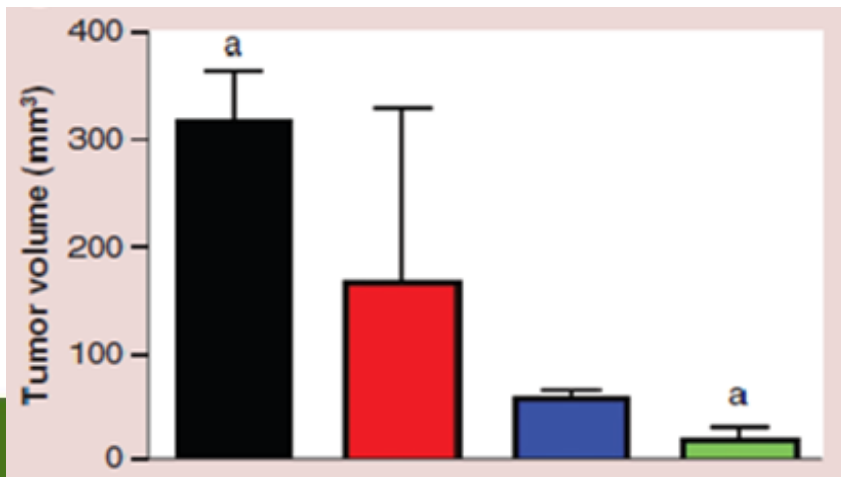
Nano-Tocotrienols

Cancer Management



- Tumour suppression up to 10 days
- Prolonged survival of 19 days

Fu et al., J Controlled Release. 2009

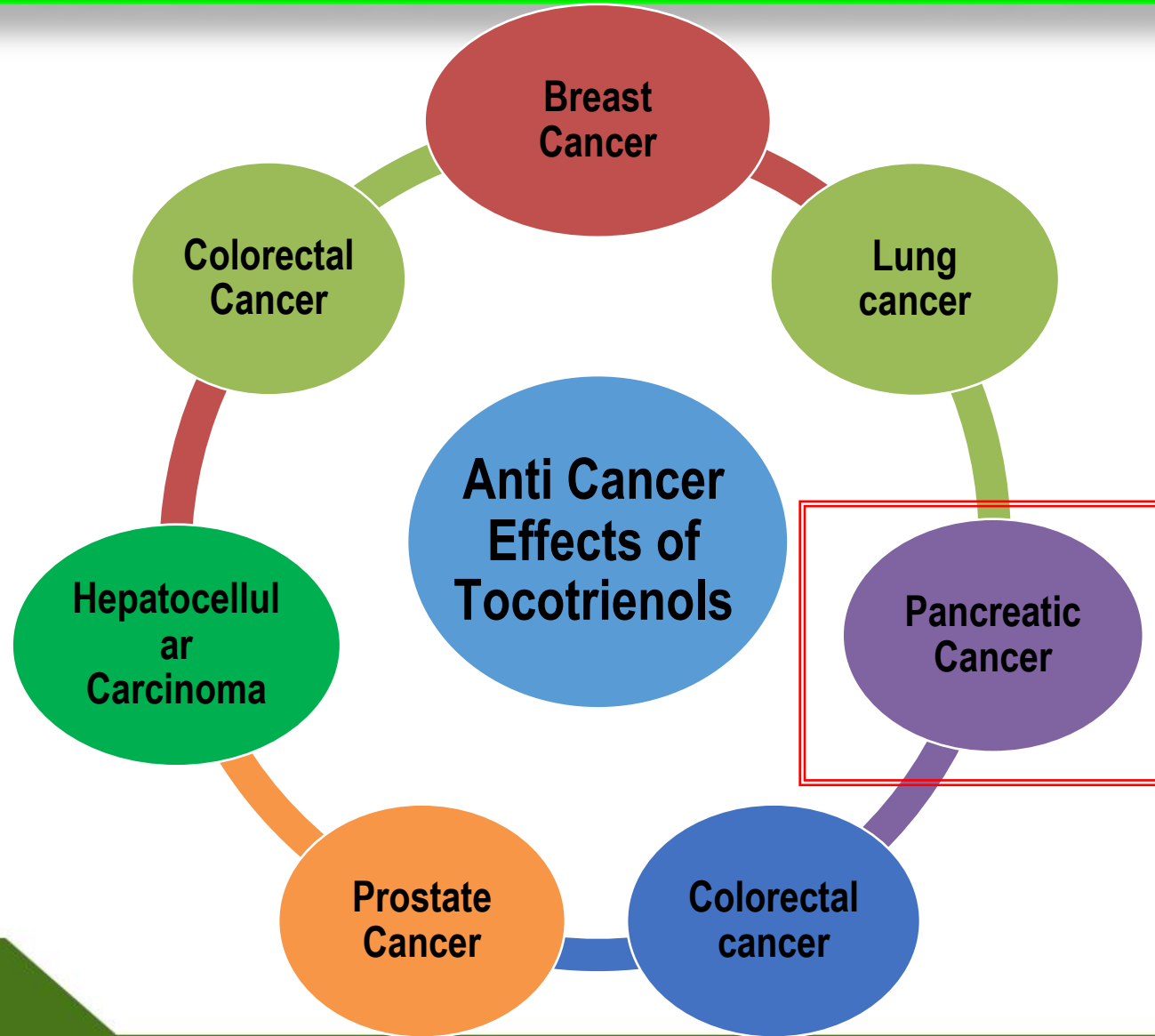


- 12-fold reduction in tumour volume was observed in mice treated with tumour-targeted nano-T3

Tan et al., Nanomedicine. 2017

Clinical trials on Tocotrienols and Cancer

Kannappan et al., 2011;
De Silva et al., 2016



Research Article

A Phase I Safety, Pharmacokinetic, and Pharmacodynamic Presurgical Trial of Vitamin E δ -tocotrienol in Patients with Pancreatic Ductal Neoplasia



Gregory M. Springett^a, Kazim Husain^a, Anthony Neuger^b, Barbara Centeno^c, Dung-Tsa Chen^d, Tai Z. Hutchinson^a, Richard M. Lush^b, Saïd Sebti^e, Mokenge P. Malafa^{a,*}

^a Department of Gastrointestinal Oncology, Tampa, FL, USA

^b Translational Research Core, Tampa, FL, USA

^c Department of Cytopathology, Tampa, FL, USA

^d Biostatistics Core, Tampa, FL, USA

^e Department of Drug Discovery, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL, USA

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Chemoprevention

ABSTRACT

Background: Vitamin E δ -tocotrienol (VEDT), a natural vitamin E from plants, has shown anti-neoplastic and chemoprevention activity in preclinical models of pancreatic cancer. Here, we investigated VEDT in patients with pancreatic ductal neoplasia in a window-of-opportunity preoperative clinical trial to assess its safety, tolerability, pharmacokinetics, and apoptotic activity.

Methods: Patients received oral VEDT at escalating doses (from 200 to 3200 mg) daily for 13 days before surgery and one dose on the day of surgery. Dose escalation followed a three-plus-three trial design. Our primary endpoints were safety, VEDT pharmacokinetics, and monitoring of VEDT-induced neoplastic cell apoptosis (ClinicalTrials.gov number NCT00985777).

Findings: In 25 treated patients, no dose-limiting toxicity was encountered; thus no maximum-tolerated dose was reached. One patient had a drug-related adverse event (diarrhea) at a 3200-mg daily dose level. The effective half-life of VEDT was ~4 h. VEDT concentrations in plasma and exposure profiles were quite variable but reached levels that are bioactive in preclinical models. Biological activity, defined as significant induction of apoptosis in neoplastic cells as measured by increased cleaved caspase-3 levels, was seen in the majority of patients at the 400-mg to 1600-mg daily dose levels.

Interpretation: VEDT from 200 to 1600 mg daily taken orally for 2 weeks before pancreatic surgery was well tolerated, reached bioactive levels in blood, and significantly induced apoptosis in the neoplastic cells of patients with pancreatic ductal neoplasia. These promising results warrant further clinical investigation of VEDT for chemoprevention and/or therapy of pancreatic cancer.

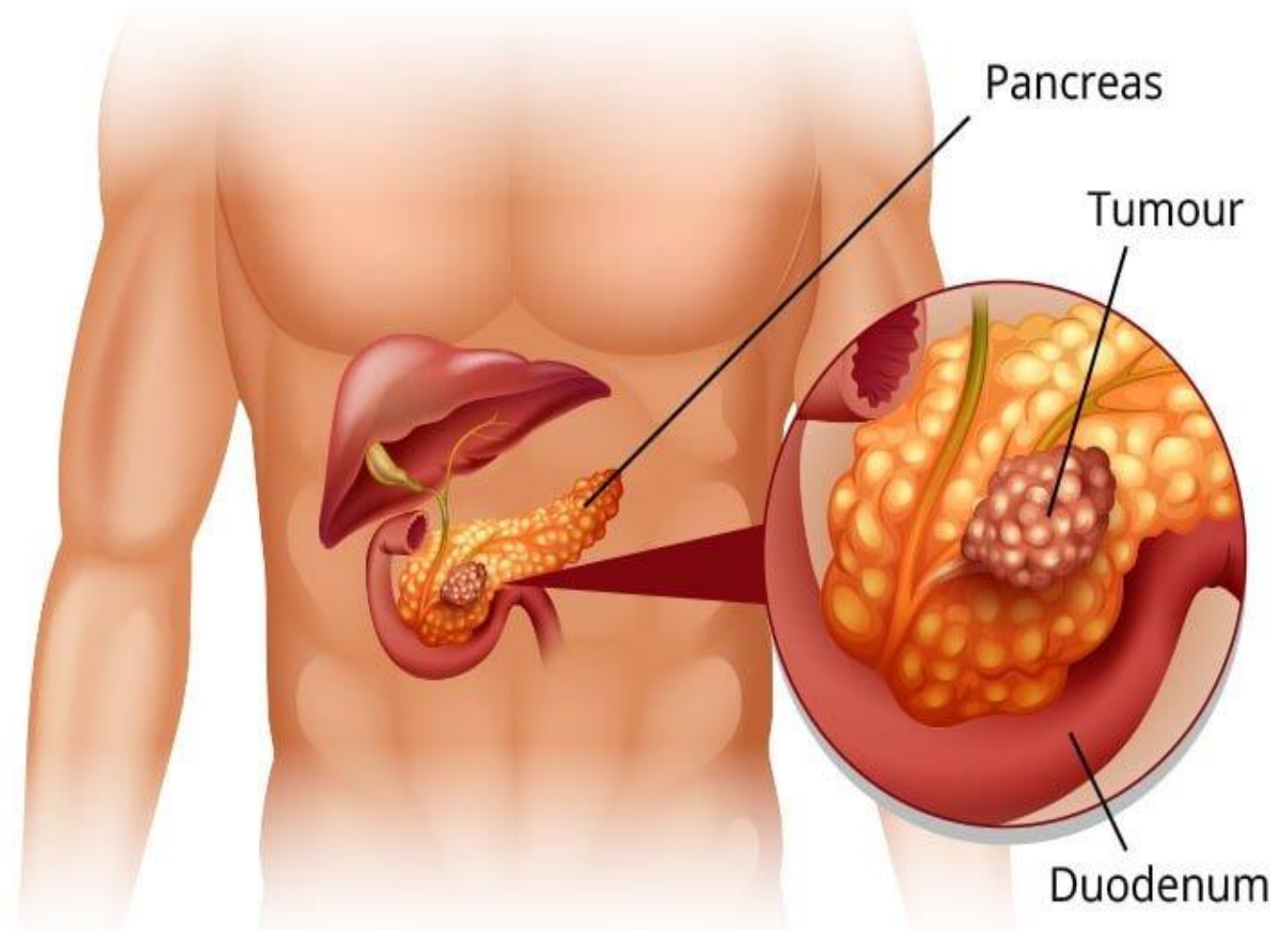
© 2015 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



(Springett et al., 2015)

Tocotrienols & Pancreatic Cancer

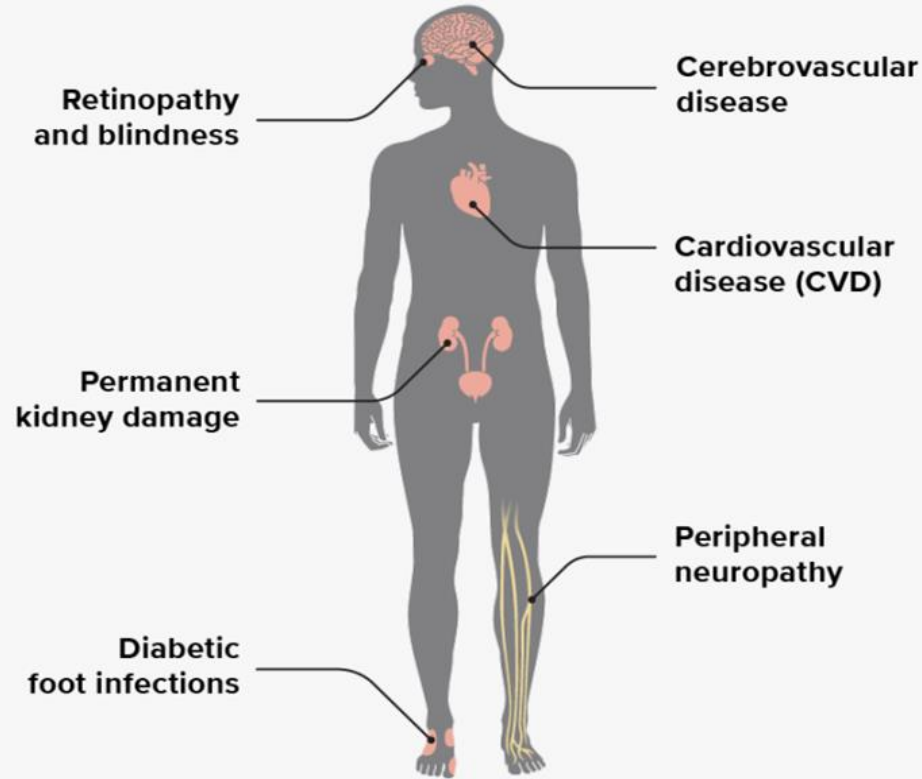
- Supplemented in pre-surgical patients
- 200 to 3200 mg of tocotrienols per day was well tolerated
- Significantly induced cell death in pancreatic ductal cancer cells



(Springett et al. EBioMedicine., 2015)

Tocotrienols & Type II Diabetes Mellitus

Type 2 Diabetes Mellitus Complications



MEDICALNEWS TODAY

- ❖ TRF reduced serum creatinine in patients with type 2 diabetes
- ❖ May be a useful addition to the current treatment for diabetic nephropathy
- ❖ TRF preventing early diabetic retinopathy progression.
- ❖ T3 reduced lancinating pain in diabetic patients with peripheral neuropathy.

Tan et al., 2018; Nutrients

Ho et al., 2022

The Vitamin E in Neuroprotection Study (VENUS) Investigators, JAMA Neurology. 2018

REGULATIONS ON PALM TOCOTRIENOLS



GRAS Status from FDA for Tocotrienols (April 2010)

Tocotrienol is now intended for use in the following foods:

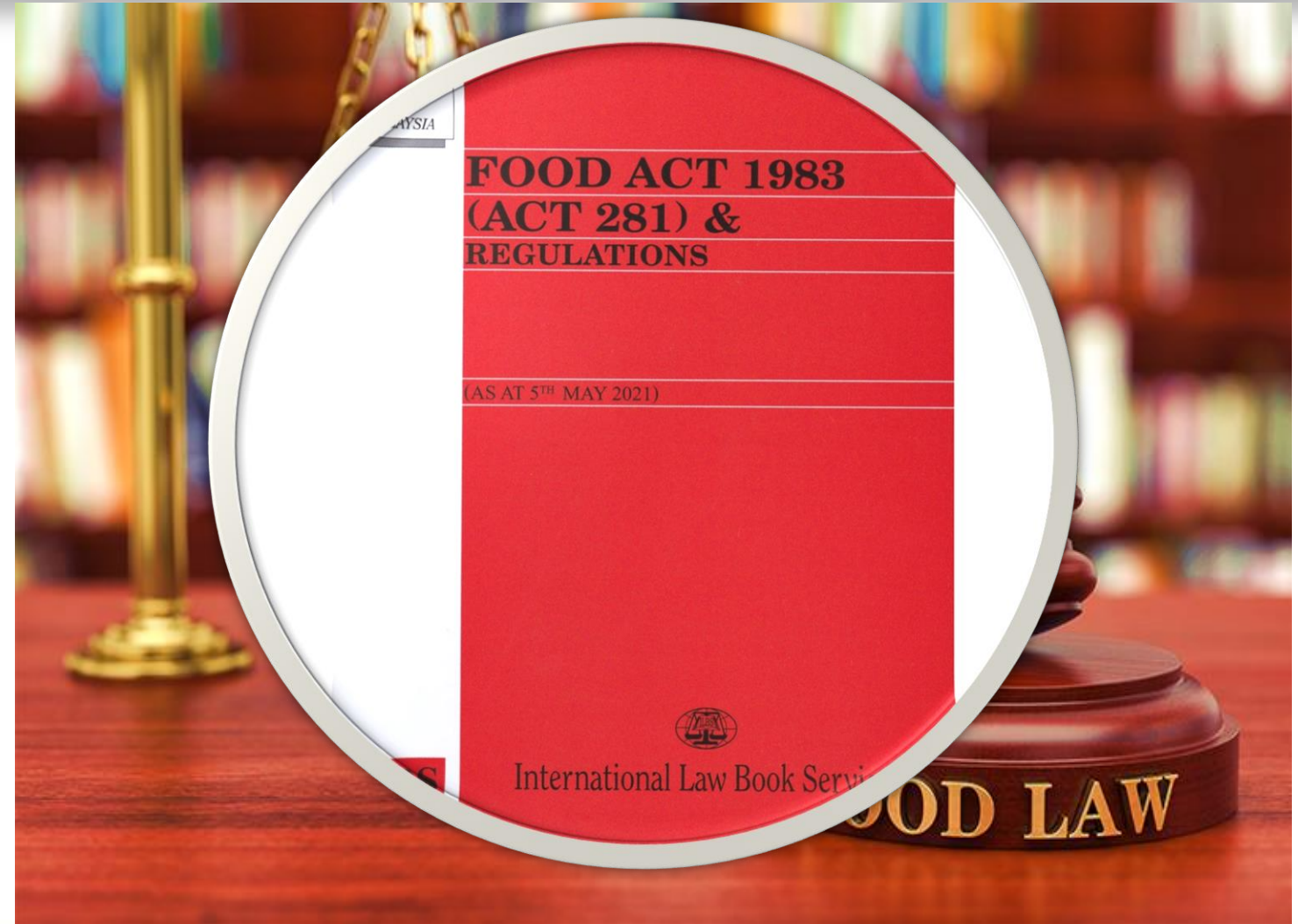
- *Margarines and spreads*
- *Designer fats and oils*
- *Salad dressing and Mayonnaise*
- *Potato chips and salty snacks*
- *Bakery products*
- *Cookies & crackers*
- *Ready To Eat (RTE) cereals, cereal bars, granola bars, protein bars and power bars*
- *Meal replacement and other functional beverage products and mixes*
- *Meatless meat products (soy-based)*





Palm Tocotrienols in the 12th Schedule of the Malaysian Food Act & Regulation 1983 (Act 281)

- Application for Palm Tocotrienols to be registered in the 12th Schedule of the Malaysian Food Act & Regulation has been approved by the Nutrition Expert Working Committee of the Ministry of Health on the 29th of September 2011
- The application has been gazetted in the Malaysian Food Act & Regulation in 2014.



PALM CAROTENOIDS



Palm Carotenes

- Crude palm oil contains 500-700 ppm carotenoids
- richest source of biologically active carotenoids
- 13 types of carotenoids are found in crude palm oil.

- The major ones are:
 - β -carotene
 - α -carotene
 - lycopene
 - phytoene
 - phytofluene



Red Palm Oil

- Red palm oil contains carotenes e.g. α -carotene, β -carotene, lycopene and the same nutrients that give tomatoes, carrots, fruits, vegetables their rich colours.
- Contains 13 other carotenes, tocopherols and tocotrienols, CoQ10, phytosterols, glycolipids.



Red palm oil, because of their purported health benefits have been:

- cold – pressed and bottled for use as cooking oil,
- blended into mayonnaise, salad oil etc
- used in other applications

Health Promoting Properties of Palm Carotenes

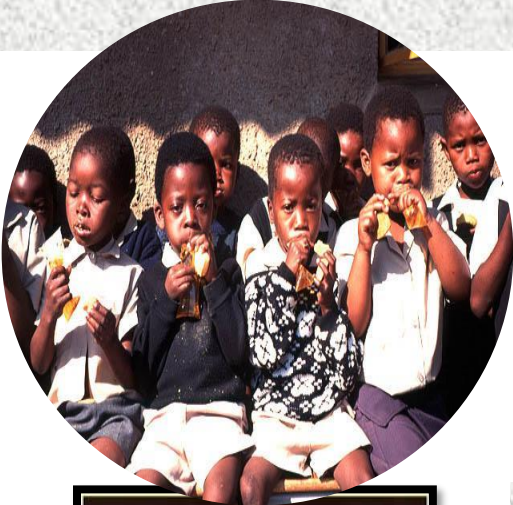
Carotenoids

- Pro-vitamin A activity
- Prevention of cardiovascular diseases
- Immuno-enhancement
- Prevention of macular degeneration
- Decrease risk of cataract formation
- Inhibition of cancer

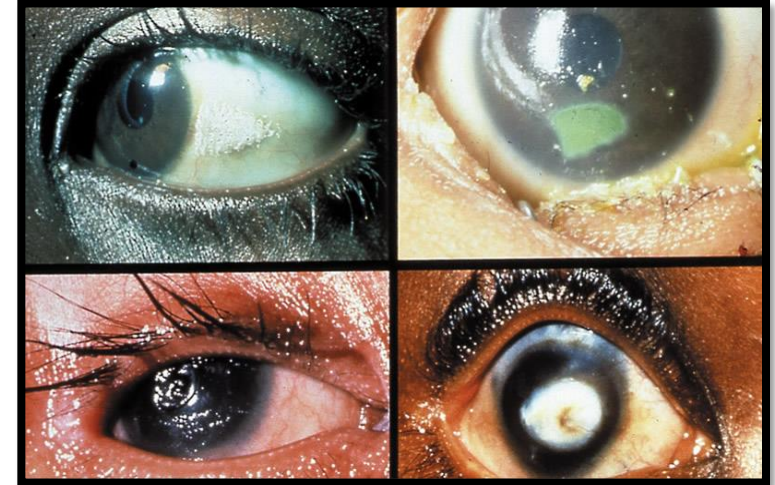


Health Benefits of Palm Carotenes

- Improves vitamin A and anti-oxidative status



Effects of Vitamin A deficiency



- Chronic malabsorption of lipids
- Impaired bile production and release
- Impaired vision/ Night blindness/Bitos's spot
- An estimated 250,000- 500,000 Vitamin A deficiency children become blind every year
- about 50% of them die within 12 months of losing their sight



Red Palm Oil Supplementation in School Children



RPO STUDY - SOUTH AFRICA

- A joint effort by PORIM, South Africa Medical Research Council and Global Palm Sdn. Bhd. (Carotino)
- Red Palm CAROTINO bakery shortening was developed to make Carotene-Rich SMART cookies
- 3 Cookies (12g each) per child each day - sufficient to overcome Vitamin A deficiency.
- Improved overall nutritional status of the child
- Resulted in a higher learning capacity

(AJS Benade, MRC, South Africa)



Source: Unnithan, Carotino Malaysia, 2011

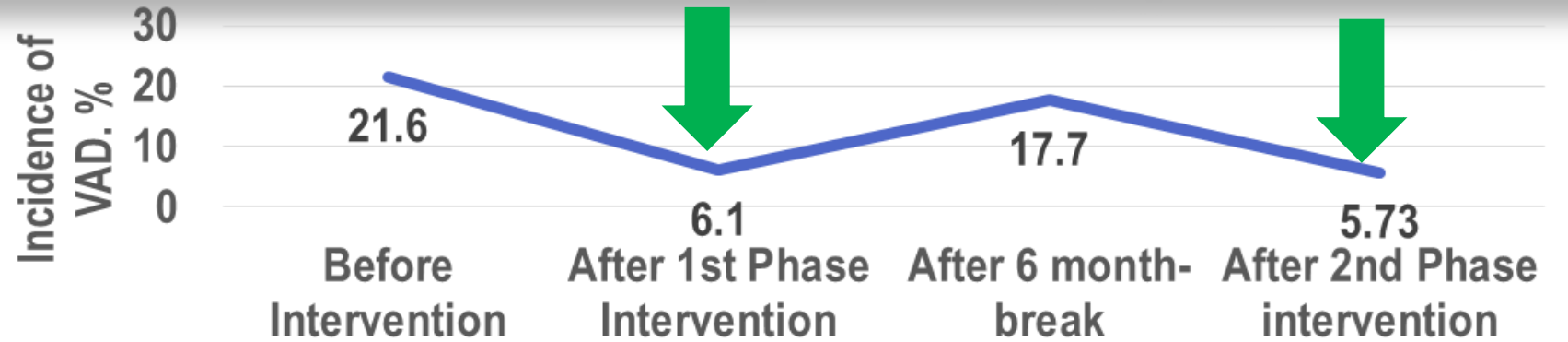


RPO STUDY – GANSU PROVINCE, LANZHOU, CHINA

Red Palm Oil Biscuit



Confirms the effects of red palm oil in reducing %VAD



Incidence of vitamin A deficiency (VAD) before and after the vitamin A intervention

1ST Phase (May – Nov 2015)



2,000 children at schools in Gansu

2nd Phase (Apr – Oct 2016)



The second phase involved 300 children at schools in Gansu

Red Palm Oil biscuit supplementation programme in Malaysian school children with Vitamin A deficiency



Phase 1: Screening

- Vitamin A deficiency = 76.8%
(Confirmed= 20.6%; Suspected= 65.1%).
- Parasitic infection = 48.7%

No of Subjects recruited (n=651)



Ocular Check



Examination with a **portable slit lamp** for signs of **xerophthalmia**



Fundus photography with portable non mydriatic camera

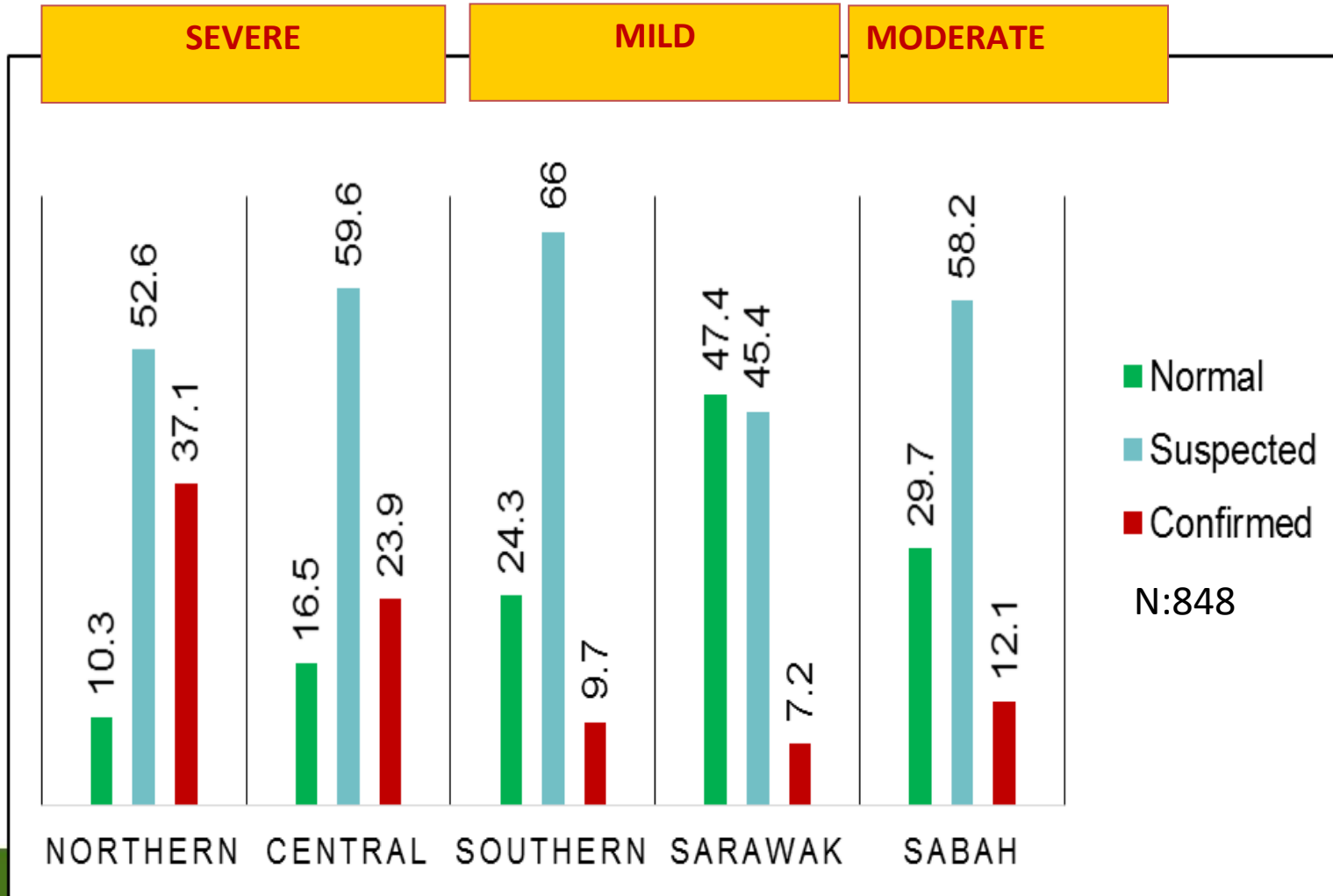


Visual acuity assessment via a **Snellen chart**



Questionnaire on night blindness symptoms

PREVALENCE OF VITAMIN A DEFICIENCY



Classification of vitamin A deficiency

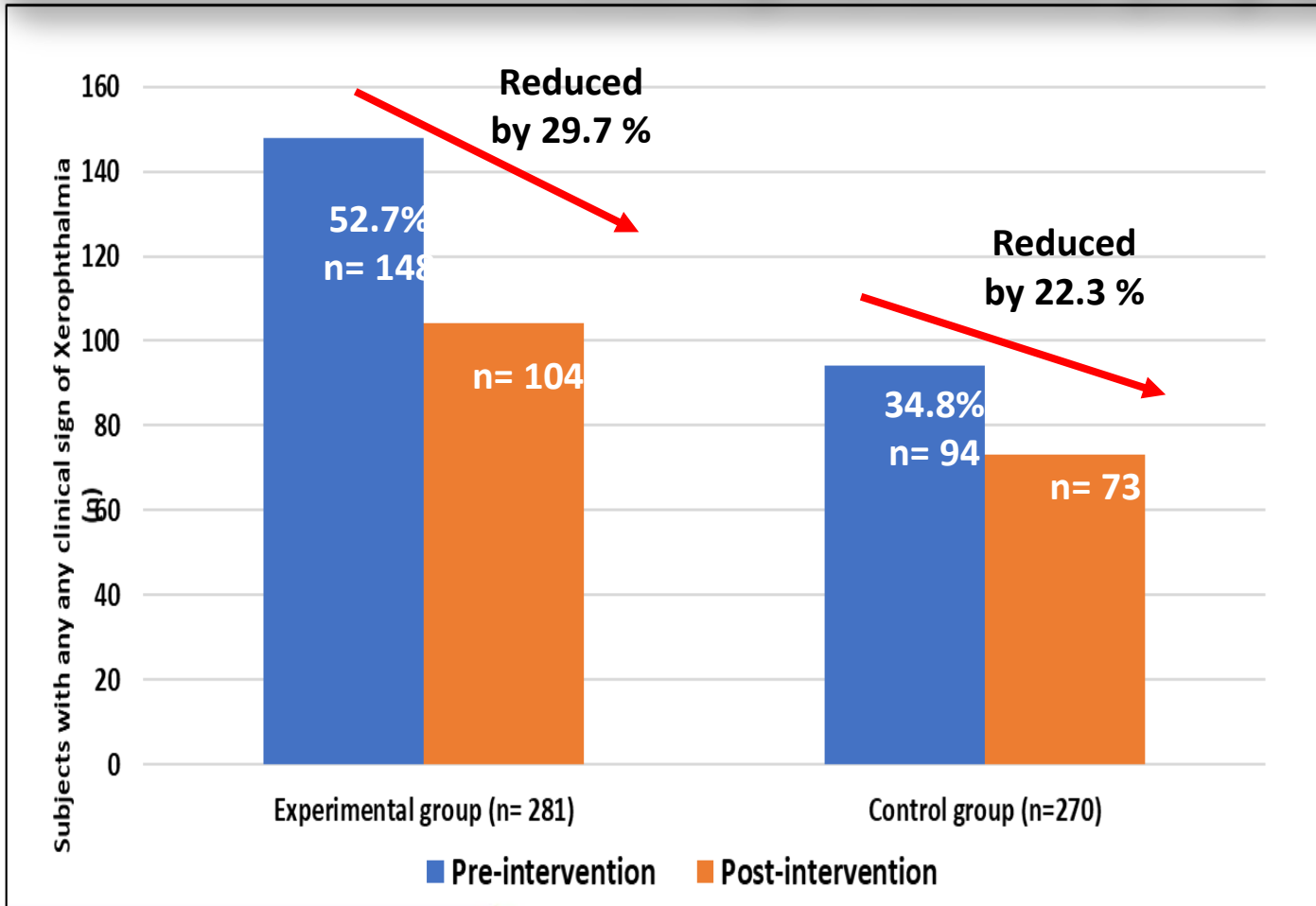
- Confirmed: <0.7 mmol/L
- Suspected: $\geq 0.7 - <1.05$ mmol/L
- Normal: ≥ 1.05 mmol/L

VAD Public Health Problem

- Mild: $\geq 2 - \leq 10\%$
- Moderate: $>10 - <20\%$
- Severe: $\geq 20\%$

WHO. Vitamin and Mineral Nutrition Information System (VMNIS).

Preliminary findings: Changes in Prevalence of Xerophthalmia (Dry Eye Syndrome)

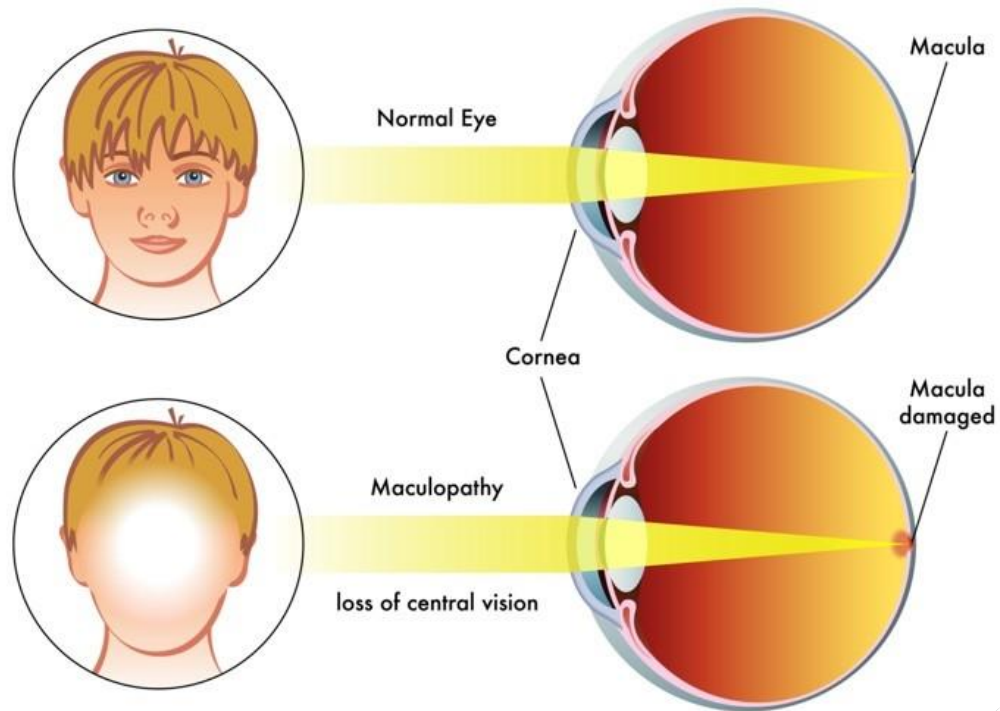


Preliminary findings – higher reduction in xerophthalmia cases in experimental arm as compared to control arm post-intervention.



PALM CAROTENES IN MANAGING AGE-RELATED MACULAR DEGENERATION

Meganathan et al., 2022, ACS Food Science & Technology (Accepted for publication)



HEALTHY EYE CONDITION



EARLY AMD



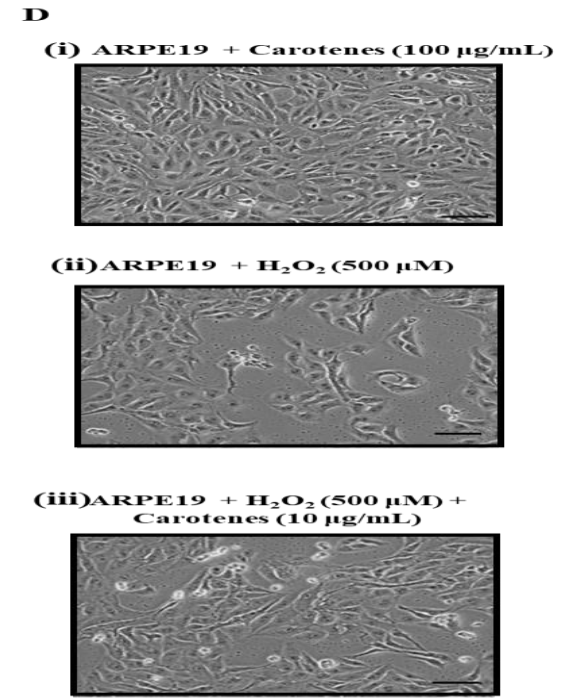
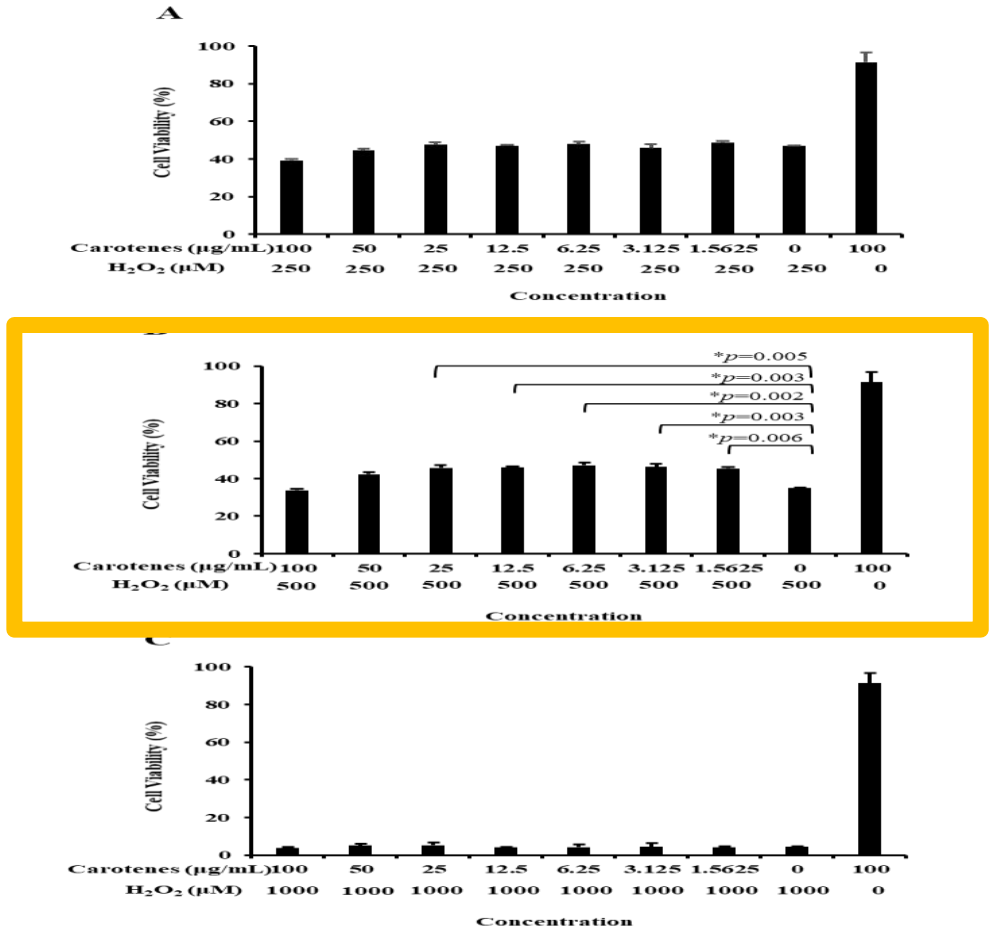
LATE AMD

PALM CAROTENES IN MANAGING AGE-RELATED MACULAR DEGENERATION



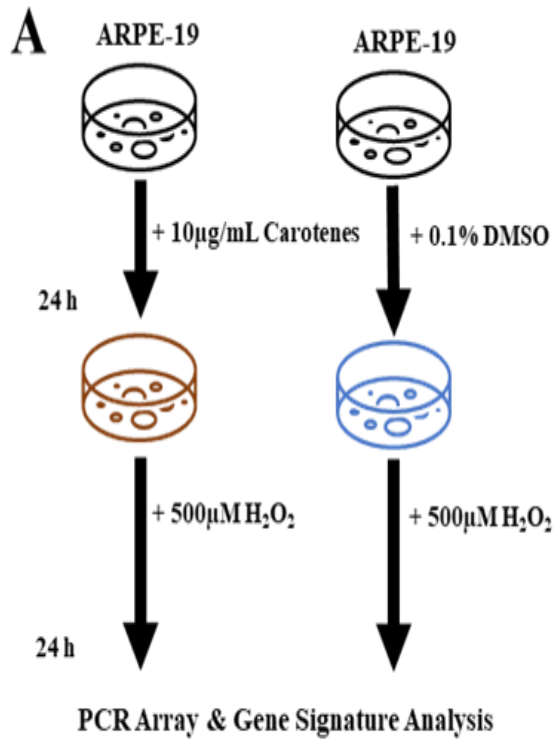
Meganathan et al., 2022, ACS Food Science & Technology (Accepted for publication)

Significant protective effect was observed when carotenes were given to the cells prior to 500 μM H_2O_2 challenge, suggesting carotenes could be a potential protective compound against H_2O_2 challenge, a model for AMD



PALM CAROTENES IN MANAGING AGE-RELATED MACULAR DEGENERATION

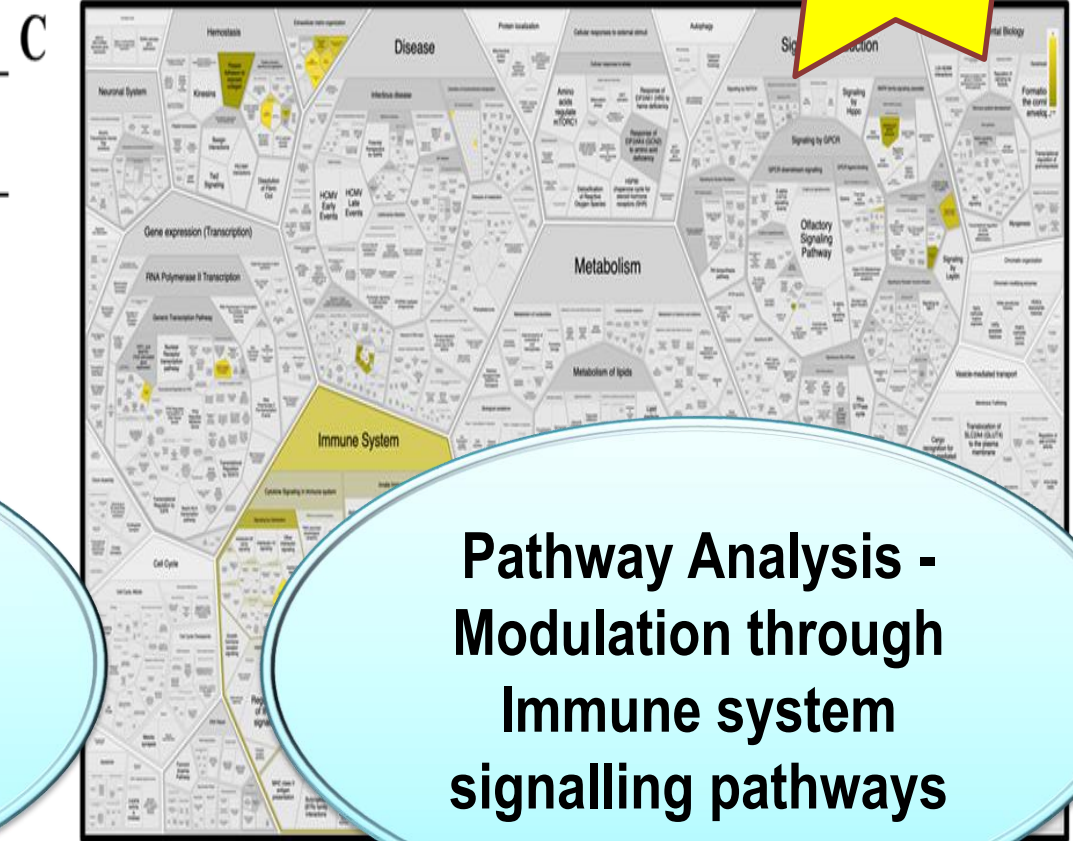
LATEST!



B

Gene	Description	Fold Change	P-value
<i>HMCN1</i>	Hemicentin 1	-3.00	0.000003
<i>FN1</i>	Fibronectin	-2.74	0.001701
<i>VTN</i>	Vitronectin	-2.56	0.019922
<i>C5</i>	Complement component 5	-2.52	0.001589
<i>TIMP3</i>	TIMP metalloproteinase 3	-2.52	0.001380
<i>CCL11</i>	Chemokine (C-C motif) ligand 11	-2.52	0.001380

Genes downregulated by carotenes - indicated potential protection against oxidative stress in AMD.



Meganathan et al., 2022, ACS Food Science & Technology (Accepted for publication)

**OTHER
PHYTONUTRIENTS IN
PALM OIL**



OTHER PHYTONUTRIENTS IN PALM OIL



Co-Enzyme Q10

Natural coenzyme in palm oil – also known as ubiquinone

Benefits:

Powerful antioxidant and free radical scavenger.
Vital role in the mitochondrial electron transport chain
Exhibit membrane stabilizing properties.
Treatment for cardiovascular ailments
Anticancer effects

Squalene

A valuable triterpene - found in shark liver oil

It is present in trace amounts in palm oil

Benefits:

Oxygen transmitter
Cardiovascular Benefits
Anti-cancer effects

Phytosterols

Major Phytosterols
sitosterol
campesterol
stigmasterol

Benefits :

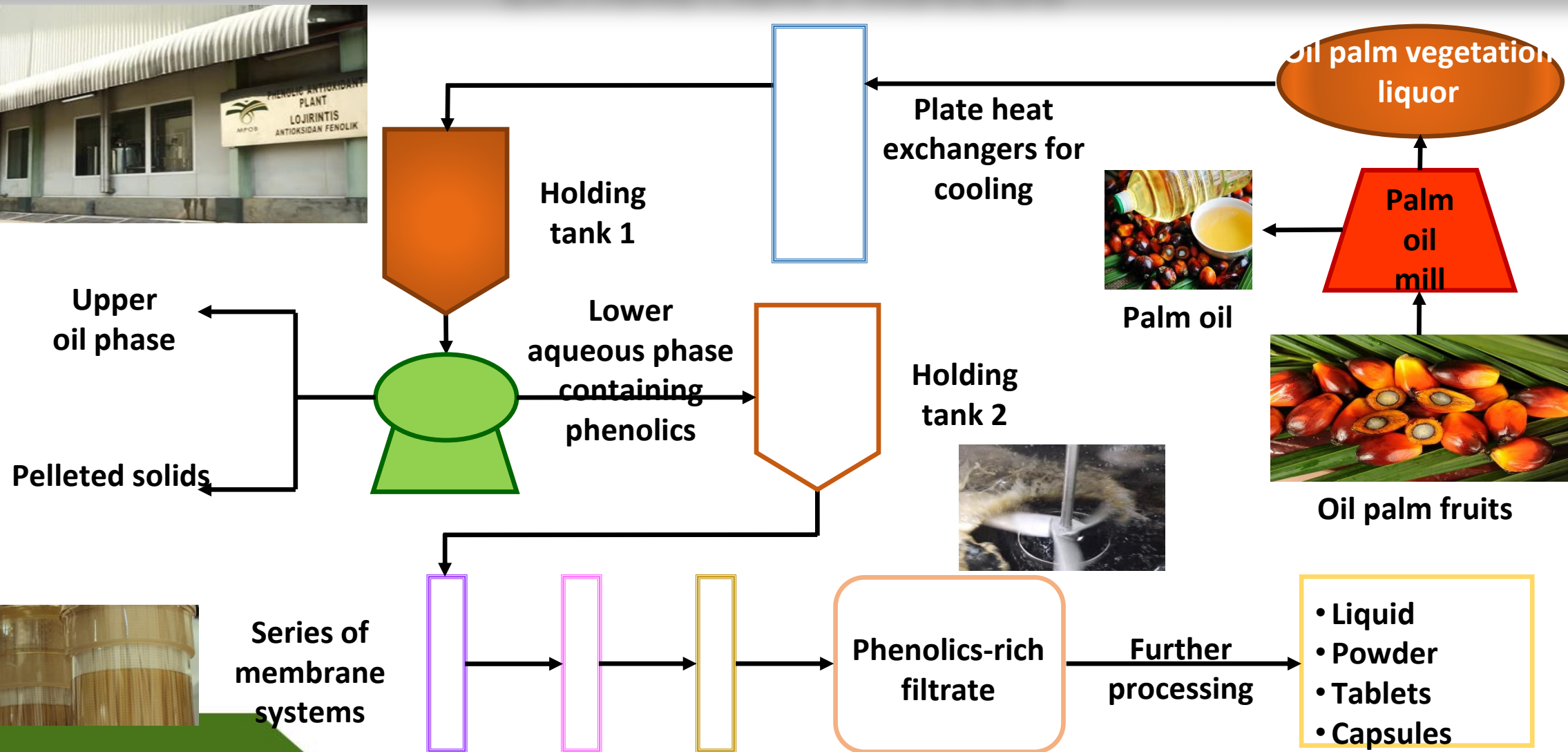
- Cholesterol lowering effect
- Inhibition of cholesterol absorption

Anticancer properties
Immune functions

WATER SOLUBLE PALM FRUIT EXTRACT



WATER-SOLUBLE PALM FRUIT EXTRACT (WSPFE): EXTRACTION PROCESS



(Sambanthamurthi *et al.*, 2008; Leow *et al.*, 2021)



WATER-SOLUBLE PALM FRUIT EXTRACT (WSPFE): PRODUCT COMPOSITION

FOOD ANTIOXIDANT
APPLICATIONS

COSMECEUTICAL
APPLICATIONS

ANTIOXIDANT

SAFETY AND
TOXICOLOGY

CARDIOPROTECTION

RADIATION
PROTECTION

**WATER-SOLUBLE
PALM FRUIT EXTRACT
(WSPFE)**



ANTI-DIABETES

ANTI-MICROBIAL

NEUROPROTECTION

PROTECTION
AGAINST
MITOCHONDRIAL
DYSFUNCTION

PROTECTION
AGAINST MACULAR
DEGENERATION

ANTI-AGEING

GUT HEALTH

ANTI-CANCER

TAKE HOME MESSAGES

- ❖ **Palm-Tocotrienols** and **Palm Carotenes** are natural, safe nutraceutical / bio components of palm oil bestowed with a bouquet of health promoting effects
- ❖ Their **health benefits** of are **scientifically evaluated** and documented for their effects on **combating Non-Communicable Diseases**
- ❖ **Palm-Phytonutrient** research has greatly evolved from **bench**
 - ❑ to **bed-side** as potential nutraceutical products and
 - ❑ to the **plate** as functional food
- ❖ **Bio-Components** of Palm Oil – Remains to be further explored



There is certainly more to come !

See You at



PIPOC 2023

MPOB INTERNATIONAL PALM OIL CONGRESS AND EXHIBITION

**7-9
NOVEMBER**

**KUALA LUMPUR CONVENTION CENTRE,
KUALA LUMPUR, MALAYSIA**



DR KANGA RANI SELVADURAY
Malaysian Palm Oil Board
E-mail: krani@mpob.gov.my
Website: www.mpob.gov.my

Malaysian Palm Oil Board (MPOB)
6 Persiaran Institusi
Bandar Baru Bangi
43000 Kajang
Selangor MALAYSIA



**THE TRANSFORMATIVE
POWER OF OIL PALM**



*MUCHAS
GRACIAS*

*THANK
YOU*

*TERIMA
KASIH*

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