

# Tocomin SupraBio™: Hair loss prevention and beyond

NUTRACEUTICALS

## INTRODUCTION

Vitamin E consists of eight similar compounds – four tocotrienols and four tocopherols. Whilst tocopherols had been intensively studied for their health benefits, many unique benefits of tocotrienols are only beginning to be brought to light by recent research. These novel health benefits include:

- A. Hair loss prevention;
- B. Potent antioxidant;
- C. Skin protection;
- D. Cardiovascular protection;
- E. Neuroprotection;
- F. Anticancer effects.

A potential impediment to the widespread use of tocotrienols or any other fat-soluble nutrient as a dietary supplement lies in poor and unpredictable oral absorption. A special self-emulsifying formula of tocotrienols (Tocomin® SupraBio™) has been developed to ensure reliable and increased oral absorption of tocotrienols.

## A. HAIR LOSS PREVENTION

Alopecia or hair loss is a common problem in males and females regardless of their age. Whilst a common problem not usually associated with physical illness, it can cause significant psychological effects such as diminished self-esteem, emotional distress, embarrassment and social inadequacy (1). Hair loss can be due to genetic factors, aging, stress, mechanical damage to scalp and hair, skin infections, diseases that affect the body generally – e.g. thyroid disease – and use of certain medications such as anti-cancer drugs.

Many attempts at classifying hair loss have resulted in complex and rather impractical classifications. Currently the widely accepted one is as follow:

- Androgenetic alopecia – also known as androgenic alopecia or male and female pattern baldness;
- Alopecia areata – also known as spot baldness;
- Telogen effluvium – shedding or thinning of hair.

Androgenetic alopecia is the most common cause of hair loss, affecting about 50% of men and women older than 40 years of age (2). Androgenetic alopecia is hereditary thinning of the hair induced by androgens (male hormones) in susceptible men and women. It usually begins between the age of 12 and 40 years old and is generally caused by three interdependent factors: male hormone dihydrotestosterone (DHT), genetic disposition and advancing age (2). DHT, a potent metabolite of the androgen testosterone, causes gradual and progressive shrinkage in hair follicles that leads to production of smaller and finer hairs. DHT also shortens the anagen growth phase of the hair follicle so the hair is shorter when it stops growing.

The treatment of hair loss ranges from the common sense to the esoteric which included almost religious like rituals. However, the commonly accepted ones include reassurance, hair prostheses, surgery and topical/oral medications (3,4). The most common pharmacological management of androgenetic alopecia is topical minoxidil and oral finasteride. Clinical trials have shown that 2% minoxidil applied topically to the scalp could stimulate hair growth in some men and women while higher percentage of 5% showed increased therapeutic efficacy (5). However, the main problem with topical minoxidil therapy is patient compliance as continued use is required to maintain hair growth (6,7). On the other hand, oral finasteride is associated with significant adverse effects such as

## SHARON LING

Carotech Ltd  
48, Hale Road  
Wendover HP22 6NF, UK  
Tel +44 1296 623 214  
sling@carotech.net



published by **B5** srl  
Via Cesare da Sesto, 10  
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Tel. 0039 02 83241119  
Fax 0039 02 8376457  
www.b5srl.com

decreased sexual drive, impotence and ejaculation disorders (8). Moreover, finasteride is not encouraged to use in female patients of childbearing age as it may cause abnormalities in male fetuses. Other drugs that have been used include exogenous estrogen, spironolactone and topical tretinoin.

Deficiency in oxygen supply as a cause of male pattern baldness was investigated by GOLDMAN *et al* (9). The results showed that penetration of oxygen was lower in bald frontal scalp than in hair bearing temporal scalp area and hence indicated that good blood supply to the scalp was essential to maintain normal cycle of hair growth.

### Randomized Placebo Controlled Clinical Trial of Tocomin SupraBio™ for Androgenetic Alopecia

Tocomin® SupraBio™ ensures approximately 300% increase in oral absorption of tocotrienols via a special self-emulsifying formulation (10). It is an advanced formulation of Tocomin®, a natural tocotrienol complex concentrated from virgin crude palm oil through a patented mild extraction process that ensures maximum preservation of phytonutrients. Tocomin® SupraBio™ is the most bioavailable tocotrienol complex available in the market.

Tocotrienols are fat-soluble vitamins related to tocopherols – the common vitamin E. Whilst tocopherols occur naturally in common vegetable oils; tocotrienols are concentrated in cereal grains, e.g. oat, barley, rice bran, with virgin crude palm oil being the richest source. Tocotrienols differ from tocopherols by having an unsaturated side tail that results in significantly different biological activities. Recent new studies brought to light many unique benefits of tocotrienols not shared by tocopherols.

Beneficial effects of vitamin E in hair care products have been reported (11) although lacking formal investigation. We conducted a double blind placebo-controlled clinical trial on volunteers with androgenetic alopecia (male pattern baldness) to evaluate the efficacy of palm tocotrienol complex oral supplementation.

### Study Design

An 8-month study was performed at the School of Pharmaceutical Sciences, University of Science Malaysia with 28 volunteers aged 18 to 59 years with mild to moderately severe hair loss. The volunteers had hair loss problem for approximately 2-5 years and most of them had hair loss pattern scale III according to the Norwood/Hamilton classification scale. They were instructed not to alter their hairstyle, hair care products (shampoo, conditioners, etc) or dye their hair during the study period.

The volunteers were randomly selected to receive palm tocotrienol complex (Tocomin® SupraBio™, Carotech Inc.) or the placebo – soft gelatin capsule containing 600 mg soya bean oil – for 8 months. The total daily intake of tocotrienols for each volunteer in the treatment group was 100 mg.

Hair counts and weight of hair in pre-selected evaluation area were measured before and every month after initiation of the study.

### Study Results

Volunteers supplemented with Tocomin® SupraBio™ showed statistically significant higher hair counts post-

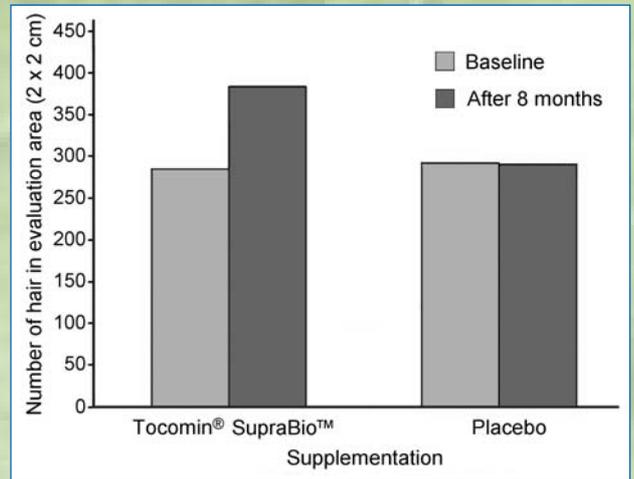


Figure 1 – Number of hair at baseline and 8 months after Tocomin SupraBio™ and placebo supplementation

supplementation ( $p < 0.01$ ). An average of 41.8% increase in the number of hair was observed after 8 months (Figure 1), whereby

- 8 volunteers (40.0%) showed >50% hair growth
- 1 volunteer (5.0%) showed 25-50% hair growth
- 9 volunteers (45.0%) showed 10-25% hair growth
- 1 volunteer (5.0%) showed <10% hair growth

Only one volunteer in the Tocomin® SupraBio™ supplemented group had a slight decrease in the number of hairs (5.0%).

Figure 2 shows one of the volunteers before taking Tocomin® SupraBio™ while Figure 3 shows the same volunteer after 8-month Tocomin® SupraBio™ supplementation.

In contrast, only 1 (12.5%) volunteer receiving placebo showed more than 20% increase in hair count while 3 volunteers (37.5%) showed negligible increase. 4 (50.0%) volunteers even had a decrease in the number of hairs. No statistically significant difference ( $p > 0.05$ ) in the number of hairs was detected between baseline and post-



Figure 2



Figure 3

supplementation, thus indicating that the placebo effect did not occur during this study and the increase in the number of hair observed in the volunteers receiving Tocomin® SupraBio™ could be ascribed to tocotrienols supplementation. Moreover, statistically significant difference ( $p < 0.01$ ) was detected in the percentage of change in the number of hair between tocotrienol supplemented group and placebo group.

In view of the proven efficacy of Tocomin® SupraBio™ in promoting hair growth in men and women suffering from androgenetic alopecia, the United States Patent and Trademark Office has granted a patent for Tocomin® SupraBio™ as a hair growth formulation (12).

## B. POTENT ANTIOXIDANT

Free radicals are highly reactive molecules that can damage biological molecules via oxidative stress. It has been implicated in many diseases and aging processes including atherosclerosis, stroke, neurodegenerative diseases, cancer, and premature aging. Alpha-Tocotrienol is 40-60 times more potent than alpha-tocopherol as an antioxidant (13). The higher antioxidant potency of  $\alpha$ -tocotrienol is due to higher recycling efficiency from chromanoxyl radicals, more uniform distribution in cell membrane and better interaction with lipid radicals. The net result is that tocotrienols are more efficient than tocopherols in scavenging and quenching the free radicals.

Researchers in Japan found that tocotrienols reduces oxidative damages and extends the mean life span of *C. elegans*, a long worm whose entire collection of genes has been decoded (14). Conversely, tocopherols did not show similar benefit. This further illustrates the efficacy of tocotrienols *in vivo* (in real life) and suggests potential anti-aging properties.

## C. SKIN PROTECTION

The antioxidant, anti-aging and moisturizing properties of vitamin E have made it a popular ingredient in cosmetic and personal care products. Tocotrienol has been shown to preferentially accumulate in the uppermost layer of the skin and is distributed uniformly on the skin surface (15). Applied topically, tocotrienols is absorbed and penetrates rapidly through the skin. The polyunsaturated side chain of tocotrienols allows them to move more efficiently across the cell membrane as compared to tocopherols. Tocotrienol

prevented skin aging and oxidation of the skin collagen matrix in animal studies (16). In addition, studies have shown that tocotrienol augmented the efficacy of sunscreen and reduces severity of sunburn (17).

Dr. NICHOLAS PERRICONE, Dermatologist at the Yale Medical Center, advocated the use of tocotrienols in cream to promote skin health and prevent skin aging in his NY Times' bestseller "The Wrinkle Cure".

## D. CARDIOVASCULAR PROTECTION

Vitamin E has been identified as a potential cardioprotective agent. However, several recent large-scale clinical trials (GISSI Prevention Trial, HOPE & HOPE-TOO Trial, Women's Health Study, Physician's Health Study II) reported that Vitamin E did not protect against cardiovascular diseases (18-21). On closer examination, all the studies used alpha-tocopherol and in some cases, the synthetic form. Synthetic alpha-tocopherol is chemically produced from petroleum byproducts. The synthetic form is a mixture of eight stereoisomers referred to as all-rac-alpha-tocopherol. Only one of these stereoisomers is bio-identical to natural alpha tocopherol (RRR-alpha-tocopherol). Synthetic alpha-tocopherol has poor bioavailability compared to the natural form. Taking an identical dosage, the concentration of synthetic alpha-tocopherol in blood and organ is only half of those of the natural form (22).

Even natural alpha-tocopherol may not be as "natural" as one would have thought since natural mixed tocopherols is converted to single alpha-tocopherol by a chemical process called methylation. In addition, taking too much alpha-tocopherol depletes the body of other Vitamin E isomers, especially gamma-tocopherol (23).

In recent years the unique cardiovascular health benefits of tocotrienols not shared by tocopherols were revealed by new research. Researchers at the School of Medicine, University of Connecticut, used various isomers of tocotrienols (Tocomin®, Carotech Inc.) to study the effects and mechanism of tocotrienols' cardioprotective function especially on their ability to improve post-ischemic ventricular function and reduce myocardial infarct size in rats. The results showed that all forms of tocotrienols – Tocomin® palm tocotrienol complex and individual tocotrienol isomers – provided significant cardioprotection. Gamma-tocotrienol was found to be the most cardioprotective isomer (24).

Tocotrienols have shown promising and unique cardioprotective properties including lowering blood cholesterol, reversing atherosclerosis, lowering blood pressure and reducing arterial stiffness.

## Cholesterol Lowering

Cholesterols are vital compounds in all animal cells and physiologically important in cell membrane function. The modern western diet however, exposes us to excessive levels of cholesterols. Coupled with genetic factors, the resultant high blood cholesterol concentration is associated with cardiovascular diseases (25). Tocotrienols inhibit cholesterol biosynthesis by inhibiting HMG-CoA reductase, the same enzyme inhibited by statins (26,27). Both animal and human studies have demonstrated the cholesterol lowering action of tocotrienols. Patients having received 100-200 mg of tocotrienols per day for 4-10 weeks had a 8-25% LDL-cholesterol reduction (28-30). Tocotrienol when taken together with lovastatin (cholesterol lowering drug) showed greater cholesterol reduction as compared to lovastatin alone (31).

In contrast, tocopherols do not possess cholesterol lowering activity. Furthermore, high concentration of alpha-tocopherol (above 30% ratio) tend to attenuate the cholesterol lowering action of tocotrienols (32).

## Reversing Atherosclerosis

Atherosclerosis is a chronic degenerative disease mainly involving arteries. Many drugs can retard the disease process but few can claim objective reversal of atherosclerosis. A double blind placebo controlled human study conducted by the Kenneth Jordan Heart Foundation and University of Elmhurst showed tocotrienols reverse atherosclerosis (33). In this study, patients with carotid stenoses (narrowing of the main artery supplying the brain) were supplemented with 240 mg/day of palm tocotrienol complex for 6 months. In the tocotrienol-supplemented group, 92% of the patient showed regression of atherosclerotic plaque or remain unchanged. In contrast, none of the patients receiving placebo showed atherosclerotic regression whilst 40% showed progressive disease. Tocotrienol is the first natural compound ever to reverse atherosclerosis in human. Its role in preventing diseases such as heart attack and stroke deserve more intensive investigation.

## Blood Pressure Lowering

High blood pressure is a complex multi-factorial disease that is a major modifiable risk factor of cardiovascular diseases. Although many effective anti-

hypertensive medicines are known, these are not without their side effects. Gamma-tocotrienol, a natural compound significantly reduced systolic blood pressure in rats (34). Similar effect was confirmed in recent human study. Patients supplemented with Tocomin<sup>®</sup> SupraBio<sup>™</sup> (Carotech Inc.) for 2 months resulted in significant reduction in aortic systolic blood pressure (35).

### Reducing Arterial Stiffness

A recent human study looked into arterial stiffness, a risk factor of cardiovascular events. Data from this randomized controlled clinical trial demonstrated that Tocomin<sup>®</sup> SupraBio<sup>™</sup> (Carotech Inc.) reduces arterial stiffness in healthy adults after 2 months of oral supplementation (36). As arterial stiffness is an independent risk factor of cardiovascular diseases, it is conceivable that improvement in arterial compliance may reduce the risk of contracting these diseases.

## E. NEUROPROTECTION – PROTECTION AGAINST STROKE-INDUCED INJURIES

Deficiency of vitamin E is a cause of neurological dysfunction. The brain is highly susceptible to oxidative damage due to its high oxygen consumption. Furthermore, the high lipid content of the brain makes it susceptible to lipid peroxidation in an antioxidant poor environment. 40-60 times more potent an antioxidant, tocotrienols are more effective than tocopherols in protecting brain cells from oxidative damage (37).

Tocotrienols exert potent neuroprotective property as proven in a number of NIH-sponsored studies (38-40). *In vitro* study showed that alpha-tocotrienol, not alpha-tocopherol, prevented neuron's death at extremely low concentration (nanomolar, 10<sup>-9</sup>). Tocotrienol-treated neurons maintained healthy growth and motility even in the presence of excess neurotoxic agent. The neuroprotective property seen at such low concentration of tocotrienol is independent of its antioxidant activity, as tocotrienols do not exhibit antioxidant properties at nanomolar concentrations. Tocotrienol only begins to show its antioxidant effects at micromolar concentrations (41).

The same researchers at the Ohio State Medical Center went on to

demonstrate that oral tocotrienols (Tocomin<sup>®</sup>, Carotech Inc.) reaches rats' brain in concentration that protected against stroke. There is reduced volume of cerebral infarct in tocotrienol-supplemented rats compared with matched controls (40). A further study showed that Tocomin<sup>®</sup> SupraBio<sup>™</sup> (Carotech Inc.) supplementation in healthy women achieved plasma levels of tocotrienols 12 to 30 times more than the required neuroprotective concentration (42).

A randomized double blind placebo controlled human study, is on course to recruit some 400 participants over the next few years to study the neuroprotective effects of tocotrienols by looking at white matter changes using magnetic resonance imaging (MRI) (43). This allows the researchers to look into early changes of the brain without having to wait for an overt clinical endpoint such as a clinical stroke. Tocomin<sup>®</sup> SupraBio<sup>™</sup> (Carotech Inc.) is used in the trial. The results of this clinical trial will shed more light on the benefits of palm tocotrienol complex in both acute neurological disorders, e.g. stroke, and chronic neurodegenerative disorders, e.g. Alzheimer's disease, Parkinson's disease.

## F. ANTICANCER

One in 3 of us will get cancer statistically. Despite billion of dollars of research into treatment, cancer remains a major cause of morbidity and mortality in a western society. Palm tocotrienol complex has anticancer properties due to its selective inhibition of cancer cell growth whilst sparing health cells. The



Figure 4

efficacy of tocotrienols in suppressing cancer cell growth has been demonstrated in cancer cells from breast, liver, lung, prostate, skin, colon, cervix, nerve and lymph node (44). In contrast, tocopherols have little or no impact on cancer cells, suggesting a mechanism independent of antioxidant activity.

The anticancer property of palm tocotrienol complex has been researched in depth in breast cancer. *In vitro* studies showed palm tocotrienol complex inhibited breast cancer cells regardless of estrogen-receptor status (45). Gamma-tocotrienol is 3 times more potent than tamoxifen – standard treatment of breast cancer – in inhibiting growth of human breast cancer cells. The inhibitory effect is 45 times more potent when tocotrienol and tamoxifen are used together, suggesting a synergistic mechanism (46).

A 5-year study involving 240 women with early breast cancer – sponsored by Malaysian Palm Oil Board – showed that combination treatment with Tocomin<sup>®</sup> SupraBio<sup>™</sup> (Carotech Inc.) and Tamoxifen resulted in higher survival rate and lower recurrence rate compared to Tamoxifen alone.

Tumour angiogenesis is the growth of new blood vessels to supply nutrients to the tumour, an important factor in tumour growth. It is possible to prevent the tumor from growing and spreading through inhibition of angiogenesis. In fact this is the main mechanism of action of several new, highly effective chemotherapeutic agents. Studies have found that tocotrienols, but not tocopherols, exert anti-angiogenesis activities, with delta-tocotrienol showing the highest activity (47,48).

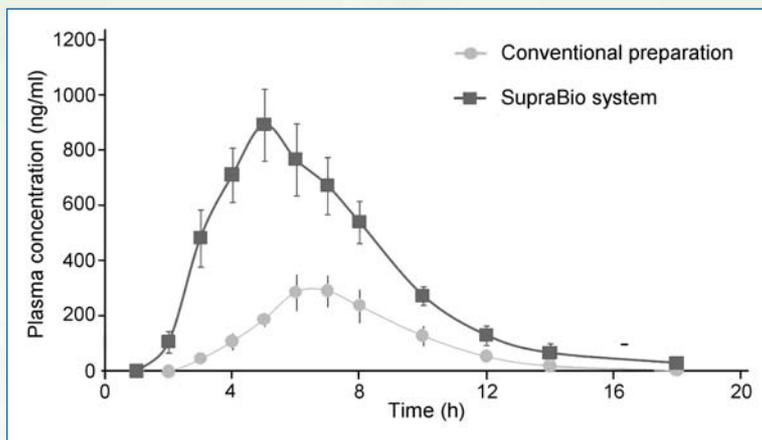


Figure 5 – Mean plasma alpha-tocotrienol versus time curves of the conventional preparation and SupraBio<sup>™</sup> system

## SUPRABIO™: PATENTED BIOENHANCED ORAL DELIVERY SYSTEM

Tocotrienols occur at very low concentration in nature with the highest concentration found in palm oil (Figure 4). Common vegetable oil such as soya bean oil, corn oil, sunflower oil does not contain tocotrienols. Due to their low level, it is practically impossible to attain biologically active concentration of tocotrienols from diet alone. For example, one has to take a cup of palm oil per day to achieve this. Therefore, dietary supplement of tocotrienols is necessary to achieve beneficial levels in the body.

Do not assume everything taken orally will be absorbed! This is true for drugs, natural compounds and even the food we eat. Like all fat-soluble vitamins, tocotrienols are poorly absorbed when taken with empty stomach or fat poor diet (49). The oral absorption of tocotrienols is low and erratic. It is similar to fat absorption, which requires physiologic processing and is highly dependent on bile secretion and emulsification in the small intestine. The efficiency of tocotrienols' absorption also depends on the type and amount of dietary fats present.

A bioenhanced oral delivery system is developed to overcome the poor absorption of tocotrienols. The patented SupraBio™ system is a self-emulsifying delivery system that provides more consistent and enhanced oral absorption of tocotrienols. It contains a mixture of oil and surfactants at optimum ratio that will self-emulsify in the gastrointestinal tract. The emulsion formed undergoes lipolysis to form particles of colloidal dimensions, mimicking the intraluminal processing essential for optimal absorption of tocotrienols. This novel delivery system results in a rapid and consistent absorption of tocotrienols independent of dietary fat or food intake. Clinical study on healthy human volunteers confirmed the efficacy of SupraBio™ system, which increased the rate and extent of tocotrienol absorption by up to 300% (Figure 5) (10).

## CONCLUSION

Although quite a few agents can effectively treat hair loss, most of these are classified as drugs and are not without side effects. Some (e.g. finasteride) can have disastrous consequences if taken in pregnancy. Palm tocotrienol complex is a

natural food supplement with no known side effects at the plasma concentration achieved via oral supplementation. At these levels, it shows very encouraging result in the prevention of hair loss and also exhibits other health benefits including skin protection, cardiovascular protection, neuroprotection and anticancer effects.

Tocomin® SupraBio™ overcome the traditional difficulties of poor oral bioavailability of fat soluble vitamins with a patented self-emulsify advanced formulation which ensures high (up to 300%) and reliable absorption of tocotrienols, allowing one to reap the maximal health benefits of tocotrienols.

For more information, please contact: Carotech, Europe Sales & Marketing Office, info@carotech.net www.carotech.net www.tocotrienol.org

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