AGE-DEFYING EYE SAVIOURS:

A randomized, double blind, placebo controlled, parallel clinical study of **XanMax®**

KATRA PHYTOCHEM

THE LONGEVITY DIVIDEND: AGEING

From the beginning of time, man has tried to understand 'Ageing'. Ageing is defined as predictable progression of events involving evolution, maturation, and declining of living organisms. It is a biological process involving rate or rates of various body functional changes. What we inherit from our ancestors has much influence on how we age, although the environmental and lifestyle factors that we adopt during our life also have a major role to play.[1]

Ageing population is a global challenge in the current century. It has been estimated that by 2050, the global population of people over 60 years of age will be 2.1 billion. The rate of geriatric population is on the rise! [2]

Ageing in human species is not a new phenomenon. During the medieval period between 8th and the 18th century, the average life of man was 25 - 35 years. But over the last 19th, 20th and the current 21st century, there has been a gradual demographic transition in most countries, a transition from high birth rates and high death rates to a state of normal birth rate and lower death rates. This difference contributes to the high elderly population. What we have observed over the years is that we have dramatically reduced early mortality. Further with advanced medications and technology interventions, lifespan over 60 years is easily achieved.[3]

Life satisfaction does not seem to decrease with Ageing despite declining health, finances and poor mobility. Global development programmes for the cause of 'Gerontology Health' is important. With longevity on the rise, development of wellness programs to lead a healthy life during old age is essential. This century will be determined by the concerns of such active and participatory elderly population.

We try our best to effectively use our body parts beyond what we refer to as "Biological Warranty Period" through some healthy lifestyle management.[4] No matter how well we manage, by and large, any of the surgical interventions become a necessity in a man's life during old age. Besides, lifestyle diseases as diabetes, osteoporosis, arthritis, hypertension, lipids imbalances and dementia have caused considerable disturbance in a man's life as he ages. But with advancement in medical sciences, many life saving drugs have quite successfully managed to prolong man's life.

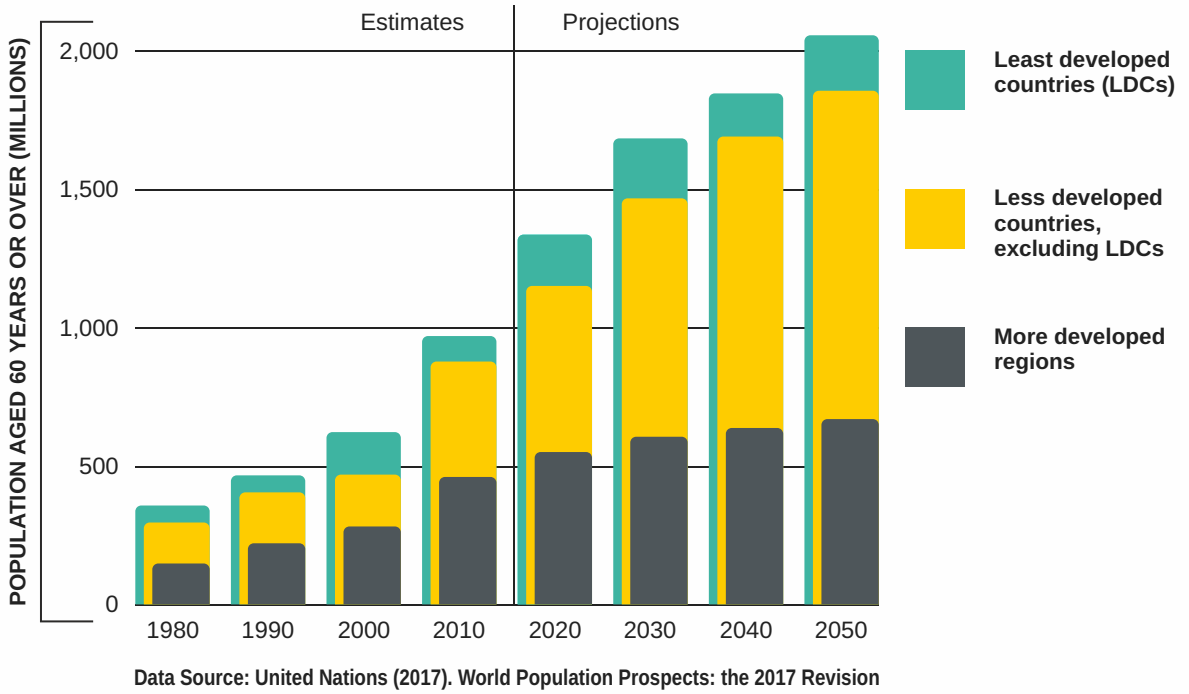
THE LONGEVITY DIVIDEND: AGEING

Lifestyle modification with nutritional supplements adequately laced with anti-ageing phytonutrients, which are natural anti-oxidants and anti-inflammatory ingredients is the key

THE LONGEVITY DIVIDEND: AGEING

Global and Regional Trends of ageing population: World Population Ageing 2017 Highlights by WHO

Number of persons aged 60 years or over by development group,[1] from 1980 to 2050



Data Source: United Nations (2017). World Population Prospects: the 2017 Revision

Reference: World Population Ageing 2017 Highlights, WHO

[1] Following common practice, the "developed regions" include Europe and Northern America plus Australia, New Zealand and Japan, while the "developing regions" include all other parts of the world. The use of these terms in the present report does not imply any judgement as to the current developmental stage of a particular country or region.

THE WINDOWS TO THE SOUL: OUR EYES

A major sensory organ that requires utmost care for a healthy life is the 'eyes'. It is one of the most susceptible organs to light damage, apart from the skin. The human eye is constantly exposed to different wavelengths and intensities of light viz. UV-B (295 - 320 nm), UV-A (320 - 400 nm) and visible light (400 - 700 nm). [Figure 1]

THE WINDOWS TO THE SOUL: OUR EYES

Photo-chemical reaction occurs in the eye only when light is transmitted to a particular ocular tissue and further absorbed by a particular chromophore. Hence exposure to intense light either causes or aggravates photo-oxidation reaction and in-turn age related ocular diseases like AMD, cataract, glaucoma among many others. [5,6]

Ocular damage can occur either through an inflammatory response or a photo-oxidation reaction.[7] Photo-oxidation reaction occurs when a chromophore absorbs light and produces harmful reactive oxygen species viz. superoxide and singlet oxygen that damages the ocular tissues. Additionally, as the eye ages, the protective chromophores become photo-toxic and has the potential to produce singlet oxygen, which are harmful.[8, 9] [Figure 2]. Hence optimal levels of anti-oxidant enzymes viz. Catalase, SOD and anti-oxidants viz. Lutein, Zeaxanthin, Vitamin C, Vitamin E; that serve to protect against photo-toxicity and oxidative stress becomes essential.[10] Lutein and Zeaxanthin are anti-oxidants that accumulate in the retina and lens of the human eye. Commonly known as 'Macular Pigments', these dietary carotenoids cannot be synthesized by mammals and must therefore be obtained from diet.[11]

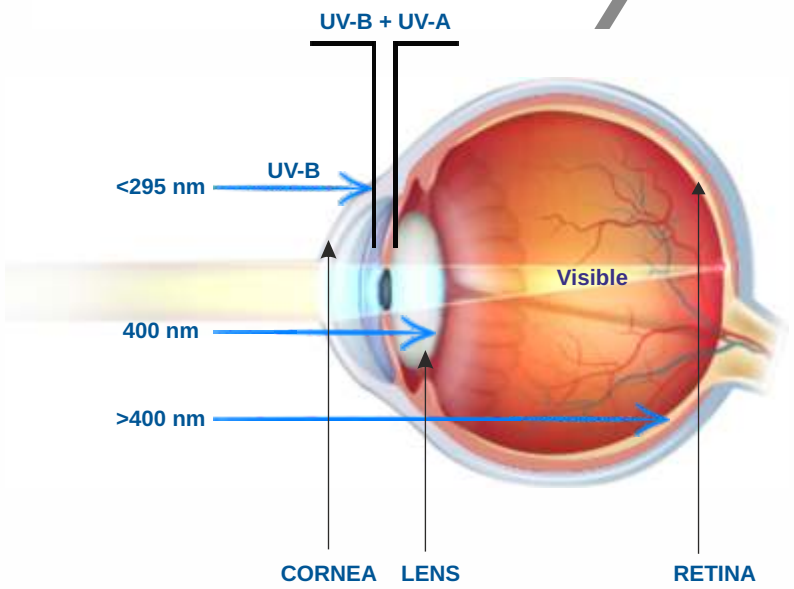


FIGURE 1 : Wavelength transmission of the adult human eye

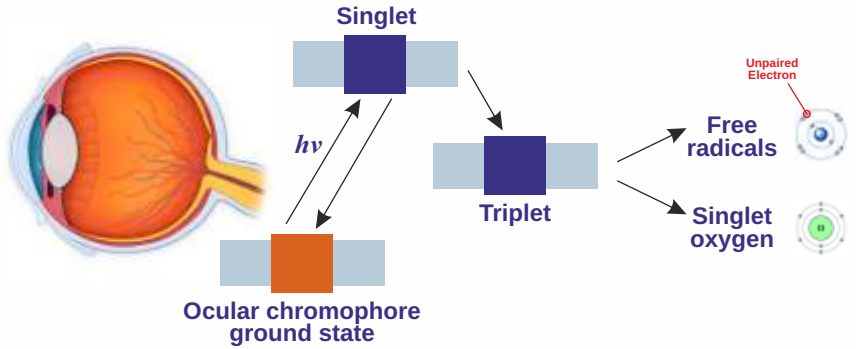
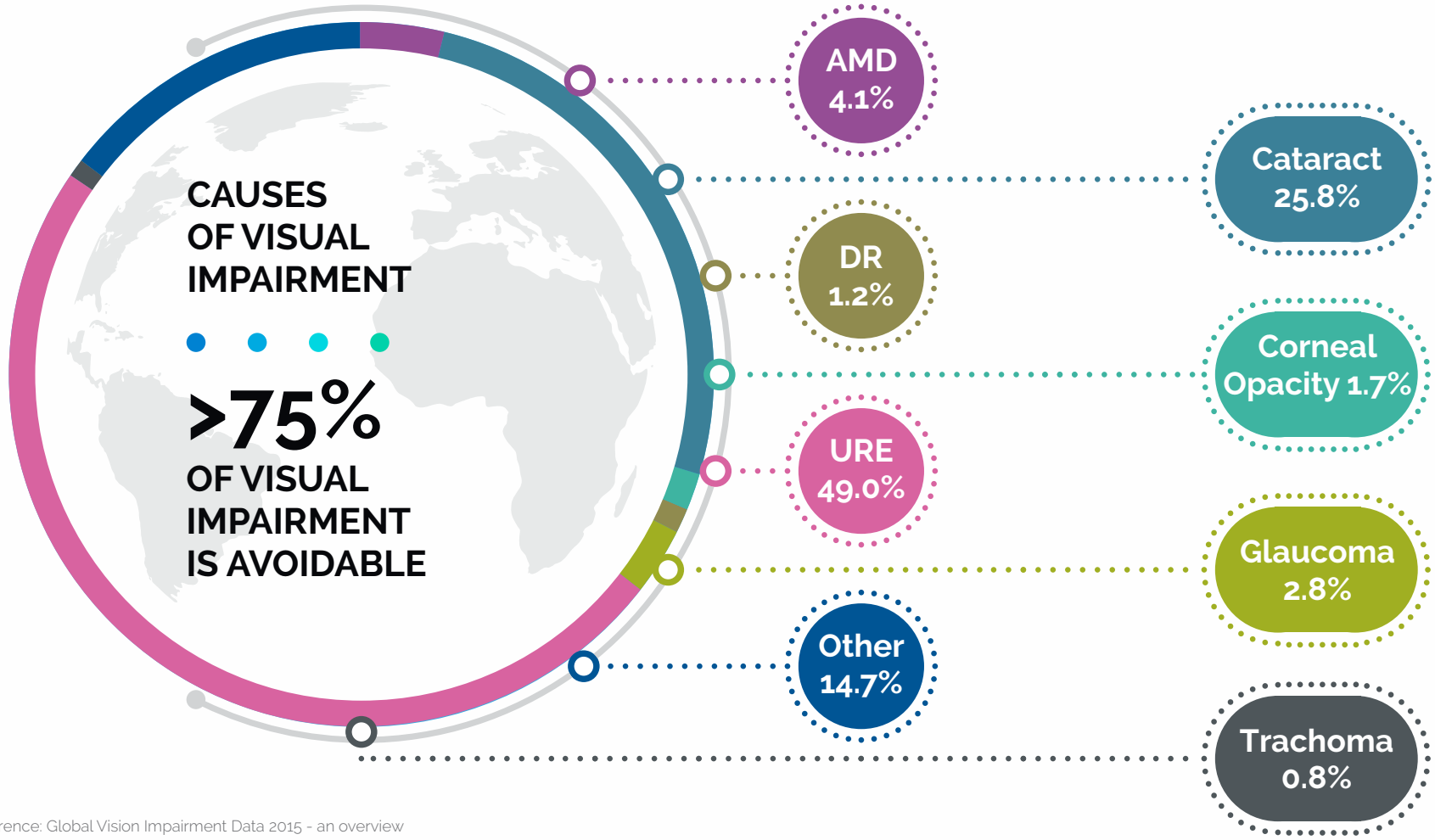


FIGURE 2 : Photo-oxidation

THE WORLD POPULATION IS **7.3 BILLION**



Reference: Global Vision Impairment Data 2015 - an overview

WHERE IT ALL STARTED: THE GOLDEN EGG?

Carotenoid pigments are counted in the many hundreds. They are a class of highly unsaturated potent phytochemicals, fat-soluble yellow to red organic pigments, occurring in plants and animals. It is usually not synthesized by human body and hence we have to obtain it from dietary sources.[12,13]

Carotenoids are nutritionally important for many animals, giving their colour. Generally, animals use these pigments to develop striking red, orange and yellow patches of color that are used as signals of quality to attract mates. It is also noted that many songbirds (like evening grosbeak, yellow warbler, common yellowthroat) deposit lutein obtained from their diet into the growing tissues, to color their feathers.[14]

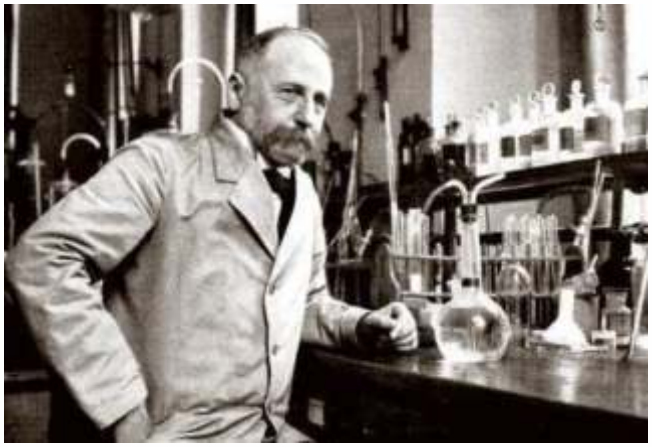


FIGURE 3 : Richard Martin Willstatter in the Laboratory

There are many chemists who have made significant contributions through their research work in the field of Phytochemistry, one such is Nobel Laureate Richard Martin Willstatter (1872-1942) (Figure 3). Though he won the Nobel prize in 1915 for his notable work on chemistry of chlorophyll, he also carried out extensive studies on carotenoids and anthocyanins. Not only did he identify lycopene in tomatoes, he and his assistant Walter Mieg identified and described xanthophylls pigment, Lutein for the first time.

Willstatter and Mieg carried out an examination of the pigment occurring in egg yolk from 6,000 hen's eggs and isolated a pigment belonging to the xanthophyll group, and to which they gave the name 'lutein.' This class of pigments was initially known as "luteines," a name that was eventually superceded by the rubric "carotenoids" or 'macular carotenoids'.[15,16]

WHERE IT ALL STARTED: THE GOLDEN EGG?

AGE-PROOF CAROTENOIDS FOR YOUR EYES: LUTEIN & ZEAXANTHIN

A paper published in Aug, 2017 in the Lancet estimates that there were, in total, 253 million people living with visual impairment in 2015. It also estimates that 1.1 billion people have near-vision impairment. The prevalence of visual impairment is known to increase rapidly with age. It is estimated that by age 60 around 1 in 9 people will be either blind or Moderate to Severe Visual Impairment (MSVI) and by age 80 the ratio increases considerably to around 1 in 3 people.[17] (Figure 4)

AGE-PROOF CAROTENOIDS FOR YOUR EYES: LUTEIN & ZEAXANTHIN

The Macular pigments are strong Anti-oxidants, is well established.

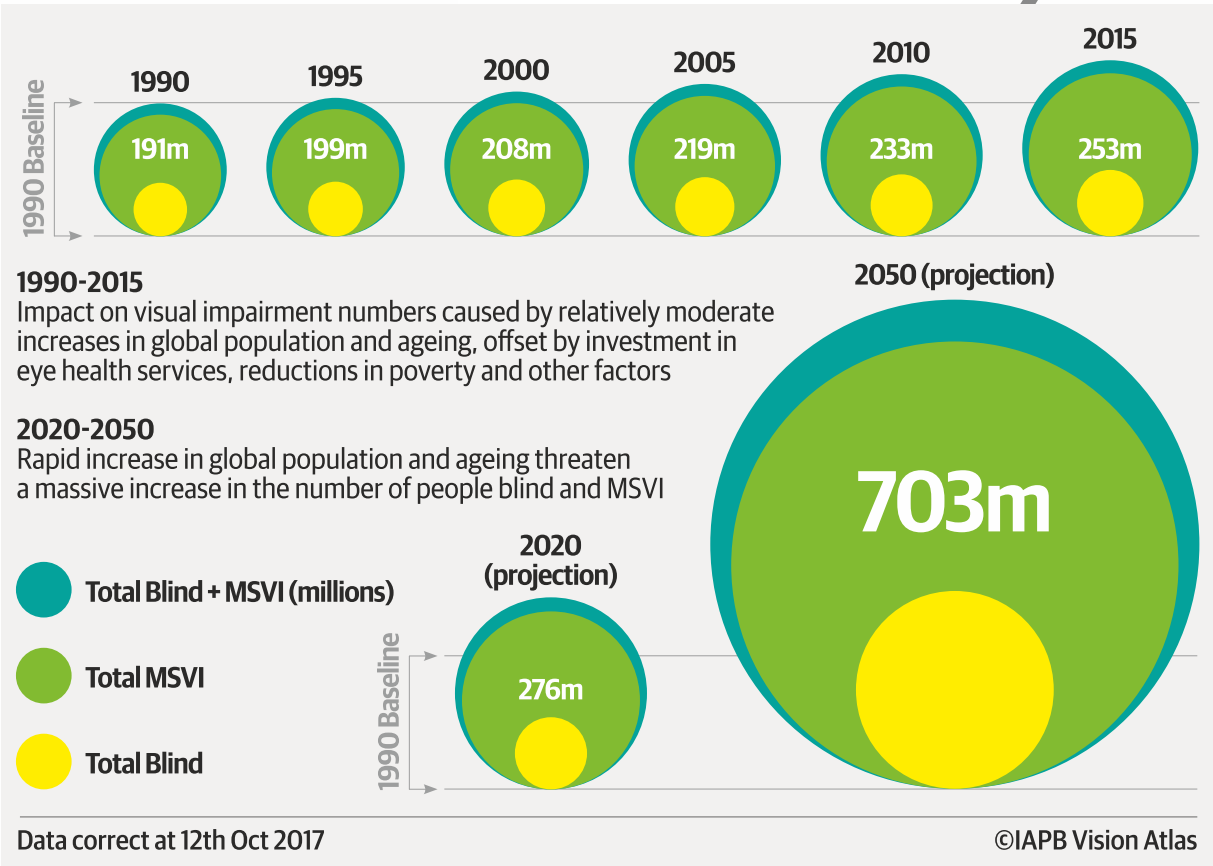


FIGURE 4 : Global number of blind and MSVI - 1990 to 2050

Deterioration of vision need not necessarily be a consequence of ageing alone. Unhealthy lifestyle, smoking, alcohol consumption, prolonged exposure to light (due to usage of mobile phones, laptops, etc.), UV damage, diabetes, and obesity can also cause visual woes.

Reference: http://atlas.iapb.org/vision-trends/impact-growing-ageing-population/

In the Eye, the retina or more particularly, the macula, is considered as the most vulnerable site for the generation of ROS, more so, the damage is caused by the long exposure to external insults.[18,19]

The ocular damage caused by phototoxic reactions can be prevented effectively by use of appropriate anti-oxidant quenchers. Studies have indicated that carotenoids in particular, Lutein and Zeaxanthin, either help prevent or reduce the risk of progression of eye diseases and macular degeneration. By acting as a blue light / UV light filter, the lens and macular pigments Lutein and Zeaxanthin can protect underlying retinal structures from light induced damage.[20,21]

Age- and diet-related loss of lutein and zeaxanthin enhance photo-toxic damage to the eye, and thus supplementation of these carotenoids becomes vital for maintaining optimal eye health.

One of the best commercial sources of pure Lutein and Zeaxanthin is marigold flowers.[22]

Most diet does not deliver adequate amounts of Lutein and Zeaxanthin because we simply do not consume as many leafy vegetables.

XanMax® has been specially formulated to bridge this gap and also to ensure optimal Lutein and Zeaxanthin supplementation, in turn sufficient protection for healthy vision, naturally.

Ample epidemiological evidence exist that Macular pigments are inversely associated with the incidence of AMD

AGE-PROOF CAROTENOIDS FOR YOUR EYES: LUTEIN & ZEAXANTHIN

ABOUT XanMax®

XanMax® is an innovative formulation with enhanced ratio of Zeaxanthin in combination with Lutein, than available from natural Marigold. These are known for delivering myriad health benefits, including healthy ageing.

XanMax® is a combination of customized natural Lutein with Zeaxanthin, offering

- Maximum Xanthophyll
- Maximum Zeaxanthin
- Maximum Bioavailability, **in turn contributing to Healthy Ageing.!!**

To understand whether regular supplementation of XanMax® (a oil soluble dietary carotenoid supplement constituting Lutein and Zeaxanthin) would help to maintain a healthy macula through deposition of optimal levels of carotenoid pigments in elderly population, **a randomized, double blind, placebo controlled, parallel study was conducted for a duration of 180 days in elderly volunteers.**

AGE-DEFYING EYE SAVIOURS: A CLINICAL STUDY

Objective of the Study: Accurate assessment of the amount of Macular pigments, expressed as Macular Pigment Optical Density (MPOD), is necessary to investigate the role of carotenoids. Primary objective of the study was to evaluate the comparative efficacy of XanMax® 2002 with that of a placebo in improving MPOD levels in elderly volunteers.

About the Product: Capsule containing the active XanMax® 2002 oil was administered.

Made from Marigold flowers, XanMax® is completely natural with high levels of Xanthophyll content and minimum impurities, using patented processing techniques. XanMax® is processed with care and precision to avoid thermal degradation of actives. XanMax® is free from xanthophylls epoxides, so as to deliver high purity xanthophylls.

XanMax® 2002 oil is a natural carotenoid supplement constituting 20% of trans-Lutein and 2% of trans-Zeaxanthin dispersed and homogenized in sunflower oil. These macular pigments were obtained by extraction, separation, and purification of the extract from the flowers of T. erecta (Marigold) using a unique process, maXavail™, to obtain a maximum bioavailability and desired eye health benefits.

maXavail™ is an innovative, proprietary technology that guarantees enhanced bioavailability of actives. This proprietary technology increases the bioavailability of actives in the body ensuring maxiumum efficacy of actives in any dosage form.

maXavail™

AGE-DEFYING EYE SAVIOURS: A CLINICAL STUDY

Study Design and Dosage: Out of 110 volunteers screened, 60 were enrolled into the study. These 60 eligible volunteers were equally randomized into one of the two arms, placebo arm and treatment arm (A & B). Elderly volunteers whose MPOD values between 0.2 and 0.4 were enrolled into the study after obtaining Institutional Ethics Committee and necessary regulatory approvals All 60 subjects received the placebo or the active product (XanMax® 2002) for a period of 180 days, one capsule once daily, to be taken 30 min after meals. Subjects were provided with subject diary and they were requested to document the daily food intake. MPOD value on baseline visit (Day 0) through the last visit (Day 180) was measured for each subject.

Statistical Analysis: Two tailed ANOVA was employed for analyzing MPOD values between and within Group A and Group B with Baseline data as co-variate, while 'p' value <0.05 was considered as statistical significance for the study.

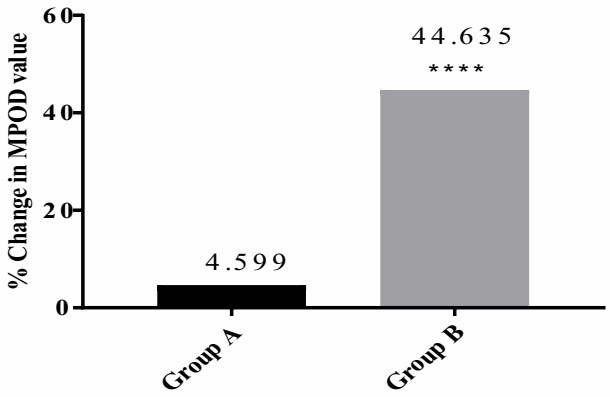


FIGURE 5: % change in MPOD values in Left eyes from Visit 1 to Visit 4 betweeen the two treatment Groups A & B

AGE-DEFYING EYE SAVIOURS: A CLINICAL STUDY

Study Results: Comparative MPOD changes from baseline to Visit 4 indicated statistical significance ($p<0.0001$) between the two groups by the end of treatment period. Furthermore, percentage change in MPOD values in the Left and right eyes from Visit 1 to Visit 4 between the two treatment Groups exhibited a statistical significance indicating intake of XanMax® 2002 improved MPOD values. [Figure 5, 6 & 7]

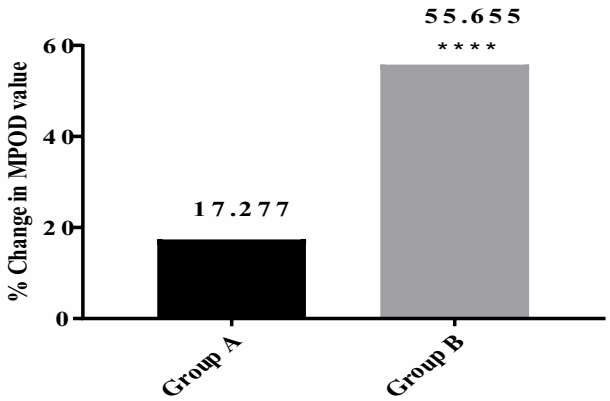


FIGURE 6: % change in MPOD values in Right eyes from Visit 1 to Visit 4 betweeen the two treatment Groups A & B

The study results shows 40% increase in the MPOD levels from Placebo to the Treatment group supplemented with XanMax® 2002 Oil

The study also demonstrated that the formulation, 2002 was safe and well tolerated when administered orally. Dilated fundus exam was performed on all the 60 enrolled subjects throughout all the 4 visits and none found to be abnormal. This infers that subjects who received active product did not show any clinically significant abnormality when compared to that of placebo group subjects

Study Conclusion: The present clinical study demonstrated better optical density values and thereby an **increase of 40% higher macular pigmentation**. It was observed that after 6 months of treatment a statistically significant improvement was seen in MPOD levels in treatment arm receiving the formulation, XanMax® 2002 constituting trans-Lutein and trans- Zeaxanthin when compared to the placebo arm. Hence, from this pilot study evaluating the efficacy of supplementation of trans-Lutein and trans-Zeaxanthin i.e. for 180 days, it can be concluded that Lutein and trans-zeaxanthin favourably influences deposition of carotenoids in macula thus positively influencing MPOD. The safety results of this study demonstrate that the formulations were safe and well tolerated when administered orally.

AGE-DEFYING EYE SAVIOURS: A CLINICAL STUDY

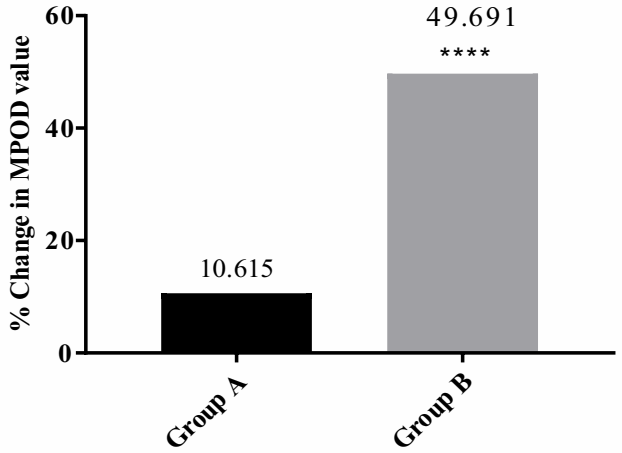


FIGURE 7: Percentage change in MPOD values in Left and Right eyes from Visit 1 to Visit 4 betweeen the two treatment Groups A& B

EYE SAVIOURS: FOR A GRACEFUL AGEING

Scientific understanding of Ageing and its related biological mechanisms became clear. Stress due to oxidation, excess Free radicals generation, coupled with faulty lifestyle all work together to cause Ageing.

Ageing is a normal, inevitable, universal, biological phenomenon. It is not reversible. We do not heal old age. We protect it and promote it. Our objective to promote healthy ageing is to prevent chronic illnesses wherever possible, to improve the quality of remaining life, prolong the period of independent living and make the extended life more happy.

EYE SAVIOURS: FOR A GRACEFUL AGEING

Scientific studies suggest that Macular pigments viz., Lutein and Zeaxanthin are a prime natural anti-ageing ingredient beneficial for healthy ageing and optimal eye health.

Epidemiological research shows an inverse relationship between macular pigment levels of lutein & zeaxanthin and ocular diseases. Increased macular pigment density has been positively linked with decreased risk and progression of ocular diseases. This in turn helps to substantiate the fact that increased pigment of lutein and zeaxanthin present in XanMax® will help in mitigating early onset of ocular diseases in young and decrease the risk of progression of ocular diseases in old, on long term supplementation.

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For further information please contact XanMax®'s European Distributor Geelawson

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