

Turmeric and bilberry: Two plants for a natural support to eye health

Vision impairment, a global issue

Quoting the recent WHO's World report on vision (1) "the most dominant of our senses plays a critical role in every facet and stage of our lives. We take vision for granted, but without vision, we struggle to learn to walk, to read, to participate in school, and to work. Vision impairment occurs when an eye condition affects the visual system and one or more of its vision functions. Vision impairment has serious consequences for the individual across the life course. Many of these consequences can, however, be mitigated by timely access to quality eye care and rehabilitation. Eye conditions are remarkably common. Those who live long enough will experience at least one eye condition during their lifetime. Globally, at least 2.2 billion people have a vision impairment or blindness, of whom at least 1 billion have a vision impairment that could have been prevented or has yet to be addressed. Eye conditions that can cause vision impairment and blindness are, for good reasons, the main focus of prevention and other eye care strategies; nevertheless, the importance of eye conditions that do not typically cause vision impairment - such as dry eye and conjunctivitis - must not be overlooked. A range of

effective strategies are available to address the needs associated with eye conditions and vision impairment across the life course. These include health promotion, prevention, treatment and rehabilitation strategies, some of which are among the most feasible and cost-effective of all health care interventions to implement" states the WHO report.

An effective support for eye wellbeing comes from the nature as well. Indena's research has been working for years on that specific area and got important results from two plants: bilberry and turmeric.

Mirtoselect[®]: the most studied bilberry on the market

Vaccinium myrtillus L. is an edible berry which grows on small wiry shrubs on hillsides

throughout Central and Northern Europe. Among the 450 species belonging to the genus Vaccinium, the traditional medicinal use of *Vaccinium myrtillus* L. has been documented since the Middle Ages, when its fruits were recommended for a variety of conditions, and from the 16th century the plant has been systematically mentioned in all major herbal treatises.

Bilberry is one of the richest sources of anthocyanins, healthy antioxidants found naturally in a number of foods - in red wine, certain varieties of cereals, and certain leafy and root vegetables (aubergines, cabbage, beans, onions, radishes) but most abundant in coloured fruits (2). In this context *Vaccinium myrtillus* L. contains the highest amounts of anthocyanins than any other berries (3).

Unlike most other berries, *Vaccinium myrtillus* L. is extremely difficult to grow; it does not produce clusters of berries, but single or, more rarely, pairs of berries, in limited numbers considering the biomass of the plant. Bilberries are softer and juicier than most other berries, and therefore more susceptible to damage and more difficult to transport. Bilberries cannot be cultivated,

and are therefore picked from wild plants growing on publicly accessible lands; nor can they be processed unfrozen, since tissue damage triggers the deglycosidation of anthocyanins, with detrimental effects on their chemical stability.

In the early 1970s, Indena developed a standardized bilberry extract whose efficacy has been extensively clinically evaluated in vascular health, with over 60 positive studies, including at least 30 controlled or double-blind studies published in peer-reviewed titles. From the beginning, the biomass collection and transportation was organized to protect wild crops. Thanks to technologically advanced process, from raw bilberries Indena produces Mirtoselect[®], a standardized bilberry extract containing \geq 36 % of anthocyanins, and characterized by a very specific and consistent HPLC profile that represents the "fingerprint" of the extract. Mirtoselect[®] is the authentic bilberry extract (*Vaccinium myrtillus* L.) obtained exclusively from fresh fruit harvested when ripe, between July and September.

Mirtoselect[®] is today not only the most extensively studied bilberry extract available, but also the market leader and benchmark. The major applications investigated so far for Mirtoselect[®] are in the realms of vascular health and ophthalmology (eye protection at the retina level).

Mirtoselect[®] has been shown to help support healthy visual function due to eye fatigue. In a crossover, double-blind, placebo-controlled study on 20 people (4), four weeks of daily supplementation with 250 mg of Mirtoselect[®], showed positive effects in subjective perceptions like the occurrence of vision sparks (80% of subjects), eyesight dimming (73% of subjects) and ocular fatigue (70% of subjects) in



computer operators. Flicker values ameliorated significantly following the administration of bilberry anthocyanins, and an overall positive effect on eye fatigue could be suggested.

Prolonged intake of Mirtoselect[®] has been associated with favourable changes in visual acuity. An 8-weeks trial (5) with a daily dosage of 150 mg of Mirtoselect[®] was carried out on 63 school children. This suggests that Mirtoselect[®] could be a powerful tool in the support of ocular health related to increased eye accommodation associated with prolonged reading and computer work, activities that are typical of school education. The anthocyanins in Mirtoselect[®] have an affinity for small blood vessels and have been shown to support the blood flow in the eye bulb tissues, activating the nutrition supply.

Through the beneficial effect on vascular circulation, Mirtoselect[®] can optimize oxygen and blood delivery to the eye, maintaining the functionality of tear secretion. Furthermore, the free radical scavenging properties balance oxidative stress, one of the major risk factors of dry eye discomfort. Recently, new positive data have emerged regarding the supportive role of Mirtoselect[®] in dry eye conditions. The new randomized, double-blinded, placebo-controlled human study (6) offers further proof of the efficacy and safety profile of Mirtoselect[®], where preserving adequate tear levels and maintaining the ocular surface healthy may possibly help in attenuating discomfort and visual disturbance. Clinical findings are also linked with an optimal tolerability profile.

Those evidences are the result of careful biomass collection, storage and consistency of batch to batch industrial production.

Meriva®: the life guardian, also for eye health

The health support of Meriva[®], Indena's turmeric formulated with Phytosome[®] delivery system, is demonstrated by 35 scientific studies in humans, of which at least a third were conducted with the randomized controlled scheme. Its tolerability and effectiveness in maintaining an overall wellbeing thus keeping low-level chronic inflammation far away, grants Meriva[®] the role of The Life Guardian[™] as it can be taken for a long-term life-maintenance strategy.

Among the fields of Meriva[®]'s application, is the eye health, as showed in the last decade by 6 human studies: one in diabetic microangiopathy, two in central serous chorioretinopathy, one in chronic anterior uveitis, one in meibomian gland disfunction and one in diabetic macular edema.

The evaluation of uveitis relapses during 1 year of supplementation with Meriva[®] and follow up compared with the previous period of 1 year before the study enrollment showed a prolonged period of eye healthy functionality in the total number of subjects with



relapses and in the total number of relapses overall (7).

Two studies on central serous chorioretinopathy showed that supplementation with Meriva[®] maintained visual acuity in 61 % of eyes, and neuroretinal or retinal pigment epithelium health in 95 % of eyes (8).

Meibomian gland dysfunction (MGD) is a chronic, diffuse abnormality of the meibomian glands. It is an inflammation-based condition and represents the main cause of dry eye. The study, focused on subjects affected by MGD, showed, after three months of dietary supplementation with Meriva®, a significant maintenance of an healthy level of TBUT (Tear Breakup Time) and, in 86 % of subjects involved, kept their cornea substantially spotless (Oxford Test) (9). Another study with Meriva® in the eye health area focused on Diabetic Macular Edema (DME), an accumulation of fluid in the macula—part of the retina that controls our most detailed vision abilities—due to leaking blood vessels. (10).

Diabetic microangiopathy and retinopathy is a consequence of long terms diabetes mellitus and its signs are increased vascular permeability, tissue ischemia and neovascularization. Along with DME, they are other areas where Meriva[®] efficacy has been studied, with results which showed positive effects on visual acuity and eye wellbeing (11).

References

1) https://apps.who.int/iris/bitstream/handle/10665/328721/WHO-NMH-NVI-19.12-eng.pdf

2) Nutrient U.S. Department of Agriculture, A.R.S., USDA Database for the Flavonoid Content of Selected Foods, Release 3.0 2011.

3) Prior R.L. et al., Antioxidant Capacity As Influenced by Total Phenolic and Anthocyanin Content, Maturity, and Variety of Vaccinium Species, J. Agric. Food Chem. 46, 2686 (1998).

4) Kajimoto O. Clinical Evaluation of the Oral Administration of Vaccinium Myr- tillus Anthocyanosides (VMA) in Mental Fatigue and Asthenopia. Scientific Report Collection 1998, 19, 143-150.

5) Kajimoto S. Recovery effect of VMA intake on visual acuity of pseudomyo- pia in primary school students. J. New Rem. Clin. 2000, 49, 72-79.

6) Riva A. et al, The effect of a natural, standardized bilberry extract (Mirtoselect®) in dry eye: a randomized, double blinded, placebo controlled trial, Europe- an Review for Medical and Pharmacologi- cal Sciences, 2017;21: 2518-2525.

7) P.Allegri, A.Mastromarino, P.Neri, Management of chronic anterior uveitis relapses: efficacy of oral phospholipidic curcumin treatment. Long -term followup, Clinical Ophtalmology, 2010.

8) F.Mazzolani, Pilot study of oral administration of a curcumin-phospholipid formulation for treatment of central serous chorioretinopathy, Clinical Ophtalmology, 2012; F.Mazzolani, S.Togni, Oral administration of a curcumin-phospholipid formulation for treatment of central serous chorioretinopathy: a 12-months follow-up study, Clinical Ophtalmology, 2013.

9) F.Mazzolani, S.Togni, L.Giacomelli, F.Franceschi, The role of a novel oral curcumin delivery form (Meriva®) dietary supplementation in meibomian gland dysfunction, Minerva Oftalmologica 2016.

10) F.Mazzolani, S.Togni, L.Giacomelli, R.Eggenhoffner, F.Franceschi, Oral administration of a curcumin-phospholipid formulation (Meriva®) for treatment of chronic diabetic macular edema: a pilot study, European Review for Medical and Pharmacological Sciences 2018.

11) R.Steigerwalt, M.Nebbioso. G.Appendino, G.Belcaro. G.Ciammaichella, U.Cornelli, R.Luzzi, S.Togni, M.Dugall, M.R.Cesarone, E.Ippolito, B.M.Errichi, A.Ledda, M.Hosoi, M.Corsi, Meriva®, a lecithinized curcumin delivery system, in diabetic microangiopathy and retinopathy, Panminerva Med, 2012.

For more information, please contact

Indena S.p.A., Marketing Department marketing@indena.com www.indena.com