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File: ■ Bilberry (*Vaccinium myrtillus*)
■ French Maritime Pine (*Pinus pinaster*)
■ Glaucoma

HC 071053-412

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RE: Bilberry Extract with Pycnogenol® Alleviates Intraocular Pressure Elevations and Improves Clinical Response to Local Medication for This Asymptomatic Condition

Steigerwalt RD, Belcaro G, Morazzoni P, Bombardelli E, Burki C, Schönlau F. Mirtogenol® potentiates latanoprost in lowering intraocular pressure and improves ocular blood flow in asymptomatic subjects. *Clin Ophthalmol*. May 2010;4:471-476.

Glaucoma is a leading cause of blindness. In most types of glaucoma, fluid and pressure build up slowly inside the eye. Excessively increased intraocular pressure damages the optic nerve, which is the nerve that transmits information from the eye to the brain. A previous exploratory pilot study found that a combination of extracts from bilberry (*Vaccinium myrtillus*) and French maritime pine (*Pinus pinaster*) bark (Pycnogenol®; Horphag Research; Geneva, Switzerland) reduced intraocular pressure and improved blood flow in the eye. The purpose of this open-label, randomized trial was to evaluate the effects of Mirtogenol®, a combination of bilberry extract and Pycnogenol, and the prescription drug latanoprost on intraocular pressure and ocular blood flow in people diagnosed with ocular hypertension.

The trial was conducted at the University of Chieti-Pescara, San Valentino, Italy. People with asymptomatic intraocular hypertension (35-40 mmHg) who were free from degenerative eye disorders, cardiovascular disease, and other systemic diseases were enrolled in the trial. The subjects were randomly assigned to 1 of 3 groups for 24 weeks. The first group used 1 drop of latanoprost (Xalatan®; Pharmacia Pfizer; New York, New York) in each eye every evening. The second group took 1 tablet of Mirtogenol every morning. One tablet of Mirtogenol contained 80 mg bilberry extract standardized to 36% anthocyanins (Mirtoselect®; Indena S.p.A.; Milan, Italy) plus 40 mg French maritime pine bark extract standardized to 70% procyanidins (Pycnogenol). The third group used both latanoprost and Mirtogenol every day. Intraocular pressure and blood flow velocity in the central retinal artery were measured on weeks 0, 4, 6, 12, 16, 20, and 24.

A total of 79 subjects were enrolled, and all subjects completed the trial. The mean age in each group ranged from 48.6 to 49.0 years. There were no significant differences in age, intraocular pressure levels, or blood flow velocity among the 3 groups at the beginning of the study.

In the latanoprost group (n=29), intraocular pressure decreased from 37.7 mmHg at baseline to 27.2 mmHg after 4 weeks ($P < 0.05$) and remained at that level until 24 weeks. In the Mirtogenol group (n=23), intraocular pressure decreased from 38.1 mmHg at baseline to

29.0 mmHg after 16 weeks ($P < 0.05$) with no further change by 24 weeks. In the combined Mirtogenol plus latanoprost group (n=27), intraocular pressure decreased from 38.0 mmHg at baseline to 27.3 mmHg after 4 weeks ($P < 0.05$), to 24.2 mmHg by 6 weeks, and further to 23.0 mmHg after 24 weeks. At all time points, pressure was significantly lower in the latanoprost group than the Mirtogenol group ($P < 0.05$). Ocular pressure was significantly lower when latanoprost and Mirtogenol were combined than when either was used alone at 16, 20, and 24 weeks ($P < 0.05$).

Blood flow velocities in the retinal artery increased gradually in all 3 groups. The improvements were similar in the Mirtogenol and latanoprost groups, with a significant increase observed at 12 weeks compared to baseline (both $P < 0.05$). Mirtogenol increased blood flow velocities significantly over latanoprost at 6 weeks for systolic and at 24 weeks for diastolic ($P < 0.05$ for both). The Mirtogenol plus latanoprost group had significantly greater improvement in diastolic blood flow velocity than either treatment by itself from 12 weeks to 24 weeks ($P < 0.05$). No adverse side effects were reported in the Mirtogenol group. Blurred vision and eyelid or conjunctival redness, which are known side effects of latanoprost, were reported in both groups using latanoprost.

In this study, Mirtogenol lowered intraocular pressure and increased retinal artery blood flow. Mirtogenol was almost as effective as latanoprost, but the improvements were seen faster with latanoprost. The additive effects of the combination of latanoprost and Mirtogenol suggest that they have different pharmacologic actions. Bilberry extracts have been shown to modify the capillaries in the ciliary body, which releases fluid within in the eye, and Pycnogenol improves the function of the endothelial cells lining blood vessels and capillaries. This suggests Mirtogenol may decrease fluid flow into the eye. Latanoprost and similar prostaglandin $F_{2\alpha}$ analogue drugs enhance fluid flow out of the eye.

The authors conclude that Mirtogenol is safe and lowers intraocular pressure in people with elevated intraocular pressure. While Mirtogenol is not a replacement for latanoprost and similar drugs for the treatment of glaucoma, it provides additional benefits when used in combination with latanoprost. Mirtogenol may be useful in preventing an increase in ocular hypertension, which would reduce the risk of developing glaucoma. Latanoprost and other drugs are not suitable for prevention because of their potential for serious side effects.

The authors mention a limitation of their study lay in the measurement of blood velocity versus volume. In addition, another limitation of the study is that the authors did not evaluate any systemic effects of Mirtogenol. The advantage of ophthalmic medications is that there are no systemic effects because the medication is given locally, and the concentration is not high enough to produce systemic effects. In contrast, when a drug is given systemically but the target is the eyes, the drug circulates through the body and most likely produces not only ocular effects but also systemic effects. Therefore, 6 months of treatment with Mirtogenol may be safe for the eyes, but the systemic safety needs to be confirmed in these patients. Systemic benefits may also accrue.

While the study confirms the findings of an earlier pilot study, additional studies using larger numbers of subjects and longer treatment duration should be conducted. This study adds to the growing evidence for benefits of bilberry extracts and Pycnogenol in maintaining eye health.

–Heather S. Oliff, PhD

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