

METHOD AND COMPOSITIONS FOR TREATMENT OF THE AGING EYE

FIELD OF THE INVENTION

A method and compositions for the prevention and treatment of orbital disorders associated with the aging eye.

BACKGROUND OF THE INVENTION

The eyes, usually the very first aspect noticed of a person's face, often show the earliest signs of the aging process. The aging process is ordinary first demonstrated by wrinkles of the eyelids, the need for glasses to correct for presbyopia, or visual loss associated with cataracts, glaucoma, diabetic retinopathy or macular degeneration.

Eyelids show age-related changes such as dry skin, wrinkles, keratoses, age spots and pigmented skin lesions. Dry eyelid skin appears dull and loses its radiance and is usually caused by low humidity, cold weather, contact pressure, detergents, solvents and some chemicals. A moisturizing topical lotion, cream or ointment usually restores the dry skin condition of the eyelids.

The skin of the upper and lower lids is unique in that it is the thinnest in the body, contains relatively little fat and subject to the most movement with blinking. Every layer of the skin changes dramatically with age. The epidermis and dermis become thinner and the density of elastic and collagen is reduced with aging. Wrinkles occur with a loss of subcutaneous fat so that the deeper layers of skin provide inadequate support for the epidermis and tiny folds appear which deepen with time.

Cataracts are the leading cause of blindness in the world, and the leading cause of reversible visual loss for persons over age 65. Cataracts are a loss of the transparency of the lens of the eye causing blurred vision, glare, sensitivity to light, poor night vision, halos around lights and color distortion. About 4 million persons have cataracts in the U.S. and 40,000 develop cataracts each year. With the life expectancy over 76 years, the incidence of cataracts is expected to double in the next 12 years. Cataract surgery is the most common surgical procedure for the elderly.

Glaucoma is the leading cause of irreversible blindness in the world, the second most common cause of irreversible blindness in the U.S. and the most common cause of blindness among blacks. An estimated 2.5 million persons in the U.S. have glaucoma. Glaucoma is not a single disease, but rather a group of disorders that damage the optic nerve. Samples J R, *Rational Drug Therapy* 1987; 21(12):1-6. Rosenberg L F, *American Family Physician* 1995;52(8):2289-2298.

Diabetes is the fourth leading cause of death affecting almost 16 million Americans, a third of them undiagnosed, costing over \$100 billion per year, 15% of U.S. health-care dollars. Some 800,000 new cases of diabetes develop every year. By the year 2030, the number could reach 50 million here and at least 300 million worldwide. Diabetes mellitus is the leading cause of new blindness among persons 20 to 74 years of age in the United States. Retinopathy begins to develop soon after the diagnosis of insulin-dependent diabetes mellitus (IDDM), and after 15 years, the prevalence is almost 100%. One million people in the U.S. have IDDM or Type I diabetes. In non-insulin-dependent diabetes (NIDDM) or Type II diabetes, currently 15 million, about 21% of the patients have retinopathy at diagnosis, and 60% after 20 years. Type II diabetics have tripled over the last 30

years, and involves half of Americans over the age of 65. Proliferative retinopathy occurs in 10-20% of NIDDM. Brechner R J, et al, *JAMA* 1993;270:1714-1718.

Macular degeneration, or age-related macular degeneration (AMD), affects the central part of the retina and is the leading cause of blindness in people over age 65 in the U.S. AMD affects 13 million people and causes impairment in about 1.2 million. About 30% of patients over 75 have AMD, and 23% of the remainder will develop it within five years. The prevalence of AMD increases with age from 16.8% in patients 55-64 to 25.6% in patients 65-74 and up to 42% in patients over 75. There currently is no known cure for dry or atrophic AMD, the form characterized by hard or soft drusen (deposits of cellular debris), changes in the retinal pigment epithelium (RPE), or atrophy of photoreceptors and RPE. This form accounts for approximately 90% of all cases. The remainder of AMD cases have the "wet" form characterized by neovascularization and exudation. Pratt S G, *Review of Ophthalmology August* 1998:42-50.

SUMMARY OF THE INVENTION

This invention relates to a method for the prevention and treatment of orbital disorders associated with the aging eye in mammals by the application of a topical composition comprising a permeation enhancing amount of one or more penetration enhancers, and one or more bio-affecting agents which penetrate into the underlying tissues and into the vascular network of the orbit. Another object of this invention is the improvement of age-related changes to the eyelids such as dry skin, wrinkles, keratoses, age spots and pigmented skin lesions. It is a further object of this invention to prevent and treat cataract formation, glaucoma, diabetic retinopathy and macular degeneration.

DETAILED DESCRIPTION OF THE INVENTION

Oxidative stress, or the predominance of free radicals over antioxidant mechanisms, has been implicated in premature aging, heart disease, arthritis, cancer, Alzheimer's disease and ocular disorders such as cataracts, glaucoma, diabetic retinopathy and macular degeneration. Free radicals are very unstable and highly reactive. They try to capture electrons from other molecules to gain stability, a process known as oxidation. They are unpaired oxygen molecules that cause cellular damage and are generated by a combination of light and oxygen or during reperfusion after an ischemic insult that deprives the eye of oxygen and nutrition. Free radicals occur naturally and cannot be avoided. Inadequate dietary intake of antioxidants can result in oxidative stress which can produce major derangement of cell metabolism, causing extensive damage to DNA, proteins and lipids.

Antioxidants are substances that significantly delay or inhibit oxidation. They neutralize free radicals by supplying electrons. Antioxidants protect from free radicals by inhibiting free radical formation, intercepting free radicals, and repairing free radical-induced injury. Antioxidant defenses involve both enzymatic and non-enzymatic systems. The enzymatic defense system includes superoxide dismutase, catalase, and glutathione peroxidase. Non-enzymatic defense systems include vitamins C and E.

The eye and the skin are the only organs of the body normally exposed to light. The eye is specifically adapted to respond to a certain band of electromagnetic wavelengths known as visible light. Infrared and ultraviolet wavelengths elicit no visual response but, nevertheless, enter the eye and may produce heating and photobiological changes. Short