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Encapsulation of natural compounds in the prevention and treatment of Diabetic Retinopathy

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INTRODUCTION

Diabetic retinopathy is a disease resulting from diabetic chronic hyperglycemia characterized by microvascular complications in the retina, where neuronal elements responsible for vision are located. Oxidative stress has been widely regarded as the main etiological factor for the emergence of ocular disease. Antioxidant therapy has been related with inhibition of diabetes-induced abnormalities of retinal metabolism. However ocular treatment effectiveness is purely low, considering the several routes of administration. The improvement of ocular bioavailability is the ultimate era of Science.

This review data encompasses new nanosystems with therapeutic potential improvements and involving routes of administration local and with a better performance facing biological barriers. Nanoparticles are described to offer real benefits to the stability, drug delivery and therapy of the patient and the most advanced treatment modalities for ocular conditions.

DIABETIC RETINOPATHY

Oxygen metabolism is essential for sustaining aerobic life and normal cellular homeostasis works on a fine balance between the formation and elimination of reactive oxygen species (ROS). Oxidative stress is a cytopathic consequence of excessive production of ROS and the reduction or suppression of ROS removal by antioxidant defense system. It is implicated in the development of many diseases, including Alzheimer disease, diabetes and its complications [Kowluru 2007].

Diabetic retinopathy, the fifth cause of blindness worldwide [Chu 2008], is progressive diabetes associated condition, compromising cells and tissues of the ocular globe and is generally recognized as a vascular disease.

OXIDATIVE STRESS AND CLINICAL IMPAIRMENT

The retina has high content of polyunsaturated fatty acid (PUFA), possess the highest oxygen uptake, glucose oxidation, lipid peroxidation and is constantly expose to light and oxygen, which makes retina more susceptible to oxidative stress than other organs or structures [Kowluru 2007]. ROS are produced continuously in all cells to support normal cellular functions.
In retinopathy, oxidative stress has been widely involved in decreased retinal blood flow, increased vascular permeability, disruption of blood-retinal-barrier and the appearance of acellular capillaries from the apoptotic loss of retinal capillary cells [Kern 2000]. Oxidative stress has also been linked to microvascular abnormalities in diabetic retinopathy, degenerative process of retinal neovascularization and the suppression of antioxidants systems [Kowluru 2002].

It is worthy to mention the various factors related to retinopathy and underline the prominent importance of oxidative stress in the development and progression of this condition [Kowluru 2007].

ANTIOXIDANT PHARMACOTHERAPY

Dietary supplementation with antioxidants has been related with inhibition of diabetes-induced abnormalities of retinal metabolism, reduction of apoptosis and partial restoration of pericytes. Antioxidants may also, inhibiting the formation of ROS, scavenge free radicals, or increase the antioxidants defense enzyme capabilities [Kalishwaralal 2010]. Moreover, the use of topical antioxidants to treat or delaying oxidative stress-related ocular manifestations is still poorly explored, while current diabetic retinopathy therapy includes invasive methods, e.g. laser photocoagulation and surgery.

Ocular antioxidant potential therapy represents a non-invasive, safe and less painful methodology, which slows the natural progress of the disease and improves the effectiveness of treatment without significant systemic toxicity [Ansari 1998]. But it may be limited by the protective physiological mechanisms in the precorneal area. Thus, strategies to overcome such barrier for the targeted ocular delivery remain a major challenge.

ENCAPSULATION OF NATURAL ANTIOXIDANTS AND DIABETIC RETINOPATHY

Nanoparticle carriers have an exceptional potential as mucosal drug delivery systems, since the colloidal systems are stable in contact with physiological fluids and barriers, control drug release and protect against adverse conditions like mucosal enzymes and biological protective fluids. The nanoparticles may possess marked mucoadhesion properties related to the combination of the particle size, particle surface chemistries and charge and potential absorption enhancing properties.

Among the different approaches explored so far, chitosan exhibits favourable and unique biological properties, such

as biocompatibility/biodegradability, non-antigenic, non-toxicity and mucoadhesiveness [Campos 2004].

Moreover, its hydrosolubility and positive charge enable interactions with macromolecules and polyanions on contact in an aqueous environment for the development of colloidal carriers [Sarmento 2007, Sarmento 2007]. Its unique ability to transiently enhance the permeability of mucosal barriers and increase cell permeability makes chitosan a useful candidate for transmucosal drug delivery. Natural extracts have been incorporated in chitosan films becoming more effective as antimicrobial or improving the antioxidant protection [Ponce 2008]

Therefore, chitosan nanoparticles could incorporate antioxidants, which would increase the exposure time in the precorneal area due to adhesive properties and make longer the penetration of drugs into the intraocular structures [Campos 2004].

The combination of antioxidants and the nanoparticles is seen as the key to success in the topical administration of therapeutic antioxidants. Pharmaceutically, the systems are expected to increase the capacity, to maintain the antioxidant activity during the preparation process, to optimize the release of the compound from the nanoparticles and to ensure a good control of the physicochemical properties and stability of the particles in order to improve bioavailability and therapeutic efficacy of diabetic retinopathy, without compromising the safety performance of the drug (Figure 1).

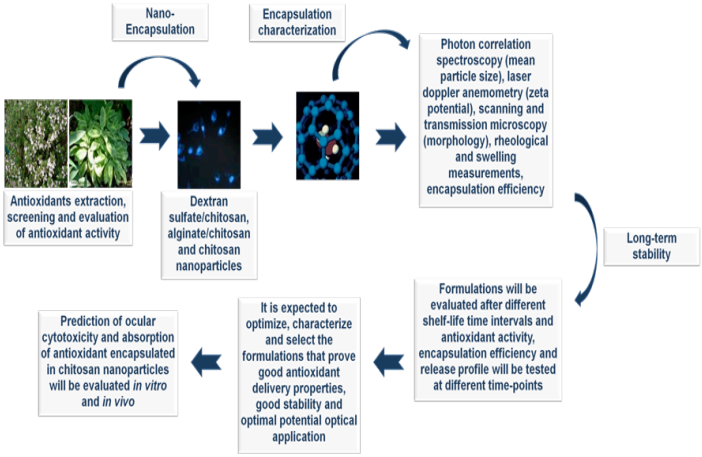

Figure 1 Schematic illustration of natural antioxidants nano-encapsulation and further characterization for long-term stability

CONCLUSION

These data have clearly underlined the emergence of innovative medicines for ocular diseases suggesting the important role of oxidative stress in the development of retinopathy and demands effective strategies to enhance the potential of antioxidant to perform this condition prophylaxis and control. Also provides a further insight on ocular delivery, benefiting from the advantages of the eye for drug delivery and, additionally, offering new potential applications of nanoparticles as drug carrier of natural antioxidants for ocular diseases.

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