EFFECTS OF CURCUMIN AND TOCOTRIENOL ON PRO-INFLAMMATORY CYTOKINES IN EXPERIMENTAL ACUTE UVEITIS

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CONTENT

ABSTRACT

Inflammation of the uvea is termed as uveitis. As in any inflammatory diseases, several inflammatory mediators are involved in the pathogenesis of the disease. Past studies has shown that tocotrienol have antioxidant, anticancer, neuroprotective and cholesterol lowering properties. Some studies have shown that tocotrienol is able to block the NF-κβ pathway, which subsequently, may also effect the several inflammatory mediators released by the activation of NF-κβ.

In our study, the rats are first induced by a single footpad injection of lipopolysaccharide (LPS) which has been dissolved in saline. Negative control rats receive footpad injection of saline only. 3 hours after injection, the rats are given empty liposomes, 0.04% or 0.03% liposomal tocotrienol. 24 hours after the induction of uveitis, slit lamp examination were done to assess the degree of inflammation and the eyes were enucleated for gene expression study.

The severity of uveitis in the group receiving treatment of 0.04% liposomal tocotrienol was higher as compared to the positive control group. On the other hand, group receiving treatment of 0.03% liposomal tocotrienol, showed much more less severity as compared to both the positive control group and group receiving 0.04% liposomal tocotrienol.

In conclusion, tocotrienol is able to reduce the degree of uveitis, but high concentration of tocotrienol could worsen the inflammation due to its pro-inflammatory activity.

CHAPTER 1

INTRODUCTION

The uvea is the vascular coat of the eye, located in between the sclera and the retina. It comprises of the iris, ciliary body and choroid. Inflammation to the uvea is termed as uveitis. Based on the International Uveitis Study Group classification system, uveitis can be classified based on the location, clinical course and laterality (Munoz-Fernandez and Martin-Mola, 2006; Foster, 2009; de Smet, Taylor, et al., 2011). For location, it can either be anterior uveitis, posterior uveitis, intermediate uveitis or pan uveitis. Out of 30% to 70% of the cases is anterior uveitis, making it the most common type (Careless and Inman, 1995). As for the clinical course, acute uveitis would normally last less than 3 months, chronic uveitis last 3 months and more, while recurrent uveitis is when an acute flare occurs after the resolution of a previous episode. And lastly, the laterality depends on whether it occurs unilateral, in one eye, or bilateral, in both eye simultaneously (Munoz-Fernandez and Martin-Mola, 2006). The etiology can either be infectious or non-infectious. In the developing countries, infectious uveitis is the most common form, accounting for 30% to 50% of all cases of uveitis. Some of the common infectious etiologies are toxoplasmosis, tuberculosis, leprosy and leptospirosis (de Smet, Taylor, et al., 2011). Genetic makeup and trauma falls under non-infectious uveitis. The best treatment for uveitis is corticosteroids, while mydriatic and cycloplegic agents used as adjuvants (Munoz-Fernandez and Martin-Mola, 2006; Foster, 2009). The Standardization of Uveitis Nomenclature (SUN) Woking Group Guideline recommended corticosteroids as the management of uveitis, but we know that prolonged use on corticosteroids leads to side effects such as glaucoma, cataract and metabolic disorders (Bittencourt, Sepah, et al., 2012). Recurrent cases of uveitis lead to complications such as cataract, macular oedema, glaucoma, destruction of intraocular tissue and ultimately blindness (Yang, Jin, et al., 2011).