ALTERED CALCIUM TO MAGNESIUM RATIO AND CALPAIN ACTIVITY AS PHARMACOLOGICAL TARGET OF ANTICATARACT EFFECT OF MAGNESIUM TAURATE

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Sincerely,

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ABSTRACT

Cataract is a condition characterized by decrease in visual acuity due to cloudiness of the lens. Magnesium deficiency coupled with lenticular ATP depletion impairs the membrane ATPases functions leads to calcium homeostasis disruption. Consequently, high calcium level leads to activation of calcium-dependent calpain which responsible in denaturation of the lenticular crystallin protein. Previous study proved that aqeous Mg taurate tends to delay the onset and progression of cataract in vivo and in vitro however, the ocular bioavailability was low. Therefore, we conducted an *in vivo* study to evaluate the anti-cataract effect of liposomal formulation of Mg taurate in the galactose-induced cataract model.

For the comparison study, forty-five (n=45) *Sprague Dawley* rats either sex weighing around 80-100g body weight were randomly divided into five groups of 9 rats each. Group 1 received normal diet and other 4 group were given 25%-galactose diet with different eye drop treatment. As for the treatment : Group 2 empty liposome, group 3 distilled water, group 4 liposomal Mg taurate and group 5 aqeous Mg taurate. For study 2, forty rats (n=40) were divided into 4 groups. Group 1 and 2 were same as study 1. Group 3 received liposomal Mg taurate and group 4 received liposomal taurine. Throughout 4 experimental weeks, weekly slit lamp examination was done for staging and opacity index determination. After 4 weeks, the rats were euthanized and lenses were extracted via posterior approach. The lenses were homogenized and centrifuged to get the supernatant for biochemical analysis. Calcium to magnesium ratio was determined by colorimetric method using Cobas Integra 400 analyzer.

CHAPTER 1

INTRODUCTION

Cataract is characterized by clouding of the lens which leads to severe visual impairment (Khaw P.T, 2004). Worldwide, cataract is the major cause of preventable blindness which contributes for approximately 51% of world blindness (WHO, 2011). In Malaysia, based on National Eye Survey 1996 has proven that cataract was the leading cause of blindness approximately 39% of blindness cases (Zainal M.I, 2002).

There are many causes of cataract which can be broadly divided to systemic disease, ocular disease, congenital and external factors. Several known systemic causes of cataract are diabetes mellitus, galactosemia and hypoparathyroidism (Crick R.P, 2003). Studies has proven that the incidence and progression of cataract is elevated in patients with diabetes mellitus (Bron, Sparrow, Brown, Harding, & Blakytny, 1993; Kahn et al., 1977). On the other hand, ocular disease that causes cataract are retinitis pigmentosa, chronic uveitis and acute angle glaucoma (Crick R.P, 2003). Besides that, rubella infection during pregnancy also may cause congenital cataract of the infant (Malhotra, 2008). Other causes of cataract include drug induced such as corticosteroid and amiodarone as well as mechanical or radiation induced trauma to the eye (Malhotra, 2008).