

UNIVERSITI TEKNOLOGI MARA

THE DEVELOPMENT AND CHARACTERIZATION OF
LIPOSOMAL FORMULATION OF MAGNESIUM
TAURATE AND STUDIES TO EVALUATE ITS OCULAR
DISTRIBUTION IN CATARACT

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ABSTRACT

Magnesium taurate is a drug potentially effective in the treatment of cataracts. However, it is a highly hydrophilic compound, which greatly reduces its ophthalmic bioavailability. An effective way to increase the bioavailability is the application of nanotechnology, in particular, the creation of liposomal drug form of magnesium taurate. Presence of amphipathic structures in liposomes facilitates their penetration into the tissue, increase the expense of bioavailability and thus increase distribution of drug throughout the ocular tissue. Liposomes were fabricated by lipid hydration method composed of L-a-phosphatidylcholine and cholesterol, dissolved in chloroform: methanol (5:1) mixture. The steps in the preparation of liposomes included evaporation, cycles of freeze-thaw, sonication and extrusion. After each step of preparation, the samples were collected and the size of liposomes was estimated using ultrasound shockwave based and dynamic light scattering based zetasizer to compare the suitability of the zetasizer in measuring the size of liposome particle and to see the effectiveness of each steps in liposomal preparation in reducing the liposomal size. 5(6)-Carboxyfluorescein-contained liposome, a hydrophilic probe, was used to evaluate liposomal distribution in ocular tissue.

Ultrasound shockwave nanosizer showed a mean liposomal particle size of 10 nm after evaporation and cycles of freeze-thaw and a mean size of 19.1 and 19.2 nm after sonication and extrusion respectively. The corresponding mean particle sizes as estimated by dynamic light scattering based zetasizer were 581.4, 561.4, 155.7 and 134.1 nm respectively with positively charged throughout the stages. Ultrasound shockwave nanosizer, although, showed homogenous size distribution, the particle size was significantly smaller than those measured by dynamic light scattering based zetasizer. Thus it seems that ultrasound shockwave based zetasizer were not really suitable in measuring the size of liposome as compared to dynamic light scattering based zetasizer as it will not only measuring the size of liposome but also reducing the size during the submission of the ultrasound wave. The presence of liposome was seen in parts of the eyes analysed: cornea, ciliary body, lens and retina. The fluorescence intensity in cornea, ciliary body and retina is clearly seen, although the distribution of the liposome within the parts of the eye may vary. However in lens, only slightly visible fluorescence can be seen. Thus the liposome, act as a carrier, able to deliver the drugs not only in the anterior segment of the eye but also to the posterior segment.

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CHAPTER 1: INTRODUCTION

1.1 Cataract

According to the World Health Organization (WHO) in 2010, estimates, there were 39 million (0.58%) blind people in the world, with global prevalence of blindness ranging from 0.3% in European Region to 0.7% in African Region, where cataract accounts for 51% of the cause of blindness in the world (Organization, 2012). In Malaysia, a report done by National Eye Survey 1996 estimates that 54000 (0.29%) Malaysians were bilaterally blind with the mean age of 60 years. Cataract was found to be the commonest cause of bilateral blindness (39.11%), followed by retinal disease (24.54%), uncorrected refractive errors (4.10%), corneal disease (3.42%), and glaucoma (1.77%) (M Zainal, 2002). The numbers of blind people due to cataract is highly likely to increase in future as a result of both growth and ageing of the population.

1.1.1 Cataract Surgery

Cataract (Figure 1.1) happens when there was a change in the lens proteins (crystalline) due to oxidative stress, which gives clouding of the lens and affects the lens in refracting light and reducing its clarity, therefore decreasing visual acuity (Figure 1). Cataract can have various causes, including, inherited metabolic disorder (Lowe's syndrome and hypocalcaemia), diabetes mellitus, drug induced (corticosteroid, amiodarone, phenothiazine, and miotics), nutritional agents, trauma radiation, eye diseases (glaucoma and uveitis) and systemic diseases (renal failure) (Bobrow, 2012), but the main cause of visually significant cataract is ageing or age-related (senile) cataract. Having cataract, does not only affect daily activities, but together with problems of mobility, pain and depression, self-care, and poor health (Aimee Teo Broman, 2002; Polack S, 2010; S Polack, 2008), thus increase dependency on others. The widely used treatment to reverse this blindness is by cataract surgery that is intracapsular cataract extraction (ICCE), extracapsular cataract extraction (ECCE) or phacoemulsification.