

Abstract

Cataract, a leading cause of blindness, accounts for nearly half (47.8%) of all cases of blindness. There were numerous studies done on magnesium and taurine independently that suggest both magnesium and taurine could delay the development of cataract in rats. Thus, the combination of both as magnesium taurate preparation should be prudent to delay the progression of galactose induced cataract in rats. This study was done to evaluate the effect of topical magnesium taurate on the development and progression of galactose-induced cataract in rats. Forty five *Sprague-Dawley* rats, weighed around 80-100g, of either sex were randomly divided into three groups; (1) normal diet (ND), (2) 30% galactose diet (GD) and (3) 30% galactose diet with topical magnesium taurate treatment (GD+MgT). The 1% magnesium taurate treatment was administered thrice daily for a period of 21 days. The weekly progression of cataract was assessed by slit-lamp examination. The staging was based on Sippel, 1966 with a slight modification made. The opacity index was also calculated for assessment of cataract development. The total serum and lenticular calcium and magnesium were measured by colorimetry. The anti-oxidant status of the lens was measured by ELISA. In our experiment, it was shown that at week 1, 16.7% lenses in GD progressed to stage 3 but all lenses were in stage 1A (33.3%) or 1B (66.7%) in GD+MgT group. At week 2, in GD group, 33.3% lenses were in stage 3 and 58.3% were in stage 2B whereas in GD+MgT group 91.7% lenses were in stage 2A. At week 3, 50% of lenses in GD group progressed to stage 4 but in GD+MgT group 83.3% lenses were still in stage 2B and only 16.7% progressed to stage 3. The opacity index (OI) was highest in GD group and treatment with MgT lowered the OI. The serum Ca/Mg ratio for the GD group was higher than the GD+MgT group although it was not statistically significant. Lenticular Ca/Mg ratio is lower in GD+MgT group (1.08 ± 0.29) as compared to the GD group (1.25 ± 0.48) although it was statistically insignificant. The superoxide dismutase activity for the GD+MgT group was significantly lower than the GD group. The glutathione activity for the GD group was higher than GD+MgT group although it was statistically insignificant. The catalase activity for the GD+MgT was significantly lower than the GD group. The histopathological grading indicated that the GD+MgT group was in lower stage than GD group. For the *in vitro* study, the highest Ca/Mg ratio was found to be in the normal group (1.69 ± 0.14) and lowest in the control group (1.56 ± 0.16). The treated group Ca/Mg ratio was lower than the normal but higher than the control group (1.65 ± 0.03). There was significant decrease in glutathione activity in control as compared to normal group ($p < 0.05$). There was significant decrease of catalase activity in the

Acknowledgement

First of all, I would like express my gratitude towards the dean, Prof. Dato' Dr. Khalid Haji Yusoff for offering me the opportunity to be enrolled in the program MBBS with Adv. Med. Sc. Also I would like to express my gratitude towards University Teknologi MARA for providing me with the funding, Dana Kecemerlangan for the research. Next, I would like to express my warmest thanks to my supervisors and co-supervisors, AP Dr Igor Iezhitsa, Dr Renu Agarwal, Dr Nor Salmah Bakar, Dr Effat Omar and Prof Dr Nafeeza Mohd Ismail for their endless guidance and support in conducting the research.

Not forgotten, lots of thanks to Prof. Alexander A. Ozerov and Alexander A. Spasov from Volgograd State Medical University, Research Institute of Pharmacology, Volgograd, Russian Federation for aiding in the synthesis of magnesium taurate salt. I would also like to thank Prof. Dr Mohamed Salama Mohamed and Mr. Ahmad Mustafa Masoud Eid from Faculty of Pharmacy, UiTM Puncak Alam for helping us to prepare the magnesium taurate eye drops.

Lots of gratitude to Dr Nor Salmah Bakar and Dr Effat Omar for helping us to develop the histopathological grading of cataract and Dr Puneet Agarwal for helping us with the slit lamp assessment of the cataract staging.

Also, I would like to extend my warmest gratitude towards my friends and everyone who had directly or indirectly help me and guide me in completing this project.

Funding statement: This work was supported in part by the DANA Kecemerlangan Penyelidikan under the project “Effect of Magnesium Taurate Eye Drops in Rats with Experimentally Induced Cataract”. Grant no. 600-RMI/ST/DANA 5/3/Dst (354/2011)

Table of contents

Contents	Page
Abstract	i
Acknowledgements	iii
Table of Contents	iv
Lists of tables and Figures	vii
List of symbols, abbreviations or Nomenclature	ix
1 Introduction	1
2 Literature Review	3
2.1 Anatomy of the eye	3
2.2 The lens anatomy	4
2.3 Physiology of the lens	5
2.4 Cataract	
2.4.1 Pathophysiology of cataract	8
2.4.2 Magnesium and cataract	11
2.4.3 Taurine and cataract	12
3 Materials and Method	
3.1 Materials	13
3.1.1 Materials for animal study	13
3.1.1.1 Test substance	13
3.1.1.2 Magnesium taurate eye drop preparation	13
3.1.1.2a List of chemicals	13
3.1.1.2b Eye drop preparation	13
3.1.2 Animals	14

1 INTRODUCTION

Cataract is the clouding of the lens of the eye or its surrounding transparent membrane that obstructs the passage of light (Merriam Webster, 2012). Cataract is the leading cause of blindness in the world as stated by WHO in 2002, accounting for 47.8% of the cases. As world population continues to increase each year, the incidence of cataract is also expected to increase. There are many factors that can cause cataract such as age, trauma, systemic disease, dermatological disorders, and ocular disease. The risk factors for development of cataract are genetic, increasing age, poor nutrition, increase sunlight and irradiation exposure, smoking, alcohol and also decrease anti-oxidant status (Wevill, 2009). Currently, the treatment for cataract is surgical intervention. However, surgical intervention of cataract is very costly and it is not affordable for most of the population (Allen and Vasavada, 2006). The lack of non-surgical treatment for cataract calls for studies to be done to find other alternatives to treat cataract.

The lens of the eye is an avascular, transparent and elliptic structure located in the posterior chamber of the eye (Dai and Boulton, 2009). The lens is able to maintain its transparency because of the short-range order of crystalline besides the lacks of organelles in the lens fibre. Various pumps, channels and transporters exist in the lens. Their function is to maintain the electrochemical gradient so that swelling of lens fibre is minimized and formation of precipitates is prevented. The lens is also rich in anti-oxidants and anti-oxidant enzymes that protect it from reactive oxygen species (Dai *et al.*, 2009). The major anti-oxidant mechanism of the lens is the glutathione system, superoxide dismutase and ascorbate system, catalase and glutathione peroxidase system and natural anti-oxidant such as glutathione and taurine. Ageing and exposure to sunlight can cause an increase in the reactive oxygen species in the lens. The reactive oxygen species can cause damage to the crystalline protein and cause cross-linkage of the protein which in turn causes opacification. Hyperglycemic condition can also cause an increase of sugar influx into the lens. Excess sugar is metabolized by the enzyme aldose reductase and the end product formed is polyol. Polyol act as an osmole and attract water into the lens and cause the swelling of lens fibre which leads to scattering of lights and opacification (Datiles, Fukui, Kuwabara and Kinoshita, 1982). The increase in polyol causes an increase the oxidative stress on the lens as the formation of polyol depletes the NADPH in the lens. NADPH is needed to convert oxidized glutathione to its reduced form and this reaction is catalyzed by glutathione reductase enzyme. The decreases in anti-oxidants exhaust the natural anti-oxidant mechanism of the lens. Nutrition such as magnesium also plays an important role in