

**UNIVERSITI TEKNOLOGI MARA**

**GENE EXPRESSION CHANGES IN SEXUALLY  
DIMORPHIC BRAIN REGION OF DOSE  
RESPONSE, BISPHENOL A TREATED MALE  
SPRAGUE-DAWLEY RATS**

**NADIA BINTI ABU BAKAR**

**Dissertation submitted in partial fulfillment of the requirement  
for the Degree of Pharmacy**

**Faculty of Pharmacy**

**November 2009**

## ACKNOWLEDGEMENT

Thanks to Allah the Almighty for His blessing that made those efforts of completing this thesis goes successfully into completion just before the time ended. Special gratitude to my supervisor, Miss Mashani Bt Mohamed for her warm guidance, time-taking draft reading and number of discussions and briefings until this study is completed accordingly. A lot of thanks go to Dr. Kalavathy Ramasamy which has been a very supportive coordinator for this subject.

Millions of thanks go to all of the lecturers involved in the BPA team as they have provided unlimited helps, guidance and teaching towards the completion of the study. To all of my lab mate, Fatin Hanis Bt. Mahmood, Shazwani Bt. Zulkifli, Nur Ezzati Bt. A.Rahman, Amilia Bt. Abd Razak and also Syukri B. Baharuddin, you guys has been such a wonderful lab mate. This still ongoing thank you-wishing goes also to all the post graduate students, lab assistants, and staffs which we bothered much, thank you for many guidance given and for being patience with our presence in the Life Sciences Research lab, the MPG lab, and the animal holding room throughout all the lab sessions. This most important part goes to the parents that I love the most Abu Bakar Ahmad and the people that I considered important in life, friends, siblings, Fazrizal Zifa; thank you for all those long lasting and non-stop supports!.

# TABLE OF CONTENTS

<b>TITLE</b>	<b>Page</b>
<b>APPROVAL</b>	
<b>ACKNOWLEDGEMENT</b>	<b>ii</b>
<b>TABLE OF CONTENTS</b>	<b>iii</b>
<b>LIST OF TABLES</b>	<b>vi</b>
<b>LIST OF FIGURES</b>	<b>vii</b>
<b>LIST OF ABBREVIATIONS</b>	<b>viii</b>
<b>ABSTRACT</b>	<b>ix</b>
<b>CHAPTER ONE (INTRODUCTION)</b>	<b>1</b>
1.1 Background of the Study	1
1.2 Objective of the Study	3
1.2.1 General Objective	3
1.2.2 Specific Objective	3
1.3 Hypothesis	3
<b>CHAPTER TWO (LITERATURE REVIEW)</b>	<b>4</b>
2.1 Bisphenol A	4
2.1.1 The Pharmacokinetic and Metabolism of Bisphenol A	6
2.1.2 The Effects of Bisphenol A	8
2.2 Brain	9
2.2.1 The Sexually Dimorphic Nuclei	11
2.3 The Sprague-Dawley Rats	13

## ABSTRACT

Bisphenol A (BPA) is one type of monomer that is widely used to manufacture polycarbonate plastic, resin lining of cans and others. The ester bond in the BPA-based polymers is so much prone to the hydrolysis, in which leaching of BPA has becoming accessible to human. BPA has been proven by many studies that it can bind weakly to both estrogen receptors; ER  $\alpha$  and ER  $\beta$ , known also as xenoestrogen. The aim of this study is to observe gene expression changes of ER $\alpha$  and ER $\beta$  receptor in brain and any physical changes in body weight of the *Sprague-Dawley* rats after exposure to BPA through force-feeding. The rats are divided into 6 groups; the positive control group, negative control group, 50 $\mu$ g/kg/day group, 500 $\mu$ g/kg/day group, 1000 $\mu$ g/kg/day group and also 5000 $\mu$ g/kg/day group in which all are treated for 14 Days and weighted daily. The rats are sacrificed and the brain is taken and kept well in the -80<sup>0</sup>C fridge. The primer for gene of interest is designed in appropriate to the gene of interest. RNA template is prepared and undergone the RT-PCR before the electrophoresis process. Based on the result of this study, it can be concluded that at lower doses, the body weight increases more ( $p < 0.05$ ) as compared to the higher doses. This study fails to obtain the band of the ER $\alpha$  and ER $\beta$  gene expression which can be due to many reasons and error such as the phenolic contamination of RNA sample, unsuitable PCR profiling and others. Many precaution steps such as proper regulation of the cleanliness and sterility of the working area can be taken to improve further study outcomes in the future.

# CHAPTER ONE

## INTRODUCTION

### 1.1 Background of the study

Bisphenol A (BPA) is a compound that has two phenol group and is a difunctional building block of several important polymers and polymers additives (Vom Saal, 2008). It is prepared by the condensation of acetone with two equivalents of phenol (Constantin *et al.*, 1991). This reaction is catalyzed by an acid and usually excess of phenol is used to ensure proper reaction to occur.

Bisphenol A comes with the molecular formula of  $C_{15}H_{16}O_2$  with  $228.29 \text{ g mol}^{-1}$  as its molar mass. Other names for BPA includes, 4,4'-(propan-2-ylidene)diphenol,p,p'-isopropylidenebisphenol, and also 4,4'-isopropylidenediphenol. The appearance of BPA seems to be in the form of white to light brown flakes or powder. There has been a high level of concerns towards the effects of BPA towards human health as there are many research are already into BPA.

Bisphenol A (BPA) is one type of monomer that is widely used to manufacture polycarbonate plastic, resin lining of cans and others. The ester bond in the BPA-