

UNIVERSITI TEKNOLOGI MARA

**OLIGOMERIC
PROANTHOCYANIDINS
INTERVENTION STUDY ON THE
INTERGENERATIONAL EFFECTS
OF MALE REPRODUCTIVE
SYSTEM IN
BISPHENOL A-EXPOSED RATS**

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ABSTRACT

Infertility is among the diverse pathological conditions that beset the human society. Birth rate in developed countries has dwindled over the years and medical cases reported related to infertility especially amongst men are increasing dramatically. Oligomeric Proanthocyanidins (OPC) is one of the most powerful antioxidants that can be found naturally in the bark, seeds, fruits and leaves of a vast range of plants in the plant kingdom that helps to cure male infertility. A total of 36 male Sprague Dawley male rats, weighing approximately 300 grams were randomly divided into 6 groups (n=6) and labeled as negative control (NEC) group, positive control (POC) group, low dose OPC (OPC10) group, high dose OPC (OPC20) group, BPA plus low dose OPC (BPA+OPC10) group and BPA plus high dose OPC (BPA+OPC20) group. Unlike in NEC, OPC10 and OPC20 groups, rats in POC, BPA+OPC10 and BPA+OPC20 groups were exposed to 200 mg/kg of Bisphenol A (BPA) for 21 days. Rats in BPA+OPC10 and BPA+OPC20 groups were then supplemented with 10 µg/kg body weight and 20 µg/kg body weight OPC, respectively. However, rats in OPC10 and OPC20 were only supplemented with respective dosage of OPC in the absence of BPA induction. After 21 days of treatment and supplementation, the male rats were randomly mated with female rats with a ratio of 1:1 to produce the F₁ generation. After the females were confirmed to be pregnant, the P generation male rats were euthanized; their sperm, blood and testes were collected to be analyzed. Similar analyses were conducted on the F₁ generation after reaching 10 weeks old. The results showed that OPC possessed powerful antioxidative characteristics and was able to alleviate the detrimental intergenerational effects of BPA. Most of the parameters analyzed in BPA+OPC10 and BPA+OPC20 groups showed a significant increase in terms of their sperm concentration, motility, anogenital distance and seminiferous epithelial height in comparison to those of the NEC and POC groups (p<0.05). In fact, OPC specifically at 10 µg/kg body weight was able to ameliorate the detrimental effects of BPA in the F₁ generation by showing significant increment in sperm concentration, motility and morphology. In conclusion, OPC is a powerful antioxidant that is capable of ameliorating the negative effects of BPA and hence, becomes an alternative to treat male infertility. However, the exact underlying mechanism of action of OPC on male reproductive system is yet to be further investigated.

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TABLE OF CONTENTS

	Page
CONFIRMATION BY PANEL OF EXAMINERS	ii
AUTHOR'S DECLARATION	iii
ABSTRACT	iv
ACKNOWLEDGMENT	v
TABLE OF CONTENTS	vi
LIST OF TABLES	x
LIST OF FIGURES	xi
LIST OF SYMBOLS	xiv
LIST OF ABBREVIATIONS	xvi
CHAPTER ONE: INTRODUCTION	1
1.1 Background of Studies	1
1.1.1 Male Infertility	1
1.1.2 Oligomeric Proanthocyanidins (OPC) as Antioxidants	1
1.2 Problem Statement	2
1.3 Research Objectives	2
1.3.1 General Objective	2
1.3.2 Specific Objectives	3
1.4 Scope and Limitations	3
1.5 Significance of Study	3
CHAPTER TWO: LITERATURE REVIEW	5
2.1 Male Reproductive System	5
2.1.1 Anatomy of the Male Reproductive System	5
2.1.2 External Organs	6
2.1.2.1 <i>Penis</i>	6

CHAPTER ONE

INTRODUCTION

1.1 Background of Studies

1.1.1 Male Infertility

Male infertility specifically refers to the incapability of a male to conceive a fertile female usually due to low sperm count and poor sperm quality. Infertility is among the diverse pathological conditions that beset the human society. Birth rates in developed countries have dwindled over the years and medical cases related to male infertility were reported to increase dramatically (Virtanen *et al.*, 2017). Cooper *et al.* (2010) reported that young men aged between 18-21 years are of poor semen quality. Recent study by Virtanen *et al.* (2017) reported that the major factor causing this problem is influenced by the man's lifestyle; men who smoke and drink alcohol are more prone to have low sperm count and poor sperm quality. The exposure to chemicals in tobacco leads to endocrine disruption which then results in infertility. Oxidative stress which results in the DNA damage of spermatozoa is closely related to poor sperm function and infertility in male (Shen *et al.*, 1999). However, of all the factors contributing to human infertility, approximately half of all cases reported is mainly caused by the male (Miyamoto *et al.*, 2012). Hence, thorough research regarding the potency and ability of antioxidant therapies must be conducted in order to cure this consequential issue. Various types of traditional herbs and natural antioxidants such as oligomeric proanthocyanidins, *Phyllanthus gomphocarpus*, *Zingiber zerumbet* et cetera can be used as alternatives to drugs and medicines to overcome this problem.

1.1.2 Oligomeric Proanthocyanidins (OPC) as Antioxidants

Antioxidants are one of the important components for couples with infertility problem. In any fertility plan, it is crucial to protect sperm cells from free radical damage as it is capable of causing spermatogenic DNA damage. One can increase the