

**UNIVERSITI TEKNOLOGI MARA**

**TRENDS OF PHOSPHODIESTERASE 5 INHIBITORS,  
GLIBENCLAMIDE, & SIBUTRAMINE ADVERSE DRUG  
REACTION REPORTING IN MALAYSIA, AUSTRALIA AND  
CANADA**

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Dissertation submitted in partial fulfilment of the requirement for  
the Bachelor of Pharmacy

**FACULTY OF PHARMACY**

**2015**

## ACKNOWLEDGEMENT

All praise to Allah SWT, who blessed us with strength to complete this research successfully. I would like to express my deepest gratitude to my supervisor, Dr. Izyan bt. Abd Wahab, for her immeasurable amount of patience and guidance along the way to complete this research.

I would like to thank Adverse Drug Reactions Monitoring & Management unit of National Pharmaceutical Control Bureau for approving this research data collection. A sincere thank to the employees of NPCB, especially Puan Rokiah and Puan Syifa Izati for their cooperation in providing me the data for this research.

I would like to thank my research colleagues, Fatin Nursyafiqah binti Anuar, Azura binti Jalil and Nur Asyikin who help me along this study was conducted. Last but not least, thanks to my family members for their immense support and motivation.

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## ABSTRACT

**Background:** Phosphodiesterase 5 inhibitors such as sildenafil was originally developed for angina treatment, then discovered to have significant effect on erectile dysfunction. Sildenafil claimed to have high safety profile, but there are reports of serious adverse drug reactions (ADRs). Glibenclamide is an antidiabetic drug under sulphonylurea class. Sulphonylureas are the most prescribed oral hypoglycemic agents in Malaysia. Sibutramine is a serotonin, norepinephrine and dopamine reuptake inhibitor. It was used in obesity treatment and was withdrawn from the market in 2010. In Malaysia, PDE 5 inhibitors, glibenclamide & sibutramine are the most common poison found in the cancelled traditional complementary products within 2008-2013. There are limited knowledge whether this products are associated with ADRs.

**Objective:** This study aims to determine and compare the trends of ADR reporting of PDE 5 inhibitors, glibenclamide, and sibutramine in Malaysia, Australia and Canada.

**Method:** Data of ADR reports of PDE 5 inhibitors, glibenclamide and sibutramine ADR reporting were collected from the Malaysia National Pharmaceutical Control Bureau (NPCB), Australia Therapeutic Goods Administrations website and Health Canada website. All data were collected from 2008-2014 for PDE 5 inhibitors and glibenclamide, and 2008-2012 for sibutramine. Then, the data were transferred onto data collection forms and ADR terms were classified according to Medical Dictionary for Regulatory (MedDRA). All ADRs were identified whether known or unknown ADR based on product information. Descriptive analyses were carried out by using Microsoft Excel software version 2013.

**Result:** Generally, there is a decreasing trends of PDE 5 inhibitors ADR reports in Malaysia, Australia and Canada from 2008 to 2014. Nervous system disorders, eye disorders and cardiovascular disorders are the common ADRs reported associated with PDE 5 inhibitors. Blindness is the similar ADRs reported in all three countries. For glibenclamide, there is an increasing trend of ADR reports in Malaysia, but a decreasing trend in Australia and Canada. Gastrointestinal disorders, nervous system



## CHAPTER ONE

### INTRODUCTION

#### 1.1 Background study

##### 1.1.1 Phosphodiesterase 5 inhibitors

For decades, researchers has taking an interest in the potential pharmacotherapeutic use of Phosphodiesterase 5 inhibitor (PDE 5 inhibitor) <sup>[1]</sup>. PDE 5 is an enzyme that catalyze the formation of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP). Both cAMP and cGMP are the second messenger of nitric oxide (NO). NO stimulate the relaxation of the smooth muscle surrounding the blood vessel and causes vasodilation <sup>[2]</sup>. PDE 5 enzyme is expresses in the lungs, platelet, heart, vascular smooth muscle and corpus covernosum in the penis <sup>[3]</sup>. PDE 5 inhibitors inhibit the degradation of cGMP, thus maintaining the effects initiated by NO which is vasodilation <sup>[2]</sup>.

In 1980s PDE 5 inhibitors are originally developed for the treatment of angina and hypertension <sup>[4]</sup>. However, during the clinical trial, PDE 5 inhibitors show greater effects on erection of the penis <sup>[4]</sup>. In 1998, the first oral PDE 5 inhibitor, sildenafil was approved by the United State Food and Drugs Administrations (FDA) to treat erectile dysfunction <sup>[4]</sup>. Consequently, about 177 million of sildenafil prescriptions have been recorded over 170 countries all over the world <sup>[4]</sup>. Sildenafil is one of the recreational drugs that have been used excessively without proper indications and prescriptions <sup>[1]</sup>. Many people who consume sildenafil because of sexual satisfaction, to impress sexual partner or merely curious about sildenafil's effect <sup>[1]</sup>.

Sildenafil is not an over the counter drugs. However, due to advance technologies, sildenafil can be obtained through private prescription from the internet <sup>[5]</sup>. In the United Kingdom, sildenafil is found to be used along with methamphetamine and ecstasy in a club for sexual satisfaction purposes <sup>[5]</sup>. In Malaysia, the majority of men who have erectile dysfunction do not seek for pharmacological treatment <sup>[6]</sup>. Fear of the possible side effects of pharmacological treatment and embrassment are the