Chapter One

Introduction

1.1 Diabetes mellitus and Glimepiride

Diabetes is a major public health problem affecting 285 million people worldwide (Schwatz P, 2010). The prevalence of diabetes is projected to double globally by 2030 (Wild & Roglic, 2004). Poorly controlled diabetes leads to nephropathy with increased risk of renal failure, neuropathy and peripheral vascular disease with potential for loss of limbs, retinopathy with increased risk of blindness, and an increased risk of cardiovascular disease and stroke (WHO, 2012). However, good glycemic control can prevent or delay chronic disease-related microvascular complications as shown by the United Kingdom Prospective Diabetes Study (UKPDS) and the landmark Diabetes Control and Complications Trial *(*Lancet. 1998) (N Engl J Med. 1993) .

The pathophysiology of type 2 diabetes mellitus (T2DM) is characterized by relative decrease in insulin secretion and/or insulin resistance. Insulin resistance is a complex phenomenon exacerbated by obesity, particularly central obesity, and is believed to start at a young age because hyperinsulinemia is observed in preteens when both parents have diabetes. (Fujimoto *et al*., 2004) T2DM results following progressive loss of insulin secretion and 50% loss of β cells by the time of diagnosis. Therefore, β cell secretagogues are useful for achieving sufficient glycemic control. (Robertson & Porte, 1973; Reaven G**,** 1988)**.**

Sulfonylureas (SUs) are widely used in the management of T2DM as insulin secretagogues and are named for their common core configuration. They are classified as first- and second-generation SUs. First-generation SUs include long-acting chlorpropamide, tolbutamide, tolazamide, and acetohexamide. Substitutions at either end of the compound result in pharmacologic and pharmacokinetic differences among SUs. (Shukla *et al*.,2004)