Chapter 1  

**Introduction**

1.0 **INTRODUCTION**

Pharmaceutical drug products have become increasingly important to providing consumers with a myriad of treatments and cures that increase life expectancy and enhance lives (Lichtenberg F.R, 2003). According to U.S. Food and Drug Administration (US FDA), any substance intended for use in the diagnosis, cure, relief, treatment or prevention of disease is called as a drug. The drug which is protected by patent is a branded drug and the drug which is a copy of branded drug and is equivalent in terms of safety, efficacy, dosage and use is called a generic drug. According to regulatory definitions, generic drug products need to be identical to their reference with respect to the active substance, the route of administration as well as quality standards (Meredith P, 2003). Generic drugs are as effective and safe as branded drugs. Moreover, the greater use of generics need not negatively impact quality and in some cases may improve it.

The essential attribute of generic drugs is that they cost less than their original brand equivalents. The rising cost of medication has been contributing to the total overall cost of health care and thus receives considerable attention globally. Pharmaceutical expenditures concern not only consumers, but government payers, private health plans, and employers as well. A major strategy for lowering the cost of medication, and thereby reducing its contribution to total health care costs, has been the introduction of generic equivalents of brand name drugs - innovator drugs (Midhal et al., 2009). Generic drugs have captured more than 65% of the global market and account for 66% of prescriptions filled in the United States but for less than 13% of the cost (Shrank et al, 2009). This strategy has been effective in reducing total prescription cost by 11% without sacrificing quality (Haas et al., 2005). Thus, because of the importance of generic drugs in health care, it is imperative that the pharmaceutical quality, safety, and efficacy of generics should be reliably compared with the corresponding innovator drugs (brand-name drugs).

Bioavailability (BA) and bioequivalence (BE) studies play a major role in the drug development phases for both new drug products and their generic equivalents, and thus attract considerable attention globally (Chen et al., 2001). For both, these studies are also important in the post-approval period in the presence of certain
manufacturing changes. These measures of systemic exposure are assumed to relate in some way to safety and efficacy outcomes that may be expressed in biomarkers, surrogate endpoints, or clinical benefit endpoints (Chen et al., 2000).

In contrast to innovator drugs, which have to demonstrate their clinical efficacy and safety, generics are considered therapeutically equivalent based on simple bioequivalence testing. BE is a strategy to introduce generic equivalents of brand-name drugs (innovator drugs) through proper assessment as directed by the international regulatory authorities.

Peptic Ulcer disease encompasses both gastric and duodenal ulcers, and are defined as breaks in the mucosal surface >5 mm in size with depth to the submucosa. The past decade has witnessed a global rise in the prevalence of peptic ulcer disease which is unrelated to non-steroidal anti-inflammatory drugs (NSAIDs) or *Helicobacter pylori* infection. Peptic Ulcer disease has a tremendous effect on morbidity and mortality until the last decades of the twentieth century, when epidemiological trends started to point to an impressive fall in its incidence.

Although the pathogenesis of peptic ulcer disease is not fully understood, the three factors recognized are: infection with gram-negative *Helicobacter pylori*, increased hydrochloric acid secretion, and inadequate mucosal defense against gastric acid. *H. pylori* infection is more prevalent in developing countries, with some regions recording background prevalence close to 100% (Jyotheswaran et al., 1998). The proportion of *H. pylori* negative peptic ulcer disease has been increasing in developed countries (Arroyo et al., 2004).

Proton pump inhibitors (PPIs) have been widely used as acid inhibitory agents for the treatment of disorders related to gastric acid secretion for about 15 years. Proton pump inhibitors are one of the most effective groups of medications for the management of acid related disorders. These agents provide the most rapid symptomatic control and best healing of acid related disorders amongst the available agents.

In 1989, the FDA approved the first proton pump inhibitor (PPI) in the United States, omeprazole (Prilosec™). Lansoprazole (Prevacid®) was the second FDA-

Esomeprazole, a new proton pump inhibitor, is the first S-isomer of omeprazole and is the first such inhibitor to be developed as a single isomer. Esomeprazole has an improved pharmacokinetic profile leading to greater acid suppression than that produced by omeprazole, lansoprazole, pantoprazole and rabeprazole. Compared with other PPIs, esomeprazole has been shown to give superior outcomes on three key measures of antisecretory effect: (i) consistency amongst individuals (ii) duration over the 24-h cycle and (iii) overall impact on pH. Esomeprazole is indicated for the treatment of symptomatic gastroesophageal reflux disease (GERD), short term treatment and maintenance of erosive esophagitis and in combination with antibiotics for the treatment of H. pylori associated peptic ulcer disease.

Therefore, this present study was planned to compare pharmacokinetic profile and establish bioequivalence between the test and the reference formulations of Esomeprazole magnesium for delayed release oral suspension in healthy adult human male subjects under fasting condition.