1.0 INTRODUCTION

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite, and poor concentration. Moreover, depression often comes with symptoms of anxiety. These problems can become chronic or recurrent and lead to substantial impairments in an individual’s ability to take care of his or her everyday responsibilities. At its worst, depression can lead to suicide. Almost 1 million lives are lost yearly due to suicide, which translates to 3000 suicide deaths every day. For every person who completes a suicide, 20 or more may attempt to end his or her life (WHO, 2012).

Depression is a significant contributor to the global burden of disease and affects people in all communities across the world. Today, depression is estimated to affect 350 million people. The World Mental Health Survey conducted in 17 countries found that on average about 1 in 20 people reported having an episode of depression in the previous year. Depressive disorders often start at a young age; they reduce people’s functioning and often are recurring. For these reasons, depression is the leading cause of disability worldwide in terms of total years lost due to disability. The demand for curbing depression and other mental health conditions is on the rise globally. A recent World Health Assembly called on the World Health Organization and its member states to take action in this direction (WHO, 2012).

The established modes of treatment of depression consist of antidepressants, electroconvulsive therapy, formal psychotherapy, and depending on the availability of resources and factors pertaining to help seeking a combination of these treatments. Over the past several decades, pharmacologic management of major depressive disorder has evolved substantially. First-line pharmacotherapy for major depressive disorder is typically chosen from among the “newer antidepressants”—selective serotonin reuptake inhibitor (SSRI) (Sidney HK and Sakina JR, 2009).

Sertraline is a Selective Serotonin Reuptake Inhibitors (SSRIs). Sertraline hydrochloride has the following chemical name: (1S-cis)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-N-methyl-1-naphthalenamine hydrochloride (Pfizer, 2005). The
sertraline is presumed to be linked to its inhibition of CNS neuronal uptake of serotonin (5HT) into human platelets. It has only very weak effects on norepinephrine and dopamine neuronal reuptake, and no significant affinity for adrenergic (alpha1, alpha2, beta), cholinergic, GABA, dopaminergic, histaminergic, serotonergic (5HT1A, 5HT1B, 5HT2), or benzodiazepine receptors; antagonism of such receptors has been hypothesized to be associated with various anticholinergic, sedative, and cardiovascular effects for other psychotropic drugs (Grimsley SR and Jann MW, 1992).

Sertraline has been shown in numerous controlled studies to have similar efficacy to other selective serotonin (5-HT) re-uptake inhibitors (SSRIs) in the treatment of depression and anxiety disorders. The efficacy of sertraline extends even beyond the treatment of depression and anxiety to include utility in eating disorders, premenstrual dysphoric disorder (PMDD) and possibly substance abuse treatment. Along with other SSRIs, sertraline offers several advantages over older antidepressants, including improved patient tolerability, low risk of lethality in overdose and no dependence potential. In head-to-head comparisons, sertraline appears to be at least as well-tolerated as other SSRIs and may even have a more favourable side effect profile. Low potential for pharmacokinetic drug interactions is another advantage of sertraline. Unlike fluoxetine, fluvoxamine and paroxetine, sertraline is not a potent inhibitor of any of the cytochrome P450 isoenzyme systems. As a result of its proven efficacy, good tolerability and lack of pharmacokinetic interactions, sertraline should be considered first-line in the treatment of anxiety and depressive disorders.

Plasma concentrations of sertraline and desmethyl sertraline (major metabolite) (Devane CL et al. 2002) slowly appeared in plasma with peak concentrations (Cmax) occurring 4-8 h after ingestion (Tmax). Co-administration with food increased Cmax by approximately 25%, while Tmax decreased from 8 h post-dosing to 5.5 h. Sertraline is highly bound to plasma proteins (Ronfeld RA et al. 1997). Sertraline undergoes extensive first pass metabolism, multiple cytochrome P450 (CYP) isoforms appear to be responsible for the metabolism of sertraline (Kobayashi K et al 1999). The plasma elimination half-life (t1/2) in healthy volunteers is approximately 26 hours (Warrington SJ, 1991).
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). This strategy has been effective in reducing total prescription cost without sacrificing quality. 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 innovator drugs (Shrank WH et al 2009). The availability of generic formulation of sertraline will increase the choices for drug prescriptions in treatment of depression.

This study was designed to evaluate the quality of the generic formulation for assuring clinicians to prescribe generic formulation interchangeably with the original formulation with similar toxicity and efficacy. Considerably, this in vivo bioavailability study was necessary for market application of the generic formulation.

Therefore, the present study was designed to compare the bioavailability of single tablet of SERLIFT 100 mg (contains Sertraline hydrochloride equivalent to 100 mg sertraline) of Ranbaxy (M) SDN BHD with two tablets of ZOLOFT (contains sertraline hydrochloride equivalent to 50 mg sertraline; total dose 100 mg) of Pfizer (Malaysia) SDN BHD, in healthy, adult human subjects under fasting condition. The present study was conducted after taking approval from the JHIRB (Jamia Hamdard Institutional Review Board)

Objectives

Primary

To compare the pharmacokinetic profile of sertraline between the test formulation, SERLIFT 100 (contains Sertraline hydrochloride equivalent to 100 mg sertraline) and the reference formulation, ZOLOFT (each tablet contains sertraline hydrochloride equivalent to 50 mg sertraline; total dose 100 mg) in healthy, adult, human subjects under fasting conditions.

Secondary

To assess the safety of SERLIFT and ZOLOFT