IN VIVO COMPARISON OF TWO PAKISTANI BRANDS OF CEPHALEXIN CAPSULES UNDER FASTING

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ABSTRACT

Comparative *in vivo* study of two commercially available cephalexin capsules (Ceporex and Zeporin) was conducted as a randomized, single-dose crossover study under fasting conditions. Serial blood samples were collected at 0.25, 0.5, 0.75, 1.25, 1.5, 2, 3, 4, 6 and 8 h. A washout period of seven days was kept between each study period. Plasma cephalexin concentrations were analyzed using a reversed-phase high-performance liquid chromatography while absorption profiles were derived using Wagner-Nelson equation. Zeporin capsules were compared with innovator brand, Ceporex using pharmacokinetic parameters C_{max}, T_{max}, AUC_{0-t}, and $AUC_{0-\infty}$. Moreover, the 90% confidence interval (CI) for the ratio of logarithmic transformed C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ was also used to determine bioequivalence. The 90% CI for the log transformed data for C_{max}, AUC_{0-t}, and $AUC_{0-\infty}$ for both the products fell within the prescribed limits of bioequivalence (90-111%). The statistical evaluation of average pharmacokinetic parameters of $AUC_{0-\infty}$, AUC_{0-t} and C_{max} demonstrated lack of statistically significant difference in two brands. No lag time was observed in any of the volunteers indicating that both the products started to release their drug content immediately after administration.

Keywords: Cephalexin, Pharmacokinetics, bioequivalence, *in vivo* performance

INTRODUCTION

Concern about lowering health care costs has resulted in a tremendous increase in the use of generic drug products; currently about one half of all prescriptions written are for drugs that can be substituted with a generic product (Miller and Strom, 1990). According to the FDA, "pharmaceutical equivalents" are drug products that contain identical active ingredients and are identical in strength or concentration, dosage form, and route of administration (FDA, 1991). The availability of different formulations of the same drug substance given at the same strength and dosage form poses a special challenge to health care professionals, making these issues very relevant to pharmacists in all practice settings.

Cephalexin is a first generation cephalosporin antibiotic and is administered by mouth for the treatment of susceptible infections including those of the respiratory and urinary tracts and of skin (Wise, 1990; Dave, 1991). In Pakistan, no regulation has been adopted to conduct *in vivo* comparison of generic formulation in the local population. Therefore, the present study was designed to determine the *in vivo* performance of two cephalexin brands in domestic situation to ensure the rational usage of this valuable medicinal agent. The protocols of the study were designed according to the guidelines of WHO/FDA for bioequivalence studies.

MATERIALS

Cephalexin (GlaxoSmithKline Pakistan Limited), methanol HPLC grade (Merck-Germany), acetonitrile HPLC grade (Merck-Germany), phosphoric acid (Merck-Germany), disodium hydrogen phosphate (Fluke-Switzerland), perchloric acid (Merck-Germany), potassium dihydrogen phosphate (Merck-Germany), Ceporex Capsules 500mg (GlaxoSmithKline, Lahore, Pakistan; Mfg Date, 10/05 and Exp. Date. 10/07) and Zeporin Capsules 500mg (Z-Jans Pharmaceuticals Ltd. Peshawar, Pakistan, Mfg Date. 12/05 and Exp. Date 12/07).

METHODS

Drug content determination

Contents of both reference Capsules, Ceporex and test Capsules, Zeporin were triturated