Introduction
Clinical Pharmacokinetic studies have indicated that variability in drug plasma concentrations may be generated by co-administration of oral drug with meals, with other drugs, or by a change in drug formulation. For drugs with a narrow therapeutic index and/or steep dose response curve, this variability may have clinically significant implications. Given the trend toward multiple drug therapy and the convenience and compliance benefits of administering drugs at meal times, the number of reports of interactions of the above types has increased.

The seriousness of some interactions has prompted regulatory review, and the pharmaceutical industry has expanded its efforts to investigate potential interactions influencing drug absorption both in preclinical screening and in clinical pharmacokinetic studies.

It is important to consider drug-food interactions because the pharmacokinetics of a prescribed drug may be affected when co-administered with food. Recently, Welling (1996), classified drug-food interactions into 5-categories: those causing reduced, delayed, increased and accelerated absorption and those in which food has no effect. The variable, but important effects of food have long been recognised. Some drugs belong to more than one category for example aspirin, avitriptan, cilazapril and pidotimod, whose absorption may be both reduced and delayed in presence of food (Singh, 1999). On the other hand, the absorption of midazolam and triazolam is delayed and the extent of bioavailability is increased when ingested with grapefruit juice (Kupferschmidt et al., 1995). There are other instances in which the rate of absorption may be decreased or delayed but the overall bioavailability remains unchanged (Singh, 1999). Also, there are few interactions in which the rate of drug absorption is slightly enhanced or accelerated, but the bioavailability is not significantly modified by food (Delhotal-Landes et al., 1988, Granneman et al., 1992, Bianchetti et al., 1995, Lukkari et al., 1996, Dingemanse et al., 1998). Thus, dietary factors have long been recognised to exert profound physiologic, biochemical and pharmacokinetic effects in laboratory animals and in human subjects.

The human diet is highly heterogeneous in preparation, chemical composition, volume and times of consumption. Accordingly, dietary effects on drug kinetics vary
widely in subjects of different age, sex, socioeconomic status, ethnic background and region. Dietary effects can vary in the same subject with time and season, as changes occur in factors that influence dietary habits (Vesell, 1984). As a result of numerous studies on food-drug interactions, several fundamental principles have emerged, as have certain problems whose resolution requires more investigation and fresh insight (Vesell, 1984).

The bioavailability of a drug is usually estimated in a fasting state to avoid the complicated interference of food. This is a regulatory requirement. However, it is important to investigate the effects of food on the bioavailability, as drugs are often administered after food intake, and alteration of the bioavailability caused by food, if it occurs, may cause significant changes in clinical response. There is considerable evidence to suggest that the absorption of various antimicrobial agents, including oral cephalosporins, is influenced by the presence of food in the gastrointestinal tract (Harvengt et al., 1973, Glynne et al., 1978, Haginaka et al., 1979).

Solid foods have been shown to decrease the stomach-emptying rate, but gastrointestinal motility increases in the presence of food. Because most drugs are absorbed from the small intestine, delayed stomach emptying may delay the onset and reduce the rate of absorption. Food may reduce the extent of absorption of drugs that are unstable at low pH. On the other hand, prolonged retention in the stomach may increase the percentage of an administered drug that is in solution when it eventually passes into the small intestine and may thereby increase the extent of absorption. For drugs that are absorbed by active and saturable processes, slow stomach emptying may increase the extent of absorption because of the non-saturation of carrier mechanisms. Increased intestinal motility in the presence of food may promote drug absorption because of the faster dissolution and greater exposure of drug molecules to the intestinal epithelium, but it may also reduce absorption because of an increased drug transit rate through the intestine.

Cephalosporins available today are members of the β-lactam group of antimicrobial drugs. The most widely used classification system is an arbitrary generation
scheme, which refers to differences in antimicrobial activity rather than dates of introduction. Cephalosporins of the second generation are characterized by a greater potency against gram-negative bacteria; like α-lactamase producing strains of *H. influenzae* and *M. catarrhalis*. Cefaclor is classified as a second-generation cephalosporin, however, the drug also displays features of a first generation cephalosporins. Cefaclor is a well tolerated, 90% of patients in clinical trials did not experience any Adverse Drug Reaction. Most frequently reported adverse reactions include hypersensitivity (about 1.4%) and diarrhea (about 1.3%). In general, adverse drug reactions are mild to moderate in nature and are either self-limited or subside upon cessation of drug exposure.

Cephalosporins antibiotics also show various phenomena as in cases in which absorption is not affected by food (Lode et al., 1979, Barbhaiya et al., 1990a), in which absorption is hindered by food intake (Harvengt et al., 1973, Hodges et al., 1978), or on the contrary in which absorption is accelerated by food intake (Chin et al., 1987, Lode et al., 1979). The bioavailability of cefaclor has been reported to be reduced by food intake (Kamiki et al., 1979, Barbhaiya et al., 1990a). However, in a recent study with the modified release formulation of cefaclor the bioavailability of cefaclor was found to be increased with the co-administration of cefaclor with food (Khan et al., 2001). Therefore, a similar study was planned with conventional formulation to rule out the effect of modified formulation in the increase of cefaclor bioavailability.

There is a wide variation in dietary practices and beliefs among populations throughout the world (Berti and Leonard 1998). The nutrients, trace substances and non-nutrients present in the food are known to influence the bioavailability of drugs (Van Bjaderen 1997, Barthe et al., 1999). The US:FDA guidelines prescribe the use of high fat non-vegetarian food for food-drug interaction studies (http://www.fda.gov/gov/cder/guidance/index.htm).

There is thus a need for a complete evaluation of the influence of different kinds of food on the bioavailability of drugs (Melander and Mc Lean, 1983). In India, the majority of population eats vegetarian food, and most non vegetarians cannot afford to
eat meat more than once a week. There is no information on the pharmacokinetics of cefaclor in the Indian population or on the effect of Indian types of food on its absorption.

In the present study, accordingly, focus was put on how the bioavailability of cefaclor would be affected by food, as well as on whether the bioavailability depends on the type of food.