LITERATURE REVIEW:

1. **Seema Gupta et. al. (2004)** showed that Itopride, a novel Prokinetic agent is unique and different from the available Prokinetics because of its dual mode of action and lack of significant drug interaction potential. Thus a Prokinetic drug like Itopride, by virtue of its efficacy and tolerability could be considered as a drug of first choice and a welcome addition to the drug armamentarium for the symptomatic treatment of NUD and other gastric motility disorders including functional bowel disorders.

2. **Hyun Chul Lim et. al. (2008)** stated that in early studies, Itopride had been known to stimulate only the upper gut. Itopride significantly increased the contractile force of only the gastric atrium and duodenum of conscious dogs. In the same study, Itopride restored dopamine induced inhibition of contractions in the gastric atrium and duodenum and the gastro duodenal responses to ACh were enhanced by Itopride and neostigmine. In their following studies, the IC50 of Itopride for guinea pig gastric AChE inhibition was 50 times as large as that of neostigmine. Therefore these authors considered that Itopride stimulates endogenous ACh release by blocking dopamine D2 receptor and accumulates endogenous ACh by anticholinesterase activity.

3. **Santosh U. Zate (2010)** studied that a number of analytical methods for quantitative estimation of Itopride hydrochloride in pharmaceutical products are known. Procedures based on LC-MS, RP-HPLC, spectrofluorimetry, and Spectrophotometry is to be found in literature. Though these methods are sensitive, they require expensive instruments and trained personnel. Despite the availability of sophisticated and sensitive instruments, for routine quantitative analysis, a simple and cost effective analytical method is always preferred.

4. **Charman WN (1997)** stated that the effect of food on drug oral bioavailability is extremely complex. Based on the physicochemical properties of the compounds, physiological changes induced by the intake of food mainly happen in slowing of gastric emptying rate and the increase in gastric pH. The pH differences in the contents of the upper GI tract between fed and fasted states can influence the dissolution and absorption of weakly acidic and basic drugs. Elevation of gastric pH following a meal may enhance the dissolution of a weak acid in the stomach but inhibit that of a weak base. Furthermore, food inhibits the rate of gastric emptying; prolonged retention in the
stomach may increase the proportion of drug that dissolves prior to passage into the small intestine, which is the primary site of drug absorption.

5. **Mohammad Yaheya Mohammad Ismail (2009)** Interaction between foods and drugs can have profound influence on the success of drug treatment and on the side effect profiles of many drugs. The clinical significance of drug-food interactions can be variable. Drug-food interactions can lead to a loss of therapeutic efficacy or toxic effects of drug therapy. Generally, the effect of food on drugs results in a reduction in the drug’s bioavailability; however, food can also alter drug clearance. Some foods greatly affect drug therapy, resulting in serious side effects, toxicity, or therapeutic failure. In some instances, the interaction may have a beneficial effect by increasing drug efficacy or diminishing potential side effects. Pharmacists in every practice setting need to be vigilant in monitoring for potential drug-food interactions and advising patients regarding foods or beverages to avoid when taking certain medications. It is imperative for pharmacists to keep up-to-date on potential drug-food interactions of medications, especially today’s new drugs, so that they may counsel properly to the patients.

6. **Booth SL et. al. (1997)** says that like food, drugs taken by mouth must be absorbed through the lining of the stomach or the small intestine. Consequently, the presence of food in the digestive tract may reduce absorption of a drug. Often, such interactions can be avoided by taking the drug one hour before or two hours after eating. Dietary fiber also affects drug absorption. Pectin and other soluble fibers slow down the absorption of acetaminophen, a popular painkiller. Bran and other insoluble fibers have a similar effect on digoxin, a major heart medication. Certain vitamins and minerals impact on medications too. Large amounts of broccoli, spinach and other green leafy vegetables high in vitamin K, which promotes the formation of blood clots, can counteract the effects of heparin, warfarin and other drugs given to prevent clotting.

7. **Williams L et. al. (1996)** stated that not all medicines are affected by food, but many medicines can be affected by the food and it's time. For example, taking some medicines at the same time with food may affect the absorption of the medicine. The food may delay or decrease the absorption of the drug. This is why some medicines should be taken on an empty stomach. On the other hand, some medicines are easier to tolerate when taken with food. It is always advised to ask the doctor or pharmacist whether it's correct
to take the medicine with a snack or a meal or whether it should be taken on an empty stomach.

8. **Hepler CD et. al. (1990)** suggested that pharmacists in every practice setting need to be vigilant in monitoring for potential drug-food interactions and advising patients regarding foods or beverages to avoid when taking certain medications. It is imperative for pharmacists to keep up to date on potential drug-food interactions of medications, especially today’s new drugs, so that they may counsel properly. In providing drug information to patients, pharmacists often discuss potential side effects and how the medication should be taken. It is important to provide information to patients on when to take their medications in relation to food intake.

9. **Syed Faisal Aman et. al. (2010)** worked regarding food-drug interactions which were studied by collecting seventy five prescriptions from various hospitals. In most of the collected prescriptions, food-drug interactions were detected using the literature available. It was also found that only few studies have been carried out so far on the effect of food on drug disposition in the Asian population. Thus more studies on food-drug interactions particularly in the local population is recommended in order to determine the effect of food and food components on drug disposition and to the kinetics of the drugs which has not yet well highlighted in this part of the world.

10. **Gibaldi M et. al. (1991)** says that food-drug interaction is a wide domain and the food that a patient takes can affect the rate and extent of drug bioavailability to the body. It is now being acknowledged by an increasing number of pharmacists, physicians and other research workers in medical sciences. The potential for food-drug interactions is sufficiently great that the US Food and Drug Administration now requires studies as to the effects of food on drug absorption as part of biopharmaceutical characterization of almost every new drug intended for oral administration and this requirement is also being applied for new dosage forms of established drugs.

11. **L. D. Bornemann et.al. (1988)**, this group designed a study to examine the effect of food on the rate and extent of Amdinocillin pivoxil absorption. According to them the bioavailability of amdinocillin was not altered when Amdinocillin pivoxil was ingested 1 h before a standard breakfast, and it increased by 20% when Amdinocillin pivoxil was ingested with or 1 h after a standard breakfast. Amdinocillin pivoxil would be convenient
for patients since it may be taken with or without food. Amdinocillin pivoxil is recommended for administration on a three times daily regimen. At some point during drug therapy, the patient may need to take the drug at mealtime. Since the bioavailability is not pronouncedly affected by food, patients may conveniently take the drug with or without food.

12. **Nai-Ning Song et. al. (2004)** showed that elevated gastric pH may afford enhanced bioavailability of acid-labile drugs such as penicillin, erythromycin, and digoxin. For example, under acidic conditions, digoxin is hydrolyzed to the digoxigenin aglycone derivative, which has reduced pharmacodynamic activity. For ionic drugs, the fraction of drug available for the absorption may be altered by changing pH values, thus affect the intestinal permeability of the drug. Besides, Ph changing can affect the dissolution of some formulations, such as some coating materials used on tablets which are PH dependent, or some formulation excipients can also cause drug release to vary with pH, or impact on the permeability of insoluble film coatings used to provide controlled release of medicaments as well as on the overall dissolution and drug release patterns from various matrix-based sustained-release formulation.

13. **Fould et al. (1996)** was conducted a study in which three new formulations of azithromycin that comprise of tablets, sachet and paediatric suspension were studied. The mean relative bioavailability of azithromycin following administration of a standard high-fat breakfast was 96% when administered as two 250 mg tablets, 113% when administered as 500 mg suspension and 112% when administered as 1000 mg sachet. It was concluded that azithromycin tablets, suspension and sachet may be given without regard to meals.

14. **D’Arcy et. al. (1985)** stated that nitrofurantoin is usually used in treating urinary tract infection and it has been stated that its bioavailability is enhanced by food or propantheline.

15. **Alkhaled et al. (2008)** did a study in which clarithromycin extended release tablets were assessed in fasting and fed conditions. In the fed study, the Cmax and AUC of both formulations were significantly increased relative to the fasting study while the arithmetic mean Tmax was 5.7 (2.8) and 6.7 (2.5) hours. The 90% CI for the ratio of log-transformed Cmax and AUC values was within the acceptance range of 0.80 to 1.25.
Thus administration with food significantly increased the rate and extent of absorption of both products in this study, with no significant effect on their bioequivalence.

16. Kshirsagar et. al. (1987) has well documented the interaction between tetracyclines and milk and dairy products. In a study conducted by him, significant differences were observed in AUC and Cmax after administration of doxycycline with food in six healthy male volunteers. Therefore, patients should be advised to avoid dairy products when are on tetracycline therapy.

17. Lecaillon et al. (1980) compared pharmacokinetic parameters of cefroxadin and cephalaxin after simultaneous oral administration of the two cephalosporins to 21 subjects in a study conducted by. Both drugs were equally well absorbed from all of the tested formulations and the same percentages of the dose were recovered in the urine in all cases. Absorption was slowed after food intake, but the amounts absorbed were almost the same as those in fasted subjects.

18. Fassbender et al. (1993) in a review evaluated the pharmacokinetics of new oral cephalosporins, including esters, non-esters and the carbacephem loracarbef in healthy volunteers, as described in the literature. Regarding the effect of food, it was stated that food increases the bioavailability of the ester cephalosporins but does not affect the absorption kinetics of the other new drugs.

19. Vasu et al. (2000) conducted a study to compare the effect of two types of Indian breakfast on the bioavailability of cefuroxime axetil in healthy volunteers. Diet-A included idly with chutney and Diet-B included poori and dal-fry. The AUC and Cmax were significantly increased after oral administration of cefuroxime axetil with Diet-B as compared to Diet-A. It was concluded that the administration of cefuroxime axetil with poori and dal-fry may enhance the bioavailability when compared with idly and chutney.

20. Karim et al. (2003) studied the effect of different types of food that includes two vegetarian (high-fat and low-fat) and two non-vegetarian (high-fat and low-fat) diets in healthy volunteers after a single dose of 250 mg cefaclor capsule, the results showed that while the rate of absorption of cefaclor is significantly decreased after food, the extent of absorption and the rate of elimination are not significantly decreased in the presence of food.
21. **Kawakami et al (1994)** studied the effect of food on the interaction of ofloxacin with sucralfate in healthy volunteers that took a single oral dose of ofloxacin (200 mg) on 4 occasions: alone after overnight fasting or after breakfast (non-fasting), and with sucralfate fasting or nonfasting. There were no significant differences in the plasma concentration-time profiles of ofloxacin after ofloxacin alone between fasting and non-fasting conditions.

22. **Shah et al. (1999)** studied the effect of food on the absorption of ciprofloxacin in healthy male subjects. The results showed that administration of ciprofloxacin suspension, in either a fasted or fed state, was not associated with significant changes in Cmax or AUC0-inf values.

23. **Lee et al. (1997)** investigated the effects of food and sucralfate on the pharmacokinetics of levofloxacin in healthy subjects. Levofloxacin was administered by oral route under three conditions: fasting, fed, and fasting with sucralfate given 2 h following the administration of levofloxacin. The only consistent outcome of the co-administration of levofloxacin with a high-fat meal for most subjects was that levofloxacin absorption was delayed and Cmax was slightly reduced. It was concluded that the absorption of levofloxacin was slightly delayed by food, although the overall bioavailability of levofloxacin following a high-fat meal was not altered.

24. **Johnson et al. (1999)** did a study in which the pharmacokinetics of a single 200-mg dose of sparfloxacin were assessed in a 3-way crossover study that included 23 healthy male volunteers who had fasted, ingested 240 mL of skim milk, or had consumed a standard high-fat breakfast. It was found that neither skim milk nor the high-fat breakfast had a statistically significant effect on sparfloxacin absorption and, therefore, sparfloxacin can be administered without regard to the ingestion of milk or meals.

25. **Lehto et. al. (1995)** evaluated the effects of milk and a standard breakfast on the oral absorption of enoxacin in eight healthy volunteers in a randomized, balanced, four-way crossover design. In this study, 400 mg enoxacin was given with water, milk, a breakfast or with a breakfast and milk. The extent of enoxacin absorption was not affected by any of the three treatments. It was concluded that enoxacin can be taken together with food and dairy products.
26. Marino et. al. (2001) stated that no significant interactions have been identified between irbesartan and hydrochlorothiazide, nifedipine, simvastatin, tolbutamide, warfarin, magnesium and aluminum hydroxides, digoxin or food. According to these workers, irbesartan has demonstrated minimal potential for drug or food interactions in trials conducted.

27. Song et. al. (2002) reviewed the pharmacokinetic properties of five newer ACE inhibitors (trandolapril, moexipril, spirapril, temocapril and imidapril. Regarding food it was stated that moexipril should be taken 1 hour before meals, whereas other ACE inhibitors can be taken without regard to meal.

28. Mantyla et al (1984) conducted a study in which single oral doses of captopril were given to healthy volunteers at three different occasions; after fasting, after a standardized breakfast or with 50 ml of an antacid suspension. The peak captopril concentrations attained were 701±81 mg/ml after fasting, 351±56 mg/ml with an antacid and 140±14ng/ml after a meal. The peak concentrations were reached in 0.5, 0.9 and 1.5 h and the areas under the blood concentration-time curves were 782±86, 456±60 and 344±47 ng x h/ml respectively. From the results it is clear that food causes a decrease in the absorption of captopril and delay the hypotensive action of the drug.

29. Thomson et al (1997) conducted a study in which the influence of food on the bioavailability of omeprazole (20 mg) enteric coated tablet under repeated dose conditions was taken into evaluation. During each treatment period, an enteric coated tablet of omeprazole was taken once daily either under fasting conditions, or immediately before or after a standardized breakfast. The maximum plasma concentration was not found to differ significantly among any of the treatment regimens but the time to reach maximum plasma concentration was significantly different when fasting and after breakfast regimens were compared. It was concluded that under repeated dose conditions, food has no influence on the bioavailability of omeprazole given as the enteric-coated tablet formulation.

30. Marathe et al. (2000) studied pharmacokinetics and bioavailability of a metformin/glyburide tablet administered alone and with food. The results showed that food do not affect the bioavailability of either component to an appreciable extent.
31. **Pargal et al (1996)** conducted a study in Asian Indian volunteers, effect of food on the sustained release dosage forms of ibuprofen and flurbiprofen was examined. In study one a single 200 mg multiple-unit sustained release capsule of flurbiprofen were given while in study two, a single 800 mg erodible sustained release matrix tablet of ibuprofen were given after an overnight fast or a heavy vegetarian breakfast. Food produced a statistically significant increase in the mean maximal plasma concentration (Cmax) and area under the plasma concentration-time curve (AUC0-48) in study one while in study two although food did not affect the bioavailability of ibuprofen yet it significantly increase mean concentration of the first peak from 14.21±1.38 mg L-1 in fasting to 20.14±1.38 mg L-1 with food. Results indicate that changes in the plasma concentration versus time curves are primarily influenced by the nature of the formulation and the type of meal.