IMPACT OF DIFFERENT SUPPLEMENT DRUGS ON THE DISSOLUTION PROFILE OF ZANTAC® AND XANTID®.

A thesis report submitted to the Department of Pharmacy, East West University, Bangladesh, in partial fulfillment of the requirements for the Degree of Bachelor of Pharmacy.

Submitted By

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July, 2016

DECLARATION BY THE RESEARCH CANDIDATE

I, Sharmin Akther Liza ID: 2012-1-70-006, hereby declare that the dissertation entitled "**IMPACT OF DIFFERENT SUPPLEMENT DRUGS ON THE DISSOLUTION PROFILE OF ZANTAC® AND XANTID®**" submitted to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Honors) is a genuine & authentic research work carried out by me. The contents of this dissertation, in full or in parts, have not been submitted to any other institute or University.

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CERTIFICATION BY THE SUPERVISOR

This is to certify that the dissertation, entitled "**IMPACT OF DIFFERENT SUPPLEMENT DRUGS ON THE DISSOLUTION PROFILE OF ZANTAC® AND XANTID® "** is a research work done by **Sharmin Akther Liza (ID: 2012-1-70-006)**, in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy under my supervision.

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ENDORSEMENT BY THE CHAIRPERSON

This is to certify that the dissertation, entitled "**IMPACT OF DIFFERENT SUPPLEMENT DRUGS ON THE DISSOLUTION PROFILE OF ZANTAC® AND XANTID® "** is a research work done by, **Sharmin Akther Liza (ID: 2012-1-70-006)** under the guidance of **Md. Anisur Rahman**, Senior Lecturer, in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

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DEDICATION

This research paper is dedicated to my beloved parents, honorable faculties & loving friends.

ABSTRACT

The work was proposed to determine the impact of different supplements on the dissolution profile of Ranitidine (H_2 receptor blocker). Here two brands of Ranitidine tablets were used, Zantac (GlasoSmithKine) and Xantid (ACI). The supplements used in this research work are Calbo 500 (Calcium Supplement), Aristcal-D (Calcium and vitamin D supplement), Acical-M (Calcium, vitamin D and Multimineral supplement), Nutrum Gold (Multivitamin and Multimineral supplement), Filwel Silver (Multivitamin and Multimineral supplement). UV Spectroscopy method was used. Distilled water was used as the dissolution medium. Dissolution tests were run for an hour and the samples were taken and diluted after 20, 40, 60 minutes and absorbance of the diluted samples were taken, by putting the value of the absorbance in the equation of the standard curve percent dissolved amount of the tablets were calculated. After an hour the percent dissolved amount of individual Zantac, Zantac with Calbo 500, Zantac with Aristocal D, Zantac with Acical-M, Zantac with Nutrum Gold and Zantac with Filwel Silver were 94.09%, 47.84%, 72.6%, 48.47%, 94.27% and 97.22% respectively. After an hour the percent dissolved amount of individual Xantid, Xantid with Calbo 500, Xantid with Aristocal D, Xantid with Acical-M, Xantid with Nutrum Gold and Xantid with Filwel Silver were 96.47%, 49.22%, 72.89%, 48.84%, 97% and 98.38% respectively. From the result it was assumed that Calbo 500 and Acical-M has extreme effect, Aristocal D has moderate effect and Nutrum Gold and Filwel Silver has no effect on the dissolution of Zantac and Xantid. Therefore, absorbance and bioavailability of the drug can be affected in the presence of Calbo 500, Aristocal D and Acical-M. So these there supplements can not be co-administered with Zantac and Xantid. Nutrum Gold and Filwel Silver can be co-administered as these supplements has no effect on the dissolution.

Key words: *Dissolution, Ranitidine, Zantac, Xantid, Calbo 500, Aristocal D, Acical-M, Nutrum Gold, Filwel Silver, Distilled water, UV spectroscopy, Dilution, Absorbance, Percent dissolve, Co-administration, Effect.*

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CHAPTER ONE INTRODUCTION

The objective of this research project was to compare the effect of calcium supplement, vitamin D and minerals on Xantid, a product from ACI Pharmaceuticals Ltd and Zantac, a product from GlaxoSmithKline Pharmaceuticals Ltd. Zantac and Xantid are both H_2 receptor Blockers in the class of Ranitidine. In market these drugs are available in the form of Ranitidine Hydrochloride. 150mg tablet dosage form was used in this research project.

To conduct the research, dissolution test of individual Zantac and Xantid and also dissolution test of Zantac and Xantid with

- Calbo 500 (Calcium supplement)
- Aristocal D (Calcium and vitamin D supplement)
- Acical-M (Calcium, Vitamin D and Multimineral supplement)
- Nutrum Gold (Multivitamin and Multimineral supplement)
- Filwel Silver (Multivitamin and Multimineral supplement) were performed.

Dissolution test was performed using distilled water as all of these drugs are soluble in water. To perform dissolution test Dissolution testing apparatus was used and dissolution was run for 1 hour. Samples were taken after 20, 40 and 60 minutes. These samples were 10 times diluted and absorbance of these samples were taken by using UV Spectroscopy.

A standard curve was prepared by plotting different concentrations of drug against different absorbance. From the standard curve an equation was found. By putting the value of absorbance (sample) in this equation the concentration of the samples after dissolution was calculated. By this concentration value the effect of calcium supplement, vitamin D, multivitamins and minerals on the dissolution of the drug was determined

To fulfill the work some important tests were done such as Weight variation test, Hardness test, Thickness test to determine the quality of the product.

1.1 INTRODUCTION OF H_2 RECEPTOR BLOCKER

1.1.1 Descriptions:

Histamine H_2-receptor antagonists, also known as H2-blockers, are used to treat duodenal ulcers and prevent their return. They are also used to treat gastric ulcers and for some conditions, such as Zollinger-Ellison disease, in which the stomach produces too much acid. In over-the-counter (OTC) strengths, these medicines are used to relieve and/or prevent heartburn, acid indigestion, and sour stomach. H2-blockers may also be used for other conditions as determined by your doctor. H2-blockers work by decreasing the amount of acid produced by the stomach. H2-blockers are available both over-the-counter (OTC) and with your doctor's prescription.

Once a medicine has been approved for marketing for a certain use, experience may show that it is also useful for other medical problems. Although these uses are not included in product labeling, H2-blockers are used in certain patients with the following medical conditions:

- Damage to the stomach and/or intestines due to stress or trauma
- Hives
- Pancreatic problems
- Stomach or intestinal ulcers (sores) resulting from damage caused by medication used to treat rheumatoid arthritis (Mayo Clinic, 2016).

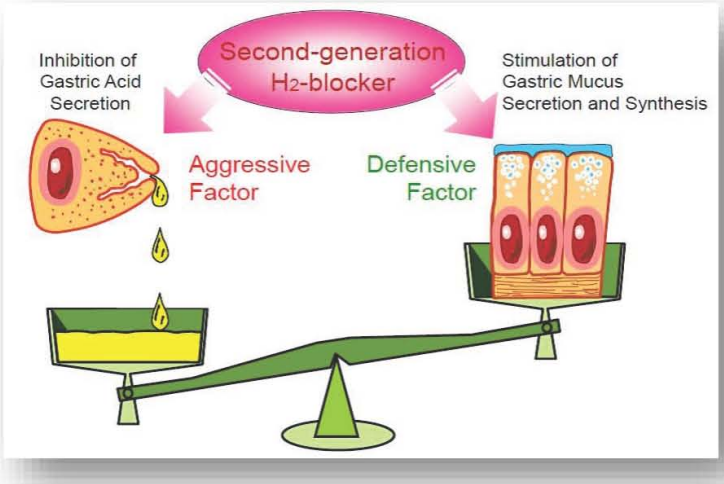

Figure 1.1: Dual action of second-generation H_2-blockers (Ichikawa and Ishihara, 2011).

1.1.2 Examples includes:

- Cimetidine
- Famotidine
- Lafutidine
- Nizatidine
- Ranitidine
- Roxatidine
- Tiotidine (Mayo Clinic, 2016).

1.1.3 Dosage Form: This product is available in the following dosage forms:

- Solution
- Tablet
- Capsule
- Suspension
- Injection
- Granule
- Capsule, Liquid Filled
- Tablet, Effervescent
- Syrup

- Powder for Suspension
- Tablet, Chewable
- Tablet, Disintegrating
- Powder for Solution (Mayo Clinic, 2016).

1.1.4 General Mechanism of H_2 Receptor Blockers

Stomach normally produces acid to help with the digestion of food and to kill germs (bacteria). This acid is corrosive so body produces a natural mucous barrier which protects the lining of the stomach.

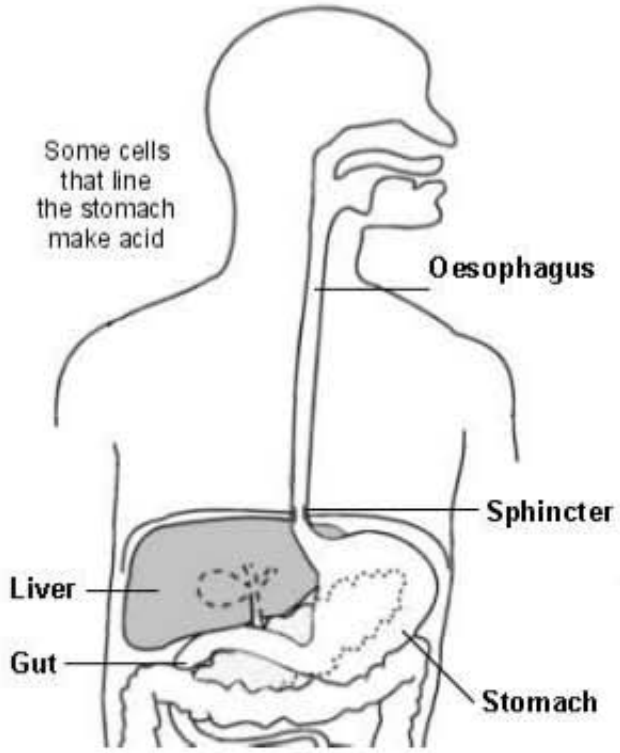

Figure 1.2: General mechanism of H_2 receptor blocker (Patient, 2013).

Histamine is a chemical naturally produced by certain cells in the body, including cells in the lining of the stomach, called the enterochromaffin-like cells (ECL cells). Histamine released from ECL cells then stimulates the acid-making cells (parietal cells) in the lining of the stomach to release acid. What H2 blockers do is stop the acid-making cells in the stomach lining from responding to histamine. This reduces the amount of acid produced by stomach. By decreasing the amount of acid, H2 blockers can help to

reduce acid reflux-related symptoms such as heartburn. This can also help to heal ulcers found in the stomach or in part of the gut (the duodenum) (Patient, 2013).

1.1.5 Side Effects:

1.1.5.1 Rare Side Effects:

- Abdominal pain
- back, leg, or stomach pain
- bleeding or crusting sores on lips
- blistering, burning, redness, scaling, or tenderness of skin
- blisters on palms of hands and soles of feet
- changes in vision or blurred vision
- confusion
- light-colored stools
- muscle cramps or aches
- sores, ulcers, or white spots on lips, in mouth, or on genitals
- sudden difficult breathing
- swelling of face, lips, mouth, tongue, or eyelids
- Swelling of hands or feet etc.

Some side effects may occur that usually do not need medical attention. These side effects may go away during treatment as body adjusts to the medicine (Mayo Clinic, 2016).

1.1.5.2 Common side effects:

- Constipation
- decrease in sexual desire
- diarrhea
- difficult urination
- dizziness
- drowsiness
- dryness of mouth or skin
- headache
- increased or decreased urination

- increased sweating
- loss of hair
- ringing or buzzing in ears
- runny nose
- Trouble in sleeping etc. (Mayo Clinic, 2016).

1.1.6 Interactions:

Certain medicines should not be used at or around the time of eating food or eating certain types of food since interactions may occur. Using alcohol or tobacco with certain medicines may also cause interactions to occur (Mayo Clinic, 2016).

1.1.7 Other Medical Problems:

The presence of other medical problems may affect the use of H_2 Blockers, especially,

- Kidney disease or
- Liver disease—The H_2-blocker may build up in the bloodstream, which may increase the risk of side effects.
- Phenylketonuria (PKU)—Some H_2-blockers contain aspartame. Aspartame is converted to phenylalanine in the body and must be used with caution in patients with PKU. The Pepcid AC brand of famotidine chewable tablets contains 1.4 mg of phenylalanine per 10-mg dose. The Pepcid RPD brand of famotidine oral dispersible tablets contains 1.05 mg of phenylalanine per 20-mg dose. The Zantac brand of ranitidine tablets contains 2.81 mg of phenylalanine per 25-mg dose and 16.84 mg of phenylalanine per 150-mg dose.
- Porphyria (rare family disease that affects the way your body digests food)—May make condition worse in patients who have acute porphyria.
- Weakened immune system (difficulty fighting infection)—Decrease in stomach acid caused by H2-blockers may increase the possibility of a certain type of infection (Mayo Clinic, 2016).

1.1.8 Precautions: Precaution should be maintained in case of,

- Allergy
- Pregnancy
- Breast feeding

It should be remembered that certain medicines, such as aspirin, and certain foods and drinks (e.g., citrus products, carbonated drinks) irritate the stomach and may make problem worse.

Cigarette smoking tends to decrease the effect of H2-blockers by increasing the amount of acid produced by the stomach. This is more likely to affect the stomach's nighttime production of acid. While taking H2-blockers, smoking should be completely stopped, or at least should not smoke after taking the last dose of the day.

Drinking alcoholic beverages while taking an H_2-receptor antagonist has been reported to increase the blood levels of alcohol worse (Mayo Clinic, 2016).

1.2 INTRODUCTION OF RANITIDINE

Ranitidine is in a group of drugs called histamine-2 blockers. Ranitidine works by reducing the amount of acid your stomach produces (Drugs.com, 2000).

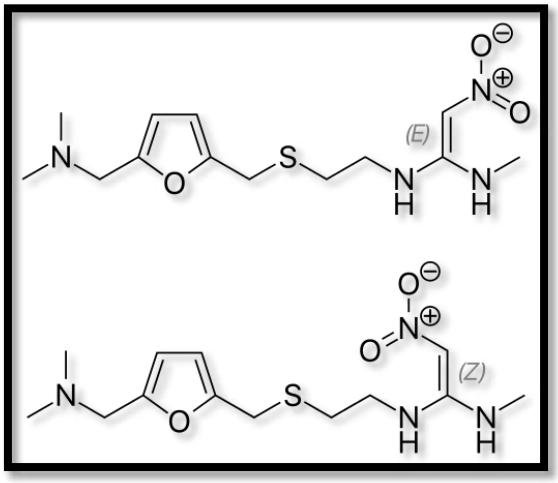

Figure 1.3: Structural formula of ranitidine (Wikipedia, 2016).

1.2.1 Systematic (IUPAC) name: N-(2-[(5-[(dimethylamino) methyl] furan-2-yl) methylthio] ethyl)-N'-methyl-2-nitroethene-1, 1-diamine (Wikipedia, 2016).

1.2.2 History:

Ranitidine was first prepared as AH19065 by John Bradshaw in the summer of 1977 in the Ware research laboratories of Allen & Han Burys Ltd, part of the Glaxo organization. Its development was a response to the first in class histamine H_2 receptor antagonist, cimetidine, developed by Sir James Black at Smith, Kline and French, and launched in the United Kingdom as Tagamet in November 1976. Ranitidine was the result of a rational drug-design process using what was by then a fairly refined model of the histamine H_2 receptor and quantitative structure-activity relationships. Glaxo refined the model further by replacing the imidazole ring of cimetidine with a furan ring with a nitrogen-containing substituent, and in doing so developed ranitidine. Ranitidine was found to have a far-improved tolerability profile (i.e. fewer adverse drug reactions), longer-lasting action, and 10 times the activity of cimetidine. Ranitidine has 10% of the affinity that cimetidine has to CYP450, so it causes fewer side effects. Ranitidine was introduced in 1981 and was the world's biggest-selling prescription drug by 1987. It has since largely been superseded by the even more effective proton-pump

inhibitors, with omeprazole becoming the biggest-selling drug for many years. When omeprazole and ranitidine were compared in a study of 144 people with severe inflammation and erosions or ulcers of the esophagus, 85% of those treated with omeprazole healed within eight weeks, compared to 50% of those given ranitidine. In addition, the omeprazole group reported earlier relief of heartburn symptoms (Wikipedia, 2016).

1.2.3 Indications:

- Relief of heartburn
- Short-term and maintenance therapy of gastric and duodenal ulcers
- Ranitidine can also be given with NSAIDs to reduce the risk of ulceration. Proton-pump inhibitors (PPIs) are more effective for the prevention of NSAID-induced ulcers.
- Pathologic gastrointestinal (GI) hyper secretory conditions such as Zollinger—Ellison syndrome.
- Gastroesophageal reflux disease (GERD).
- Erosive esophagitis.
- Part of a multidrug regimen for *Helicobacter pylori* eradication to reduce the risk of duodenal ulcer recurrence.
- Recurrent postoperative ulcer.
- Upper GI bleeding.
- Prevention of acid-aspiration pneumonitis during surgery.
- Prevention of stress-induced ulcers in critically ill patients (Wikipedia, 2016).

1.2.4 Pharmacodynamics: Ranitidine is a histamine H2-receptor antagonist, is used to block the action of histamine on parietal cells in the stomach, decreasing acid production by these cells. These drugs are used in the treatment of dyspepsia, however their use has waned since the advent of the more effective proton pump inhibitors. Like the H1-antihistamines, the H2 antagonists are inverse agonists rather than true receptor antagonists (Drugs.com, 2000).

1.2.4.1 Mechanism of action: The H2 antagonists are competitive inhibitors of histamine at the parietal cell H2 receptor. They suppress the normal secretion of acid by parietal cells and the meal-stimulated secretion of acid. They accomplish this by two mechanisms: histamine released by ECL cells in the stomach is blocked from binding

on parietal cell H2 receptors which stimulate acid secretion, and other substances that promote acid secretion (such as gastrin and acetylcholine) have a reduced effect on parietal cells when the H2 receptors are blocked (Drugs.com, 2000).

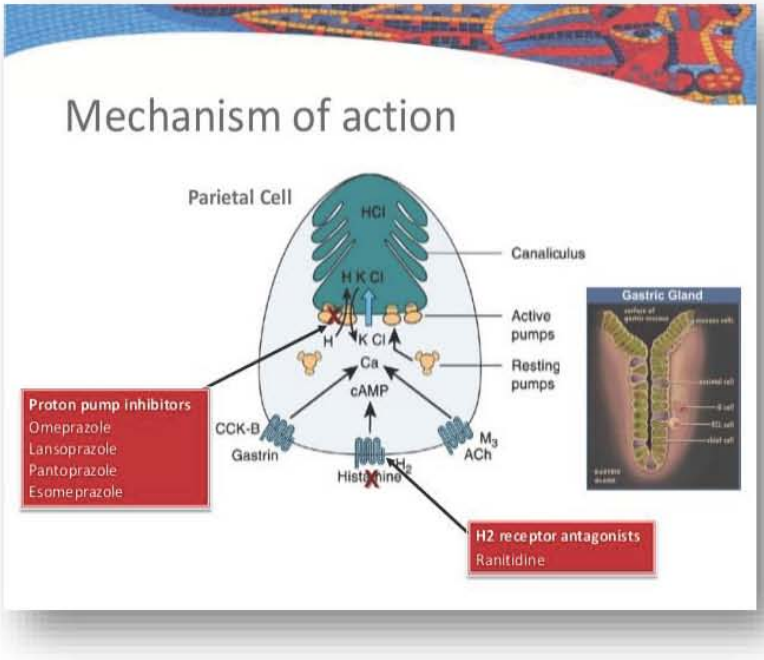

Figure 1.4: Mechanism of action of Ranitidine (Ichikawa and Ishihara, 2011).

1.2.5 Some other factors of ranitidine, (Drug Bank, 2005),

1.2.5.1 Absorption: Approximately 50% bioavailability orally.

1.2.5.2 Volume of distribution:

- 1.4 L/kg
- 1.76 L/kg [clinically significant renal function impairment (creatinine clearance 25 to 35 mL/min)]

1.2.5.3 Protein binding: 15%

1.2.5.4 Metabolism: Hepatic. Ranitidine is metabolized to the N-oxide, S-oxide, and N-dimethyl metabolites, accounting for approximately 4%, 1%, and 1% of the dose, respectively.

1.2.5.5 Route of elimination: The principal route of excretion is the urine (active tubular excretion, renal clearance 410mL/min), with approximately 30% of the orally administered dose collected in the urine as unchanged drug in 24 hours.

1.2.5.6 Half-life: 2.8-3.1 hours

1.2.5.7 Clearance:

- 29 mL/min [clinically significant renal function impairment]
- 3 mL/min/Kg [neonatal patients]

1.2.5.8 Toxicity: LD_{50}=77mg/kg (orally in mice). Symptoms of overdose include muscular tremors, vomiting, and rapid respiration.

1.2.5.9 Affected organisms: Humans and other mammals.

1.2.6 Ranitidine side effects: (Drugs.com, 2000),

1.2.6.1 Serious side effects are,

- Chest pain, fever, feeling short of breath, coughing up green or yellow mucus.
- Easy bruising or bleeding, unusual weakness
- Fast or slow heart rate.
- Problems with your vision.
- Fever, sore throat, and headache with a severe blistering, peeling, and red skin rash or nausea, stomach pain, low fever, loss of appetite, dark urine, clay-colored stools, jaundice (yellowing of the skin or eyes).

1.2.6.2 Less serious side effects are,

- Headache (may be severe).
- Drowsiness, dizziness.
- Sleep problems (insomnia).
- Decreased sex drive, impotence, or difficulty having an orgasm or
- Swollen or tender breasts (in men).

- Nausea, vomiting, stomach pain or
- Diarrhea or constipation.

1.2.7 Dosing:

1.2.7.1 For oral dosage forms (syrup, tablets, and effervescent tablets): (Mayo Clinic, 2016),

To treat active duodenal ulcers:

- Older adults, adults, and teenagers—150 milligrams (mg) two times a day. Some people may take 300 mg once a day at bedtime.
- Children and infants—2 to 4 mg per kilogram (kg) (1 to 2 mg per pound) of body weight twice a day. However, the total dose will not be more than 300 mg a day.

To maintain healing of duodenal ulcers:

- Older adults, adults, and teenagers—150 mg once a day at bedtime.
- Children and infants—2 to 4 mg per kg (1 to 2 mg per pound) of body weight once a day. However, the total dose will not be more than 150 mg a day.

To treat erosive esophagitis:

- Older adults, adults, and teenagers—150 mg four times a day
- Children and infants—5 to 10 mg per kg (2.3 to 4.6 mg per pound) of body weight per day, usually divided and given in two doses during the day.

To treat benign gastric ulcers:

- Older adults, adults, and teenagers—150 mg two times a day.
- Children and infants—2 to 4 mg per kg (1 to 2 mg per pound) of body weight twice a day. However, the total dose will not be more than 300 mg a day.

To maintain healing of gastric ulcers:

- Older adults, adults, and teenagers—150 mg once a day at bedtime.

- Children and infants—2 to 4 mg per kg (1 to 2 mg per pound) of body weight once a day. However, the total dose will not be more than 150 mg a day.

To treat heartburn, acid indigestion, and sour stomach:

- Adults and teenagers—150 mg with water when symptoms start. The dose may be repeated once in twenty-four hours. Do not take more than 300 mg in twenty-four hours.
- Children—Dose must be determined by doctor.

To prevent heartburn, acid indigestion, and sour stomach:

- Adults and teenagers—150 mg with water taken thirty to sixty minutes before eating a meal or drinking beverages you expect to cause symptoms. Do not take more than 300 mg in twenty-four hours.
- Children—Dose must be determined by doctor.

To treat gastroesophageal reflux disease:

- Older adults, adults, and teenagers—150 mg two times a day. Your dose may be increased if needed.
- Children and infants—5 to 10 mg per kg (2.3 to 4.6 mg per pound) of body weight per day, usually divided and given in two doses during the day.

1.2.7.2 For injection dosage form: (Mayo Clinic, 2016),

To treat duodenal ulcers, gastric ulcers, or conditions in which the stomach produces too much acid:

- Older adults, adults, and teenagers—50 milligrams (mg) injected into a muscle every six to eight hours. Or, 50 mg injected slowly into a vein every six to eight hours. Instead, you may receive 6.25 mg per hour injected slowly into a vein around the clock. However, most people will usually not need more than 400 mg a day.

To treat duodenal or gastric ulcers:

- Children—2 to 4 mg per kilogram (kg) (1 to 2 mg per pound) of body weight per day, usually divided and injected slowly into a vein every six to eight hours. However the total dose will not be more than 50 mg every six to eight hours.

1.2.8 Warnings and precautions: (Wikipedia, 2016),

1.2.8.1 Disease-related concerns:

With gastric malignancies, relief of symptoms due to the use of ranitidine does not exclude the presence of a gastric malignancy. In addition, with kidney or liver impairment, ranitidine must be used with caution. Finally, ranitidine should be avoided in patients with porphyria, as it may precipitate an attack.

1.2.8.2 Pregnancy:

This drug is rated pregnancy category B in the United States.

1.2.8.3 Lactation:

Ranitidine enters breast milk, with peak concentrations seen at 5.5 hours after the dose in breast milk. Caution should be exercised when prescribed to nursing women.

1.2.8.4 Children:

In children, the use of gastric acid inhibitors has been associated with an increased risk for development of acute gastroenteritis and community-acquired pneumonia. A cohort analysis including over 11,000 neonates reported an association of H_2 blocker use and an increased incidence of necrotizing enterocolitis in very-low-birth-weight (VLBW) neonates.

1.3 INTRODUCTION OF ZANTAC (Ranitidine)

Each tablet contains 150 mg of ranitidine as ranitidine hydrochloride (Drugs.com, 2016).

1.3.1 Indications and Usage for Zantac: (Drugs.com, 2016),

Zantac is indicated in:

1. Short-term treatment of active duodenal ulcer. Most patients heal within 4 weeks. Trials available to date have not assessed the safety of ranitidine in uncomplicated duodenal ulcer for periods of more than 8 weeks.

2. Maintenance therapy for duodenal ulcer patients at reduced dosage after healing of acute ulcers. No placebo-controlled comparative trials have been carried out for periods of longer than 1 year.

3. The treatment of pathological hyper secretory conditions (e.g., Zollinger-Ellison syndrome and systemic mastocytosis).

4. Short-term treatment of active, benign gastric ulcer. Most patients heal within 6 weeks and the usefulness of further treatment has not been demonstrated. Trials available to date have not assessed the safety of ranitidine in uncomplicated, benign gastric ulcer for periods of more than 6 weeks.

5. Maintenance therapy for gastric ulcer patients at reduced dosage after healing of acute ulcers. Placebo-controlled trials have been carried out for 1 year.

6. Treatment of GERD. Symptomatic relief commonly occurs within 24 hours after starting therapy with Zantac 150 mg twice daily.

7. Treatment of endoscopically diagnosed erosive esophagitis. Symptomatic relief of heartburn commonly occurs within 24 hours of therapy initiation with Zantac 150 mg 4 times daily.

8. Maintenance of healing of erosive esophagitis. Placebo-controlled trials have been carried out for 48 weeks.

Concomitant antacids should be given as needed for pain relief to patients with active duodenal ulcer; active, benign gastric ulcer; hyper secretory states; GERD; and erosive esophagitis.

1.3.1.1 Usual Adult Dosage: One tablet daily after the evening meal, at bedtime, or as directed by a physician.

1.3.2 Side effects: This medicine can cause,

- Diarrhea, constipation
- Dizziness, drowsiness, headache, nausea, gas, trouble sleeping, vomiting, blurred vision, confusion, hallucination (hearing or seeing things that aren't there)
- Breast development (males)
- Change of heartbeat (faster, slower, or irregular)
- hair loss
- skin rash or hives
- signs of kidney problems (e.g., increased urination at night, decreased urine production, blood in the urine)
- Signs of liver problems (e.g., nausea, vomiting, diarrhea, loss of appetite, weight loss, yellowing of the skin or whites of the eyes, dark urine, pale stools) (Medbroadcast, 2016).

1.3.3 Drug interactions: following drugs can interact with Zantac, (Medbroadcast, 2016),

- Amiodarone
- Atorvastatin
- Warfarin
- Carvedilol
- Carbamazepine
- Cefuroxime
- Cyclosporine
- Delaviridine
- Grapefruit juice
- HIV protease inhibitors (e.g., darunavir, indinavir, lopinavir, saquinavir, tipranavir)
- Nefazodone
- Prazosin
- Procainamide
- Progesterone
- Propranolol
- Quinidine
- Quinine
- Rifampin
- Sulfonylureas (e.g., glyburide, gliclazide)
- Tyrosine kinase inhibitors (e.g., dasatinib,

1.3.4 Contraindications: Zantac is contraindicated for patients known to have hypersensitivity to the drug or any of the ingredients (Drugs.com, 2016).

1.3.4.1 Precautions:

1. Symptomatic response to therapy with Zantac does not preclude the presence of gastric malignancy.

2. Since Zantac is excreted primarily by the kidney, dosage should be adjusted in patients with impaired renal function. Caution should be observed in patients with hepatic dysfunction since Zantac is metabolized in the liver.

3. Rare reports suggest that Zantac may precipitate acute porphyric attacks in patients with acute porphyria. Zantac should therefore be avoided in patients with a history of acute porphyria (Drugs.com, 2016)

1.3.5 Storage condition: It should be store between 15 and 30 degree Celsius in a dry place and should be protected from light. Should not be used if printed safety seal under cap is broken or missing (Drugs.com, 2016).

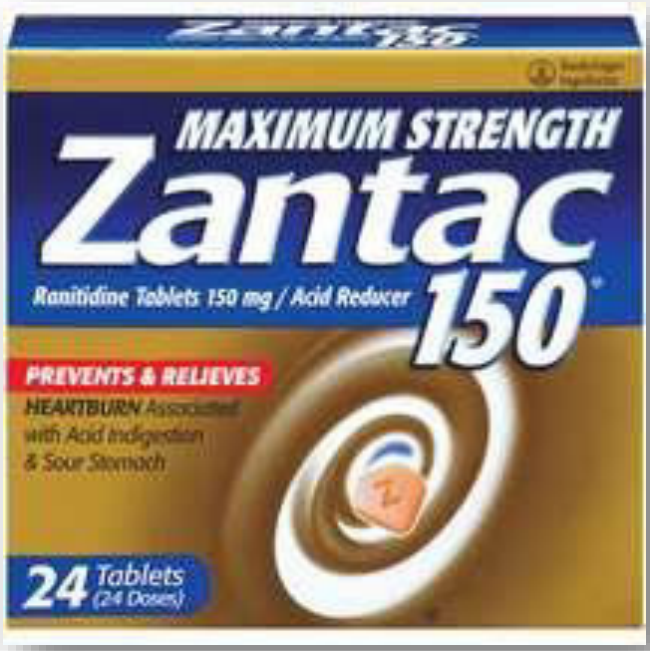

Figure 1.5: Zantac (Medbroadcast, 2016).

1.4 INTRODUCTION OF XANTID (Ranitidine)

Each tablet contains Ranitidine 150mg as Hydrochloride USP (Aci, 2016).

1.4.1 Indications:

- Xantid is indicated for the treatment of duodenal ulcer and benign gastric ulcer, including that associated with non-steroidal anti-inflammatory agents.
- Xantid is also indicated for the treatment of postoperative ulcer, oesophageal reflux disease and Zollinger-Ellison Syndrome.
- Ranitidine treatment is beneficial for patients with chronic episodic dyspepsia, characterized by pain (epigastric of retrosternal), which is related to meals or disturbs sleep but is not associated with the preceding conditions. Xantid is indicated for conditions where reduction of gastric secretion and acid output is desirable , such as
    - The prophylaxis of gastrointestinal hemorrhage from stress ulceration in seriously ill patients,
    - The prophylaxis of recurrent hemorrhage in patients with bleeding peptic ulcers and before general anesthesia in patients considered to be at risk of acid as piration (Mendelson's Syndrome) particularly obstetric patients during labour. Concomitant antacid may be given as needed for relief of pain (Aci, 2016).

1.4.2 Dosage and administration:

1.4.2.1 Adults: The usual dosage is 150mg Xantid twice daily, taken in the morning and evening. Alternatively, patients with duodenal ulceration gastric ulceration or oesophageal reflux disease may be treated with a single bed-time dose of 300mg Xantid. lt is not necessary to time the dose in relation to meals. In most cases of duodenal ulcer, benign gastric ulcer and post-operative ulcer, healing occurs in 4 weeks. A further 4 weeks of treatment may be needed in those patients whose ulcers have not fully healed after the initial course of therapy.

In ulcers following non-steroidal anti-inflammatory drugs therapy or associated with continued non-steroidal anti-inflammatory drugs, 8 weeks treatment may be necessary. In duodenal ulcer 300mg twice daily for 4 weeks results in rapid healing than those at

4 weeks with Ranitidine 150 mg twice daily or 300 mg once at bed-time. For patients with a history of recurrent ulcer or after a short-term therapy, maintenance treatment at a reduced dosage of 150mg at bedtime is recommended.

ln the management of esophageal reflux disease, the recommended course of treatment is either 150mg twice daily or 300mg at bedtime for up to 8 weeks. In patients with severe esophagitis, and those who fail to respond to standard doses of Ranitidine, the dosage of Ranitidine may be increased to 300mg four times daily for up to 8 weeks. The increased dose has not been associated with an increased incidence of unwanted effects.

In patients with Zollinger Ellison Syndrome, the starting dose is 150mg three times daily and this may be increased up to 6gm daily as necessary and these doses have been well tolerated.

For patients with chronic episodic dyspepsia the recommended course of treatment is 150mg twice daily for up to 6 weeks. Anyone not responding or relapsing shortly afterwards should be investigated. In the prophylaxis of hemorrhage from stress ulceration in seriously ill patients or the prophylaxis of recurrent hemorrhage in patients bleeding from peptic ulceration, treatment with Xantid 150mg twice daily may be used.

Patients thought to be at risk of acid aspiration syndrome a dose of 150mg can be given 2 hours before induction of general anesthesia, and preferably also 150mg the previous evening (Aci, 2016).

1.4.2.2 Children: Use of Ranitidine in children has not been fully evaluated in clinical studies. However, it has been used successfully in children aged 8 to 18 years in dose up to 150mg (2 mg/kg) twice daily (Aci, 2016).

1.4.2.3 Parenteral administration: ln some hospitalized patients with pathological hyper secretory conditions or intractable duodenal ulcers, or in patients who are unable to take oral medication, Xantid may be administered parenterally according to the following recommendations,

1.4.2.3.1 Intramuscular injection: 50mg (2ml) every 6 to 8 hours (No dilution necessary) (Aci, 2016).

1.4.3 Precautions: Histamine H2-antagonist may mask symptoms associated with carcinoma of the stomach and may therefore delay diagnosis of the condition. As Ranitidine is excreted through kidney, in severe renal impairment plasma level of the drug increases. Therefore, it is recommended that the dosage of Ranitidine in such patients be 150mg at night for 4 to 8 weeks. Lf ulcer is not healed after treatment the standard dosage regimen of 150mg twice daily be instituted, followed if need be, by maintenance treatment at 150mg at night. Regular supervision of patients with peptic ulcer and on non-steroidal anti- inflammatory drugs is recommended, especially in elderly. Ranitidine crosses the placenta but therapeutic doses administered to obstetric patient's in-labor or undergoing cesarean section have been without any adverse effect on labor, delivery or subsequent neonatal progress. Ranitidine is also excreted in human breast milk. Like other drugs Ranitidine should only be used during pregnancy and lactation if essential (Aci, 2016).

1.4.3.1 Use in elderly patients: In clinical trial the ulcer healing rates have been found similar in patients age 65 and over with those in younger patients. Additionally, there was no difference in the incidence of adverse effects (Aci, 2016).

1.4.3.2 Over dosage: Ranitidine is very specific in action and accordingly no particular problems are expected following overdosage with the-drug. Symptomatic and supportive therapy should be given as appropriate. If required, the drug may be removed from the plasma by hemodialysis (Aci, 2016).

1.4.3.3 Pharmaceutical precautions: Should be Stored in a cool and dry place should be protected from light (Aci, 2016).

1.4.4 Side effects: ln clinical trials or in the routine management of patients treated with Ranitidine the following events have been reported. The relationship to Ranitidine therapy has not been established in many cases. Transient and reversible changes in liver function tests can occur. Occasionally hepatitis (hepatocellular, hepatocanalicular or mixed) with or without jaundice has been reported. These were usualty reversible. In rare occasions reversible leucopenia and thrombocytopenia have been observed in patients.

Rare cases of agranulocytosis or of pancytopenia, sometimes with marrow hyperplasia, or aplasia have been reported. Hypersensitivity reactions (urticaria, angioneurotic

oedema. fever, bronchospasm, hypotension, anaphylactic shock) have been seen rarely following the administration of Ranitidine. These reactions have occasionally occured after a single dose.

As with other H2-receptor antagonists, there have been rare reports of bradycardia and A-V block. Headache, sometimes severe, and dizziness have been reported in a very small oroportion of patients. Rare cases of reversible mental confusion and hallucinations have been reported predominantly in severely ill and elderly patients. Skin rash has been rarely reported.

Ranitidine does not interfere significantly with endocrine or gonadal function. Few reports of breast symptoms (swelling and/or discomfort; in men taking Ranitidine have been reported; some cases have resolved on continued Ranitidine treatment. Discontinuation of therapy may be necessary in order to establish the underlying cause (Aci, 2016).

1.4.5 Package quantities: (Aci, 2016).

Xantid Tablets: Carton of 150 tablets in blister.

Xantid-hs Tablets: Carton of 100 tablets in blister.

Figure 1.6: Xantid (Aci, 2016).

1.5 INTRODUCTION OF CALBO 500 (Calcium supplement)

1.5.1 Composition: Each tablet contains Calcium Carbonate BP 1.25 gm equivalent to 500 mg of Calcium (Square, 2016).

1.5.2 Pharmacology: Calcium carbonate reacts with gastric acid to produce a salt and water. For calcium carbonate the postulated chemical reaction is:

$$CaCO_3 + 2HCl = CaCl_2 + H_2O + CO_2$$

Two grams of calcium carbonate will readily bring 100 ml of hydrochloric acid to a pH above 6. The increase in gastric pH diminishes the activity of pepsin in the gastric secretion. Up to 30% of the oral calcium load may be absorbed (Square, 2016).

1.5.3 Indications:

Calbo 500 (Calcium Carbonate) is used for the treatment or prevention of calcium depletion in patients in whom dietary measures are inadequate. Conditions that may be associated with calcium deficiency include hyperparthyroidism, achlorhydria, chronic diarrhea, vitamin D deficiency, steatorrhea, sprue, pregnancy and lactation, menopause, pancreatitis, renal failure, alkalosis, and hyperphosphatasemia. Calcium Carbonate is being used increasingly often to treat hyperphosphatasemia in chronic renal failure as well as those on continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis. Many patients are unable to tolerate sufficient doses for complete phosphate control and require additional measures such as stringent dietary phosphate restriction or relatively small doses of aluminum hydroxide. Calcium Carbonate containing preparations can provide short term relief of dyspeptic systems but are no longer recommended for long term treatment of peptic ulceration (Square, 2016).

1.5.4 Dosage and Administration: Calcium Carbonate is always used orally and when used as an antacid the recommended doses for adults are equivalent to 540-2000 mg Calcium Carbonate per day, doses for children being half of those for adults. As a dietary supplement, such as for the prevention of osteoporosis, 1250-3750mg Calcium Carbonate (500-1500 mg calcium) daily is recommended in general, but again this will need to be tailored to the individual patient depending on any specific disease such as Calcium deficiency, malabsorption or parathyroid function (Square, 2016).

1.5.5 Side effects: Orally administered Calcium Carbonate may be irritating to the GI tract. It may also cause constipation. Hypocalcaemia is rarely produced by administration of calcium alone, but may occur when large doses are given to patients with chronic renal failure (Square, 2016).

1.5.6 Contraindications and Precautions:

- Hypercalcaemia and hyperparathyroidism
- Hypercalciuria and nephrolithiasis
- Zollinger-Ellison syndrome
- Concomitant digoxin therapy (requires careful monitoring of
- serum calcium level)

Calcium salts should be used cautiously in patients with sarcoidosis, renal or cardiac disease, and in patients receiving cardiac glycosides (Square, 2016).

1.5.6.1 Drug interactions: Calcium Carbonate may enhance the cardiac effects of digoxin and other cardiac glycosides, if systemic hypercalcemia occurs. Calcium Carbonate may interfere with the absorption of concomitantly administered tetracycline preparations and in chronic renal failure modification of vitamin D therapy may be required to avoid hypercalcemia when Calcium Carbonate is used as the primary phosphate binder (Square, 2016).

1.5.6.2 Use in pregnancy and lactation: Calcium containing drugs have been widely used in pregnancy by way of oral calcium supplementation or antacid therapy. Calcium Carbonate can be used in lactating women too (Square, 2016).

1.5.6.3 Use in children: Calcium carbonate has been extensively studied in children and infants with chronic renal failure and is both safe and effective (Square, 2016).

1.5.6.4 Use in elderly:

In case of elderly patients with renal failure when calcium carbonate is taken constipation may be troublesome one for this group. For this reason, monitoring of serum calcium and phosphate is of course indicated for elderly patients (Square, 2016).

1.5.7 Storage condition: It should be Stored in a cool, dry place in controlled room temperature (Square, 2016)**.**

Figure 1.7: Calbo 500 (Square, 2016).

1.6 INTRODUCTION OF ARISTOCAL D (Calcium and Vitamin D supplement)

1.6.1 Description: Aristocal D is a combined preparation of Calcium and Vitamin D (Cholecalciferol) specially designed to promote bone health (Beximcopharma, 2014).

1.6.2 Indications:

- Prevention and treatment of osteoporosis.
- For the treatment of hypocalcemic states dietary supplementation
- Healthy bone formation and maintenance.
- To reduce phosphate absorption from the gut in patients with hyperphosphatemia.
- Treatment of chronic renal failure (Beximcopharma, 2014).

1.6.2.1 Dosage and Administration: One tablet twice daily with food (Beximcopharma, 2014).

1.6.3 Contraindications: Aristocal D is contraindicated in patients who have known hypersensitivity to any of the components of this preparation (Beximcopharma, 2014).

1.6.4 Precautions:

Caution should be taken in patients with,

- Renal impairment,
- Sarcoidosis,
- Hypercalcemia and Hypercalciuria (Beximcopharma, 2014).

1.6.4.1 Use in Pregnancy & Lactation: Aristocal D should be used considering the risk benefit ratio (Beximcopharma, 2014).

1.6.4.2 Pharmaceutical Precaution: It should be stored in a cool and dry place, away from light and should keep out of reach of children (Beximcopharma, 2014).

1.6.5 Adverse Reactions: Aristocal D is well tolerated. Mild gastrointestinal disturbances may occur (Beximcopharma, 2014).

1.6.5.1 Drug Interactions: Concurrent administration of Thiazide diuretics may increase the risk of hypercalcemia. Bran decreases the gastro-intestinal absorption of calcium, and may therefore decrease the efficacy of calcium supplements. Calcium salts reduce the absorption of a number of other drugs such as Biphosphonates, Fluoride, some Fluoroquinolones and Tetracycline's (Beximcopharma, 2014).

1.6.6 Commercial Pack: Aristocal D Tablet: Box containing 50'stablets in 5 x 10's blister strips. Each tablet contains 500 mg Elemental Calcium (as Calcium Carbonate USP) and 200 IU Vitamin D USP (Beximcopharma, 2014).

Figure 1.8: Aristocal D (Beximcopharma, 2014).

1.7 INTRODUCTION OF ACICAL-M (Calcium, Vitamin D and Mineral supplement)

1.7.1 Description: Nutrition is the most important strategy to prevent osteoporosis and other bone related diseases. Calcium, magnesium and Vitamin D are the macro nutrients for bone. Without vitamin D very little calcium is absorbed. Like calcium, magnesium increases bone strength and rigidity. Recent epidemiological studies show that some micro nutrients like copper, manganese, zinc and boron play an important role in bone health. Deficiency of the micro nutrients is noticed in patients with osteoporosis (Aci, 2016).

1.7.2 Indications & Uses:

- Prevention and treatment of osteoporosis
- To maintain strong bone growth and teeth
- For proper functioning heart, muscle and nerves
- As nutritional supplement
- For bone development and constant regeneration of bone

- Pregnancy & lactation
- Deficiency state of calcium, vitamin D, magnesium, zinc, copper, manganese & boron (Aci, 2016).

1.7.2.1 Dose & Administration: 2 tablets per day, preferably 1 tablet in the morning and 1 tablet in the evening (Aci, 2016).

1.7.3 Side effects:

The use of calcium supplements has, rarely, given rise to mild gastro-intestinal disturbances, such as constipation, flatulence, nausea, gastric pain, diarrhoea. Following administration of vitamin D supplements occasional skin rash has been reported. Hypercalciuria, and in rare cases hypocalcaemia have been seen with long term treatment at high dosages. Side-effects from micronutrient are rare (Aci, 2016).

1.7.4 Precautions: Patients with mild to moderate renal failure or mild hypercalciuria should be supervised carefully. Periodic checks of plasma calcium levels and urinary calcium excretion should be made in patients with mild to moderate renal failure or mild hypercalciuria (Aci, 2016).

1.7.4.1 Pregnancy and Lactation: During pregnancy and lactation treatment should always be under the direction of a physician. During pregnancy and lactation, requirements for calcium and vitamin D are increased but in deciding on the required supplementation allowances should be made for availability of these agents from other sources (Aci, 2016).

1.7.4.2 Pharmaceutical precautions: Should be stored in cool place (below 30ºc) and dry place. Keep out of reach of children (Aci, 2016).

1.7.5 Contraindications: Hypersensitivity to any of the tablet ingredients. Absolute contraindications are hypercalcemia resulting for example from myeloma, bone metastases or other malignant bone disease, sarcoidosis, primary hyperparathyroidism and vitamin D overdosage. Severe renal failure (Aci, 2016).

1.7.6 Drug interactions: It has possible interaction with digoxin, antacids containing calcium, aluminum or magnesium, other calcium supplements, calcitriol or other

vitamin D supplements; tetracycline, doxycycline, minocycline or oxytetracycline etc. So before taking any of these drugs with Acical-M, suggestions of the physicians are needed (Aci, 2016).

1.7.7 Overdose: The most serious consequences of acute or chronic overdose is hypercalcemia (Aci, 2016).

1.7.8 **Presentation**: Acical-M Tablet: A light orange color, vanilla flavor, oblong film coated tablet, break line on one side & another side engraved with ACI. Each tablet contains Cholecalciferol (as vitamin D3) 200 IU, Calcium (as Calcium Carbonate) 600 mg, Copper (as Cupric oxide) 1 mg, Magnesium (as Magnesium Oxide) 40 mg, Manganese (as manganese Sulphate) 1.8 mg, Zinc (as Zinc Oxide) 7.5 mg, Boron (as Boron Citrate) 0.25 mg (Aci, 2016).

1.7.8.1 Package quantities:

Acical-M Tablet: Each container contains 30 tablets (Aci, 2016).

Figure 1.9: Acical-M (Aci, 2016).

1.8 INTRODUCTION OF NUTRUM GOLD (Multivitamin & Multimineral Supplement)

1.8.1 Description:

Nutrum Gold tablet is a complete well-balanced multivitamin and multimineral supplement designed for the adults (Acme, 2014).

1.8.2 Composition:

Vitamin A (20% as Beta-Carotene) 5000 IU, Thiamine 1.5 mg, Riboflavin 1.7 mg, Pantothenic Acid 10 mg, Vitamin B6 2 mg, Vitamin B12 6 mcg, Vitamin C 60 mg, Vitamin D 400 IU, Vitamin E 30 IU, Vitamin K 25 mcg, Niacin 20 mg, Folic Acid 400 mcg, Lutein 250 mcg, Biotin 30 mcg, Iodine 150 mcg, Potassium 80 mg, Magnesium 100 mg, Boron 150 mcg, Selenium 20 mcg, Nickel 5 mcg, Copper 2 mg, Silicon 2 mg, Manganese 2 mg, Tin 10 mcg, Calcium 162 mg, Chromium 120 mcg, Vanadium 10 mcg, Iron 18 mg, Molybdenum 75 mcg, Phosphorus 109 mg, Chloride 72 mg & Zinc 15 mg (Acme, 2014).

1.8.3 Indications: Indicated for adults for treatment & prevention of vitamins & minerals deficiencies (Acme, 2014).

1.8.3.1 Dosage and administration: One tablet daily with food (Acme, 2014).

1.8.4 Precautions:

Vitamin A, in high doses, may be associated with birth defects. Pregnant women and women who may become pregnant should not exceed the recommended doses without medical advice (Acme, 2014).

1.8.4.1 Use in pregnancy and lactation: As with any supplement, pregnant women or nursing mother should consult with a doctor (Acme, 2014).

1.8.4.2 Warnings:

Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of reach of children. In case of accidental overdose immediately call a doctor (Acme, 2014).

1.8.5 Drug interactions:

No prominent drug interactions have been reported (Acme, 2014).

1.8.5.1 Contraindications:

This product is contraindicated in patients with known hypersensitivity to any of its ingredients (Acme, 2014).

1.8.6 Side effects: Generally well tolerated. Allergic sensitization has been reported following oral administration of folic acid (Acme, 2014).

1.8.7 Important information:

Long-term intake of high levels of vitamin A (excluding that sourced from beta carotene) may increase the risk of osteoporosis in postmenopausal women. Do not take this product if taking other vitamin A supplements (Acme, 2014).

1.8.7.1 Way of supply:

30-Tablet Pack: Each airtight plastic container contains 30 tablets (Acme, 2014).

15-Tablet Pack: Each airtight plastic container contains 15 tablets (Acme, 2014).

Figure 1.10: Nutrum Gold (Acme, 2014).

1.9 INTRODUCTION OF FILWEL SILVER (Multivitamin and Multimineral supplement)

1.9.1 Composition: Filwel Silver Each tablet contains Vitamin A 3500 IU, Vitamin C 60 mg, Vitamin D 400 IU, Vitamin E 45 IU, Vitamin K 10 mcg, Thiamin 1.5 mg, Riboflavin 1mg, Niacin 20 mg, Vitamin B6 3 mg, Folic acid 400 mcg, Vitamin B12 25 mcg, Biotin 30 mcg, Pantothenic acid 10 mg, Calcium 200 mg, Phosphorous 48 mg, Iodine 150 mcg, Magnesium 100 mg, Zinc 15 mg, Selenium 20 mcg, Copper 2 mg, Manganese 2 mg, Chromium 150 mcg, Molybdenum 75 mcg, Chloride 72 mg, Potassium 80 mg, Boron 150 mcg, Nickel 5 mcg, Silicon 2 mg, Vanadium 10 mcg, Lutein 250 mcg, Lycopene 300 mcg (Square, 2016).

1.9.2 Indications:

Filwel Silver is specially formulated for the prevention and treatment of vitamin and mineral deficiencies for adults over 45 years of age. Filwel Silver is also indicated to meet the increase demands of vitamin and minerals for adults over 45 years of age (Square, 2016).

1.9.2.1 Dosage and administration:

One tablet daily with food. Not formulated for use in children (Square, 2016).

1.9.3 Side effects:

Generally, this preparation is well tolerated. Diarrhea may occasionally occur during treatment with beta carotene and the skin may assume a slightly yellow discoloration. The side effects of vitamin A are reversible. Vitamin C and vitamin E may cause diarrhea and other gastrointestinal disturbances (Square, 2016).

1.9.4 Contraindications and precautions: This product is contraindicated in patients with known hypersensitivity to any of the ingredients. Do not take this product if taking other vitamin A supplements. Long term intake of high levels of vitamin A (excluding that sourced from beta carotene) may increase the risk of osteoporosis in postmenopausal women (Square, 2016).

1.9.4.1 Use in pregnancy and lactation: Recommended by the consultation with physician (Square, 2016).

1.9.4.2 Drug interactions:

No drug interactions have been reported (Square, 2016).

1.9.5 Storage condition: It should be stored in a cool and dry place protected from light and moisture. Keep the container tightly closed. Keep out of reach of children (Square, 2016).

1.9.5.1 Supply condition: 30 tablets in HDPE bottle (Square, 2016).

Figure 4.11: Filwel Silver (Square, 2016).

CHAPTER TWO

LITERATURE REVIEW

2.1 LITERATURE REVIEW

Comparative dissolution test was run in three ranitidine tablets marketed in Bahia, Brazil. Dissolution was done by using a USP type 2 apparatus at 50 rpm with 900 ml of distilled water at 37.0 ± 0.5 ºC for 1h. The dissolution test was performed in compliance with the American Pharmacopoeia (USP-32). All the products released ranitidine satisfactorily, at least 80% of the drug dissolved within 30 minutes (Santos *et al.,* 2014).

Zantac (reference drug) and 10 domestic and foreign generics of ranitidine hydrochloride (150mg) was studied using the pharmacopoeic (USP 29) dissolution test. Analyses showed insignificant differences in the excipients entering into the compositions of ranitidine generic tablets registered in Russia. From this study It was demonstrated that the *in vitro* dissolution test recommended by WHO can be used for determining the bioequivalence of ranitidine generics (Smekhova *et al.,* 2009).

In this study, an analytical technique was developed to determine the composition of two solid forms of ranitidine hydrochloride. Two peaks of Fourier transform infrared (FTIR) spectra were used. The solubility data were modeled using the group contribution parameters and Universal Quasi-Chemical (UNIQUAC) theory. No solid–solid transformation was observed due to grinding or compressing the pure samples (Mirmehrabia *et al.,* 2004).

The purpose of this study was to evaluate the pharmaceutical properties of few selected generic products of ranitidine hydrochloride tablets available in retail pharmacies of Bangladesh. The various parameters of the selected samples such as diameter, shape, size, weight variation, thickness, hardness, disintegration, dissolution and potency was determined according to the American Pharmacopoeia USP 27 requirements. It was found that all ten selected products met the USP 27 specifications (Azad *et al.,* 2013).

Different brand of ranitidine tablets such as ranitidine produced by BIPI (Boehringer Ingelheim Pharmaceuticals Inc.), and Zantac Tablets (GSK) was taken for dissolution testing by using paddle and basket apparatus. Results showed that dissolution artifacts for ranitidine tablets could be reduced by the use of baskets or tablet sinkers (Cappola, 2001).

The purpose of this study was to design, formulate and physicochemical evaluation of the effervescent ranitidine hydrochloride (HCl) tablets. Fusion and direct compression methods used to prepare the effervescent tablets. Result showed that fusion method is the best alternative in terms of physicochemical and physical properties (Aslami and Jahangiri, 2013).

The study was run to determine the impact of the super-disintegrants incorporation mechanism on the immediate realese of the ranitidine 150 mg tablets. Ranitidine dissolution was higher in the extragranular incorporation. For the product quality the extragranular addition mode seemed the best method to incorporate the superdisintegrant (Postolache and Gafitanu, 2012).

A floating type of dosage form of ranitidine hydrochloride in the form of microspheres (capable of floating on simulated gastric fluid) was prepared by solvent evaporation technique. Microspheres were prepared with ethyl cellulose, Eudragit RS100 alone or in combination. This study suggested that ethyl celluose, Eudragit RS100 alone or in combination with added pH modifiers was useful in floating microspheres and was also beneficial to enhance the bioavailability of ranitidine hydrochloride (Kotagale *et al.,* 2011).

Safety and efficacy of Omeprazole (20 mg) and Ranitidine (150 mg) was compared in one hundred and fifty-two patients with endoscopically verified erosive and ulcerative esophagitis. Healing rate was higher with omeprazole which was also accompanied by a significantly faster and more substantial improvement in reflux symptoms. However, both omeprazole and ranitidine were well tolerated, and there were no adverse effects and no clinically significant changes in the laboratory values were attributed to the trial medications (Sandmark *et al.,* 1988).

Ranitidine and omeprazole was given in twelve volunteers to suppress nocturnal acid secretion. From this study it was established that, bedtime ranitidine is more effective than bedtime omeprazole on residual nocturnal acid. It was also suggested that fasting breakthrough of nocturnal acid secretion in patients receiving omeprazole is most likely histamine related (Peghini *et al.,* 1998).

In this study the relapse rate of symptomatic esophagitis during maintenance was investigated after treatment with omeprazole or ranitidine. In this study omeprazole was significantly better than the dose of ranitidine (Hallerback *et al.,* 1994).

Nocturnal gastric acid breakthrough (NAB) was studied in ten male volunteers without *Helicobacter pylori* infection received. The used drugs were rabeprazole and ranitidine. It was established that the inhibitory effect of ranitidine was declined administration in *H. Pylori*-negative subjects when it combined with rabeprazole. Split dosing of rabeprazole was more effective than the single morning dose for inhibiting nocturnal gastric acid secretion (Adachi *et al.*, 2003).

Pharmacokinetic characteristics of ranitidine (100, 150, 200, 400 mg) was evaluated in this study. Pre-dose ranitidine concentrations did not increase with multiple dose administration. This study indicated that the pharmacokinetics of ranitidine was linear in the dose range of 100 mg to 400 mg and were similar with both single- and multiple-dose administrations (Dyal *et al.,* 1985)

To treat gastro-esophageal reflux disease omeprazole (20 mg) and ranitidine (150 mg) were compared. 704 patients were under this treatment procedure. Omeprazole was more efficient than ranitidine in the treatment of gastro-esophageal reflux disease (Wiklund *et al.,* 1998).

Ranitidine and omeprazole was used in patients with bleeding ulcer. As both drugs can maintain high intragastric pH values in patients with bleeding ulcers so continuous infusions of high dose ranitidine and omeprazole were given to the patients. It was concluded that Primed infusions of omeprazole produced consistently high intragastric pH values in patients with bleeding peptic ulcers, whereas primed infusions with ranitidine were less effective. It was assumed that the loss of effectiveness of ranitidine was due to tolerance (Labenz *et al.,* 1997).

Ranitidine (300 mg) and ranitidine (300 mg) plus triple therapy was given to 109 patients infected with *H. pylori.* The recurrence rate of ulcer in patients who received ranitidine plus triple therapy was significantly lower than the patients who received ranitidine alone. But the triple therapy failed to eradicate *H. pylori* (David *et al.,* 1992).

To eradicate of H. pylori and reduce ulcer recurrence ranitidine bismuth citrate plus antibiotic clarithromycin and ranitidine bismuth citrate was compared to determine the

efficacy. From this study it was determined that the co administration of ranitidine bismuth citrate plus clarithromycin is a simple well-tolerated and effective treatment for active H. pylori- associated duodenal ulcer disease (Peterson *et al.*, 2006).

Ranitidine was compared to misoprostol in the prevention of gastric ulcer and duodenal ulcers in patients on chronic NSAID therapy. Patients were given chronic NSAID therapy and were experiencing NSAID-related upper gastrointestinal (UGI) pain. Misoprostol was significantly more effective than ranitidine in the prevention of NSAID-induced gastric ulcers. However ranitidine was as effective as misoprostol for the prevention of NSAID-induced duodenal ulcers (Jeffrey *et al.*, 1996).

Ten healthy volunteers (20-24 years) were given oral 500 mg sodium bicarbonate. After 1 hour they were given intravenous injection of 100 mg ranitidine. A glass pH electrode was used for continuous gastric juice pH measurements and a tonomitor catheter were placed 10 cm distally from the gastro-oesophageal junction. After ranitidine, the gastric juice pH increased while basal $iPCO_2$ did not change after sodium bicarbonate (Kolkman *et al.*, 1994).

This study was conducted to evaluate the drug-drug interaction of Etravirine, a non-nucleoside reverse transcriptase inhibitor (NNRTI) and Ranitidine (H_2-receptor blocker). Ranitidine slightly decreased etravirine exposure. But co-administration of a single dose of etravirine and ranitidine was safe and well tolerated. So it was concluded that Etravirine can be co-administered with H_2 antagonists without dose adjustments (Thomas *et al.*, 2008).

This study assessed the efficacy of ebrotidine and ranitidine in preventing gastroduodenal lesions induced by piroxicam. Patients were endoscopically examined before and after treatment. Lanza's score was also determined, and laboratory tests were performed. The results of this study showed that the most powerful protective effect against mucosal gastric lesions induced by piroxicam was achieved with ebrotidine. Ranitidine did not protect gastric mucosa, and showed a poor gastro-protective effect (Puscas *et al.*, 1997).

Three hundred fifty-three patients with an active, nonmalignant gastric ulcer at least 5 mm in diameter confirmed by endoscopy and biopsy and who continued to receive stable doses of NSAIDs were randomized to receive ranitidine hydrochloride (150 mg

) or lansoprazole, (15 mg or 30 mg) .Healing was assessed by endoscopy at 4 and 8 weeks. *Helicobacter pylori* status was assessed by histological examination. After 8 weeks it was concluded that the patients who require continuous treatment with NSAIDs, lansoprazole is superior to ranitidine for healing of NSAID-associated gastric ulcers. Healing is not delayed by the presence of *H pylori* infection (Naurag *et al.*, 2000).

Twelve healthy volunteers took part in a randomized placebo-controlled cross-over study. Each subject received on three separate occasion's placebo, cimetidine (400 mg) or ranitidine (150 mg) for 24 h before and 48 h after a single oral dose of nebivolol (5 mg). Nebivolol and its individual (+) and (−) enantiomers were determined by H. P. L. C. There was no interaction between ranitidine and nebivolol. Although cimetidine inhibited nebivolol metabolism (Kamali *et al.,* 1997).

This study was conducted to estimate healing and relapse rates in acute and maintenance treatment of GERD with the newer PPIs pantoprazole, rabeprazole and pantoprazole compared with omeprazole, ranitidine, and placebo. In this study, the newer PPIs were of similar efficacy to omeprazole in terms of heartburn control, healing rates, and relapse rates. All the PPIs were superior to ranitidine and placebo in healing erosive esophagitis and decreasing relapse rates (Caro et *al.,* 2001).

To examine the effect of common excipients such as sugars (sorbitol vs. sucrose) on bioequivalence between pharmaceutical formulations, ranitidine and metoprolol was used as model drugs. Two single-dose, replicated, crossover studies were first conducted in healthy volunteers to compare the effect of sorbitol and sucrose on bioequivalence of 150 mg ranitidine or 50 mg metoprolol in aqueous solution, followed by a single-dose, non-replicated, crossover study was conducted to determine the threshold of sorbitol effect on bioequivalence of 150 mg ranitidine in solution. It was concluded that Sorbitol decreased the systemic exposure of ranitidine (Chen *et al.,* 2007).

Seven Norwegian centres recruited 61 female and 54 male patients with non-ulcer dyspepsia (NUD). Their mean age was 40 years. After 6 weeks double-blind alternating treatment with 150 mg ranitidine twice daily, the overall effect of ranitidine in patients with NUD was due to good symptomatic effect in a subpopulation characterized by

meal-related heartburn regurgitation, large body mass index, first-degree relatives with gastrointestinal diseases, a relatively low frequency of gastrointestinal symptoms per week, and absence of soft stools (Farup *et al.,* 1991).

To assess endoscopically the effect of prophylactic short-term ranitidine treatment in the prevention of stress-induced gastric lesions in neonatal intensive care unit (ICU) patients. Fifty-three infants were enrolled in a randomized, controlled study. A histamine-2-receptor blocker, ranitidine, was given prophylactically after birth for 4 days to infants mechanically ventilated and treated in the neonatal ICU. It was conclude that short-term prophylactic ranitidine treatment prevents gastric mucosal lesions in newborn infants under stress (Kuusela *et al.,* 1997).

To investigate the influence of food and administration of an antacid (aluminum-magnesium hydroxide) or ranitidine on the absorption of BAY 59–7939 (rivaroxaban), 4 randomized studies were performed in healthy male subjects. Plasma samples were obtained to assess pharmacokinetic and pharmacodynamic parameters of BAY 59–7939. No significant difference in C_{max} and AUC was observed with co-administration of BAY 59–7939 and ranitidine or antacid (Dagmer *et al.,* 2006).

High-performance liquid chromatography has been used for the qualitative analysis of ranitidine in the urine from subjects given oral and intravenous doses of ranitidine. A selected-ion monitoring technique was used. A normal-phase system consisting of methanol-propan-2-ol-5 M ammonium acetate (50:50:1) was used, and because of this the volume of urine which could be injected on-column without deterioration of the chromatography was limited to 10 µl. This limited the sensitivity of the method to 1.0 µg of ranitidine per milliliter of urine (Martin *et al.*, 1982).

This study compared the effects of cimetidine, ranitidine, and antacids on oesophageal pH levels. Forty-five patients were confirmed as having a gastro-esophageal acid reflux by 3-hour postprandial metered pH measurements. The 20-hour measurement demonstrated a significant decrease with all three drugs in the number of acid reflux incidences compared to the untreated control patients, the ranitidine group had a significant decrease in the percentage of time with acid pH (Desechalliers *et al.*, 1984).

CHAPTER THREE MATERIALS & METHODS

3.1 MATERIALS

3.1.1 Sample Collection: To observe the change in dissolution in ranitidine with other drugs 50 tablets (150 mg) of Zantac, Xantid and 10 tablets of Aristocal D, Calbo 500 mg, Acical M, Nutrum Gold, Filwel Silver were collected from the local drug store in Dhaka as a sample.

3.1.2 Samples:

Table 3.1: Samples used in the experiment including source

Name	Source
Zantac® tablets	GlaxoSmithKline Bangladesh Limited
Xantid® tablets	ACI Pharmaceuticals Limited
Aristocal® D	Beximco Pharmaceuticals Limited
Acical-M®	ACI Pharmaceuticals Limited
Calbo® 500	Square Pharmaceuticals Limited
Nutrum Gold®	Acme Laboratories Limited
Filwel Silver®	Square Pharmaceuticals Limited

3.1.3 Dissolution Medium:

As Ranitidine is soluble in water so distilled water was prepared in the laboratory of East West University and was used as dissolution medium for dissolution test.

3.1.4 Equipment and Instrument:

Table3.2: Lists of equipment used for the experiment

Serial no.	Equipment	Source (Supplier Name)	origin
1	UV-Spectrophotometer	Shimadzu UV-1800	Japan
2	Dissolution tester	SMIC	China
3	Distill water Plant	SMIC	China
4	Electronic balance	Precisa XB 120A	Switzerland
5	Vernier Caliper	China Supplier	China
6	Hardness tester	Manually operated hardness tester	India

3.1.5 Images of Instruments:

Some images of important instruments those were used in different testes during research work.

Figure 3.1: Dissolution apparatus.

Figure 3.2: UV-1800 Double Beam Spectrophotometer

Figure 3.3: Distilled Water apparatus

Figure 3.4: Hardness tester

Figure 3.5: Electronic Balance

Figure 3.6: Vernier Caliper

3.1.6 Apparatus:

Some apparatus are listed in following table those were used throughout the experiments.

Table 3.3: Representing the apparatus

Serial no	Apparatus
1	Beakers
2	Test tubes
3	Volumetric flasks
4	Filter paper
5	Spatula
6	Mortar and pestle
7	Pipette pumper
8	Pipette (1ml & 10 ml)
9	Glass and plastic funnel
10	Syringe & pipes

3.2 METHODS

3.2.1 Standard curve preparation:

3.2.1.1 Preparation of stock solution for Standard Curve:

Ranitidine is soluble in water. So distilled water was used as stock solution to make the standard curve. By using distilled water apparatus in the East West University 500 ml distilled water was made and that was used to prepare the standard curve.

3.2.1.2 Preparation of Standard Curve:

1. To prepare the standard curve, at first different concentrations (5, 10, 15, 20 and 25) µg/ml of Ranitidine was prepared.
2. For the preparation of different concentrations of ranitidine,
3. First Zantac (Ranitidine) tablet was crushed in mortar and pestle.

4. From the crushed tablet 25 mg was taken and was dissolved in 50 ml of distilled water.
5. By this procedure the concentration of the stock solution became 0.5mg/ml or 500 µg/ml.
6. This solution was filtered in the volumetric flask.
7. After that the solution was 50 times diluted and the concentration of the solution become 50 µg/ml.

For the preparation of 5 µg/ml,

S_1= 50 µg/ml

S_2= 5 µg/ml

V_2= 10 ml

V_1=?

$V_1= S_2 * V_2 / S_1$

= 1 ml

This 1 ml stock solution was added with 9 ml of distilled water to obtain 10 ml.

Same calculation was followed for the preparation of 10, 15, 20, 25 µg/ml

For,

10 µg/ml, 2ml stock solution was added with 8 ml of distilled water.

15 µg/ml, 3ml stock solution was added with 7 ml of distilled water.

20 µg/ml, 4 ml stock solution was added with 6ml of distilled water.

25 µg/ml, 5ml stock solution was added with 5 ml of distilled water.

- Then spectrophotometer was turned on and 314nm wave length was set up.
- Then the spectrophotometer was adjusted for 0 and 100% T.
- The solutions were placed on spectrophotometer to measure the absorbance.
- Then the absorbance was plotted against concentration.
- A straight line was found.

Table 3.4: Concentrations of Ranitidine

Serial no	Concentration(µg/ml)
1	5
2	10
3	15
4	20
5	25

3.2.2 Preparation for dissolution test:

3.2.2.1 Preparation of dissolution medium:

Distilled water was prepared in the laboratory and was used as dissolution medium for dissolution test. For each batch 6L of distilled water was prepared.

3.2.2.2 Method for dissolution test of Zantac (Ranitidine) or Xantid (Ranitidine)

1. 6L (6000ml) of stock solution (distilled water) was prepared.
2. Each vessel of dissolution tester was filled with 900 ml of stock solution (distilled water)
3. Time 1 hour, rpm 50 was set up in the dissolution machine.
4. Then the machine was allowed to warm up until it reached at 37.5 degree C.
5. Then 1 Zantac or Xantid tablet was placed in every vessel.
6. After 20, 40 and 60 minutes 10 ml of solution was collected from each vessels and filtered, then from that 1 ml of solution was taken in another test tube and 9 ml distilled water was added to make it 10 ml.
7. At last UV absorbance off the solutions were taken where the wave length was 314nm.

3.2.2.3 Method for dissolution test of Zantac (Ranitidine) or Xantid (Ranitidine) with Calbo 500 (calcium supplement):

1. 6L (6000ml) of stock solution (distilled water) was prepared.
2. Each vessel of dissolution tester was filled with 900 ml of stock solution (distilled water)
3. Time 1 hour, rpm 50 was set up in the dissolution machine.
4. Then the machine was allowed to warm up until it reached at 37.5 degree C.
5. Then 1 Zantac or Xantid tablet and 1 Calbo 500 were placed in every vessel.
6. After 20, 40 and 60 minutes 10 ml of solution was collected from each vessels and filtered, then from that 1 ml of solution was taken in another test tube and 9 ml distilled water was added to make it 10 ml.
7. At last UV absorbance off the solutions were taken where the wave length was 314nm.

Same procedure was followed in the dissolution tests of Zantac or Xantid with Aristocal D, Acical-M, Nutrum Gold and Filwel Silver.

3.2.3 Determination of physical parameters

3.2.3.1 Weight Variation Test

3.2.3.1.1 Procedure:

- 10 tablets were taken and weighed.
- The average was taken and it was considered as the standard weight of an individual tablet.
- All tablets were weighed individually and observed whether the individual tablets are within the range or not.

N.B: The variation from the average weight in the weights not more than two tablets must not differ more than the percentage listed below:

Table 3.5: Accepted percentage list for weight variation test of tablets

Weight of tablets	Percentage difference
130 mg or less	±10%
More than 130 to 324 mg	±7.5%
More than 324 mg	±5%

(Scribd, 2016).

3.2.3.1.2 Equation:

Following equation was used to determine % weight variation of tablets

$$\% \text{ Weight Variation} = (A\text{-}I/A) \times 100$$

Where,

Initial Weight of Tablet, I (gm.)

Average weight of Tablets, A (gm.)

3.2.3.2 Thickness test

3.2.3.2.1 Procedure

- First the tablet was placed between the two jaws of the Vernier caliper.
- Then the main scale reading was taken.
- Next Vernier scale reading was taken also.
- The two readings were added together for multiplying with the Vernier constant 0.1Cm.

3.2.3.2.2 Calculation

Following formula was used to determine thickness of tablets.

Thickness of the tablet = Reading of Cm scale + Reading of Vernier scale × Vernier constant (0.01) + Vernier error

3.2.3.3 Hardness test

3.2.3.3.1 Procedure:

- The slide scale of hardness tester was made zero.
- One tablet was placed vertically between the two jaws of the tester.
- Force was applied with a screw thread and spring until tablet fractured.
- Reading in Kg was taken from the sliding scale.

CHAPTER FOUR RESULTS

4.1 RESULTS

4.1.1 Standard curve preparation:

Table 4.1: Concentration and Absorbance for standard curve of Ranitidine.

Serial number	Concentration (µg/ml)	absorbance
1	0	0
2	5	0.247
3	10	0.471
4	15	0.698
5	20	0.937
6	25	1.132

By plotting the concentration against the absorbance of ranitidine a straight line was found. From the standard curve of Ranitidine an equation was derived, Y=.045x+.012 & R^2=0.999. This equation was used to get the concentration from different sample absorbance.

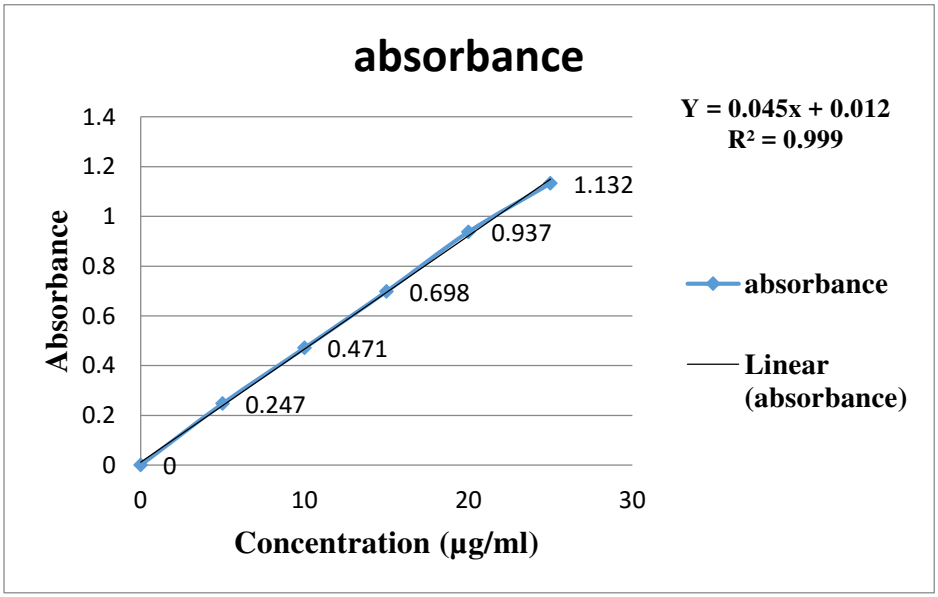

Figure 4.1: Plot showing straight line for absorbance with respect to concentration for Ranitidine.

4.1.2 Result of the dissolution test of individual Zantac and Zantac with Calbo 500, Aristocal D, Acical-M, Nutrum Gold and Filwel Silver.

4.1.2.1 Dissolution test of Zantac (Ranitidine) without any supplement:

Table 4.2: UV absorbance of Zantac (Ranitidine)

	Absorbance		
Serial number	After 20 minutes	After 40 minutes	After 60 minutes
1	0.564	0.653	0.603
2	0.415	0.605	0.694
3	0.486	0.707	0.761
4	0.424	0.659	0.744
5	0.439	0.643	0.753
6	0.438	0.651	0.751

4.1.2.1.1 Calculation of dissolved amount for Zantac (Ranitidine):

From the standard curve an equation was found which is, Y= 0.045x+0.012

Here, Y= Absorbance

X=concentration=?

Dilution factor=9000

If the absorbance is 0.564, then by putting the value in this equation,

0.564=0.045x + 0.012

0.045X=0.564-0.012

0.045x=0.552

X=0.552/0.045

X=12.27

Dissolve amount=12.27*9000/1000= 110.40mg

By putting the other absorbance value in this equation different dissolved amount of Zantac (ranitidine) was calculated.

Table 4.3: Determination of Dissolved amount of Zantac (Ranitidine) without any supplement.

	After 20 minutes		After 40 minutes		After 60 minutes	
Serial number	Absorbance	Dissolved amount (mg)	Absorbance	Dissolved amount (mg)	Absorbance	Dissolved amount (mg)
1	0.564	110.40	0.653	128.20	0.603	118.20
2	0.415	80.60	0.605	118.60	0.694	136.40
3	0.486	94.80	0.707	139.00	0.761	149.80
4	0.424	82.40	0.659	129.40	0.744	146.40
5	0.439	85.40	0.643	126.20	0.753	148.20
6	0.438	85.20	0.651	127.80	0.751	147.80

4.1.2.2 Dissolution test of Zantac (ranitidine) with Calbo 500 (Calcium supplement):

Table 4.4: UV absorbance of Zantac (Ranitidine) with Calbo 500 (Calcium supplement).

	Absorbance		
Serial number	After 20 minutes	After 40 minutes	After 60 minutes
1	0.314	0.331	0.367
2	0.211	0.346	0.372
3	0.206	0.35	0.414
4	0.236	0.361	0.421
5	0.313	0.329	0.33
6	0.268	0.319	0.321

4.1.2.2.1 Calculation for dissolved amount (mg) of Zantac (ranitidine) with Calbo 500 (Calcium supplement).

By using, Y= 0.045x+0.012 equation dissolved amount of Zantac (ranitidine) with Calbo 500 (Calcium supplement) was calculated.

Table 4.5: Determination of Dissolved amount of Zantac (Ranitidine) with Calbo 500 (Calcium supplement).

	After 20 minutes		After 40 minutes		After 60 minutes	
Serial number	Absorbance	Dissolved amount (mg)	Absorbance	Dissolved amount (mg)	Absorbance	Dissolved amount (mg)
1	0.314	60.40	0.331	63.80	0.367	71.00
2	0.211	39.80	0.346	66.80	0.372	72.00
3	0.206	38.80	0.35	67.60	0.414	80.40
4	0.236	44.80	0.361	69.80	0.421	81.80
5	0.313	60.20	0.329	63.40	0.33	63.60
6	0.268	51.20	0.319	61.40	0.321	61.80

4.1.2.2.2 Comparison of dissolved amount and percent dissolved amount between Zantac(Ranitidine) and Zantac(Ranitidine) with Calbo 500 (Calcium supplement) and impact on dissolution calculation after 20,40 and 60 minutes.

4.1.2.2.2.1 Impact of Calbo 500 on the dissolution of Zantac after 20 minutes.

Table 4.6: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Calbo 500 (Calcium supplement) and impact on dissolution calculation after 20 minutes.

Zantac without any supplement				Zantac with Calbo 500				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
110.4		73.6		60.4		40.27		
80.6		53.73		39.8		26.53		
94.8	89.8	63.2	59.87	38.8	49.2	25.87	32.8	-45.21
82.4		54.93		44.8		29.87		
85.4		56.93		60.2		40.13		
85.2		56.8		51.2		34.13		

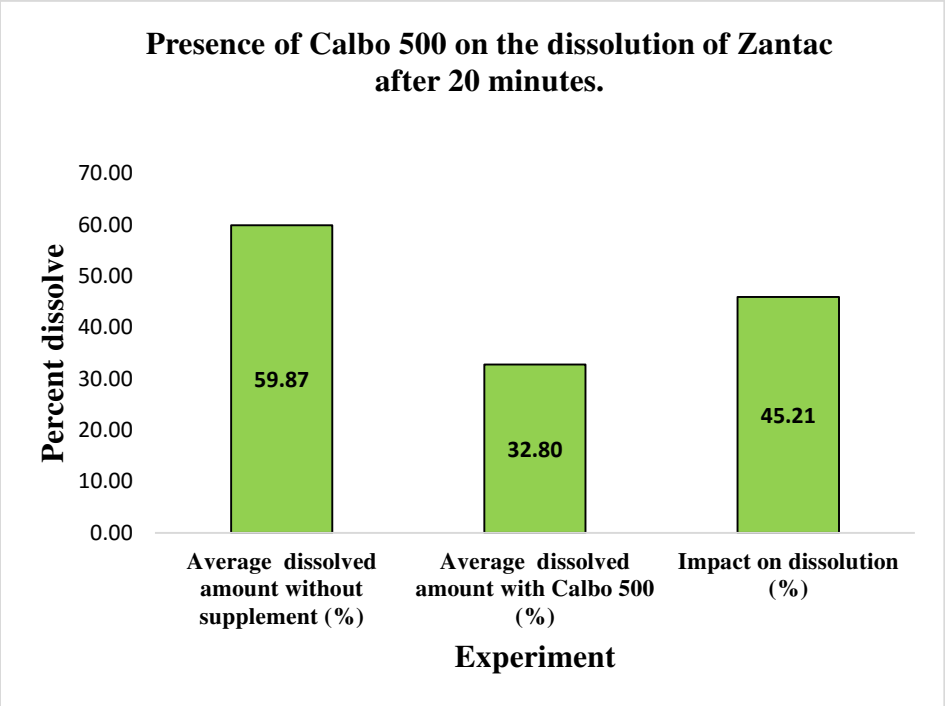

Figure 4.2: Graph represents the presence of Calbo 500 on the dissolution of Zantac after 20 minutes.

4.1.2.2.2.2 Impact of Calbo 500 on the dissolution of Zantac after 40 minutes.

Table 4.7: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Calbo 500 (Calcium supplement) and impact on dissolution calculation after 40 minutes.

Zantac without any supplement				Zantac with Calbo 500				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
128.2		85.47		63.8		42.53		
118.6		79.07		66.8		44.53		
139	128.2	92.67	85.47	67.6	65.47	45.07	43.64	-48.94
129.4		86.27		69.8		46.53		
126.2		84.13		63.4		42.27		
127.8		85.2		61.4		40.93		

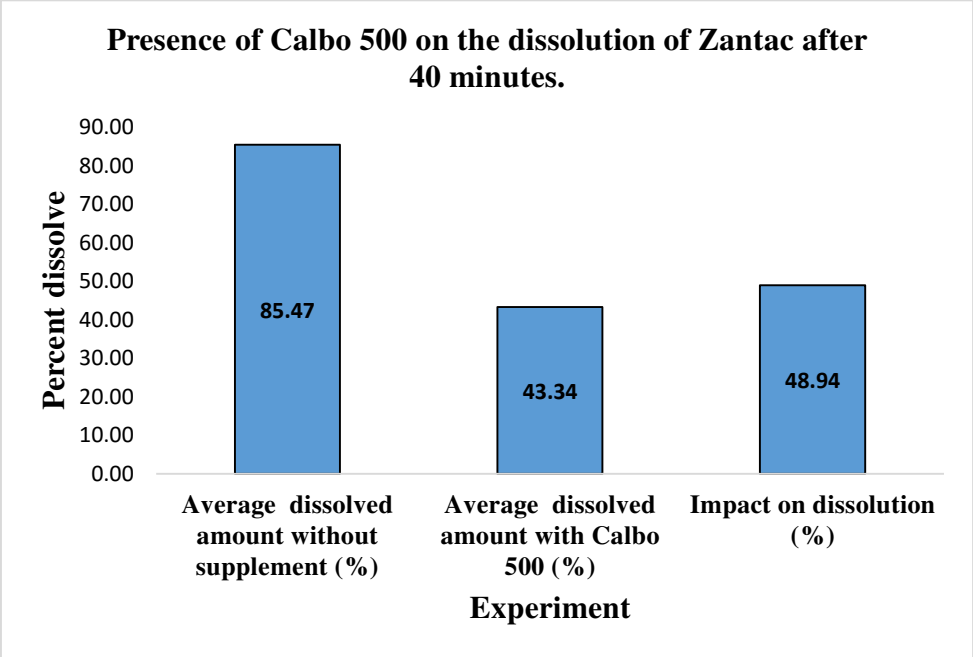

Figure 4.3: Graph represents the presence of Calbo 500 on the dissolution of Zantac after 40 minutes.

4.1.2.2.2.3 Impact of Calbo 500 on the dissolution of Zantac after 60 minutes.

Table 4.8: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Calbo 500 (Calcium supplement) and impact on dissolution calculation.

Zantac without any supplement				Zantac with Calbo 500				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
118.2		78.8		71		47.33		
136.4		90.93		72		48		
149.8	141.13	99.87	94.09	80.4	71.77	53.6	47.84	-49.87
146.4		97.6		81.8		54.53		
148.2		98.8		63.6		42.4		
147.8		98.53		61.8		41.2		

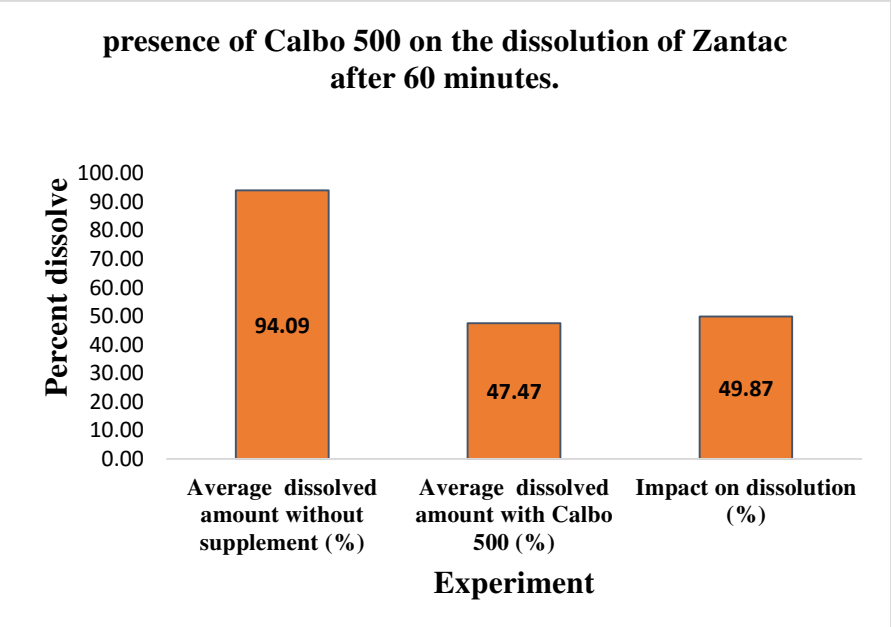

Figure 4.4: Graph represents the presence of Calbo 500 on the dissolution of Zantac after 60 minutes.

4.1.2.3 Dissolution test of Zantac (ranitidine) with Aristocal D (Calcium and vitamin D supplement):

Table 4.9: UV absorbance of Zantac (Ranitidine) with Aristocal D (Calcium and vitamin D supplement.

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.315	0.506	0.509
2	0.370	0.498	0.566
3	0.476	0.581	0.606
4	0.359	0.485	0.528
5	0.390	0.487	0.599
6	0.321	0.468	0.531

4.1.2.3.1Calculation for dissolved amount (mg) of Zantac (Ranitidine) with Aristocal D (Calcium and vitamin D supplement.

By using, Y= 0.045x+0.012 equation dissolved amount of Zantac (ranitidine) with Aristocal D (Calcium and vitamin D supplement) was calculated.

Table 4.10: Determination of Dissolved amount of Zantac (Ranitidine) with Aristocal D (Calcium and vitamin D supplement).

	After 20 minutes		**After 40 minutes**		**After 60 minutes**	
Serial number	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**
1	0.315	60.60	0.506	98.80	0.509	99.40
2	0.370	71.60	0.498	97.20	0.566	110.80
3	0.476	92.80	0.581	113.80	0.606	118.80
4	0.359	69.40	0.485	94.60	0.528	103.20
5	0.390	75.60	0.487	95.00	0.599	117.40
6	0.321	61.80	0.468	91.20	0.531	103.80

4.1.2.3.2 Comparison of dissolved amount and percent dissolved amount between Zantac (Ranitidine) and Zantac(Ranitidine) with Aristocal D (Calcium and vitamin D supplement) and impact on dissolution calculation after 20, 40 and 60 minutes.

4.1.2.3.2.1 Impact of Aristocal D on the dissolution of Zantac after 20 minutes.

Table 4.11: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Aristocal D (Calcium and vitamin D supplement) and impact on dissolution calculation 20 minutes.

Zantac without any supplement				Zantac with Aristocal D				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent Dissolved amount (%)	Impact on dissolution (%)
110.4		73.6		60.6		40.4		
80.6		53.73		71.6		47.73		
94.8	89.8	63.2	59.87	92.8	71.97	61.87	47.98	-19.86
82.4		54.93		69.4		46.27		
85.4		56.93		75.6		50.4		
85.2		56.8		61.8		41.2		

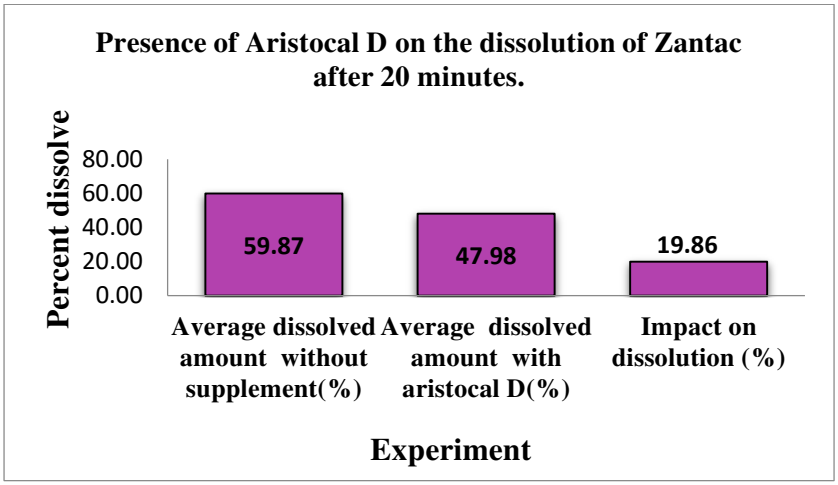

Figure 4.5: Graph represents the presence of Aristocal D on the dissolution of Zantac after 20 minutes.

4.1.2.3.2.2 Impact of Aristocal D on the dissolution of Zantac after 40 minutes.

Table 4.12: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Aristocal D (Calcium and vitamin D supplement) and impact on dissolution calculation after 40 minutes.

Zantac without any supplement				Zantac with Aristocal D				
Dissolved amount (mg)	Average Dissolved amount (mg)	Percent dissolved amount (%)	Average percent Dissolved amount (%)	Dissolved amount (mg)	Average Dissolved amount (mg)	Percent dissolved amount (%)	Average percent Dissolved amount (%)	Impact on dissolution (%)
128.2		85.47		98.8		65.87		
118.6		79.07		97.2		64.8		
139	128.2	92.67	85.47	113.8	98.43	75.87	65.62	-23.22
129.4		86.27		94.6		63.07		
126.2		84.13		95		63.33		
127.8		85.2		91.2		60.8		

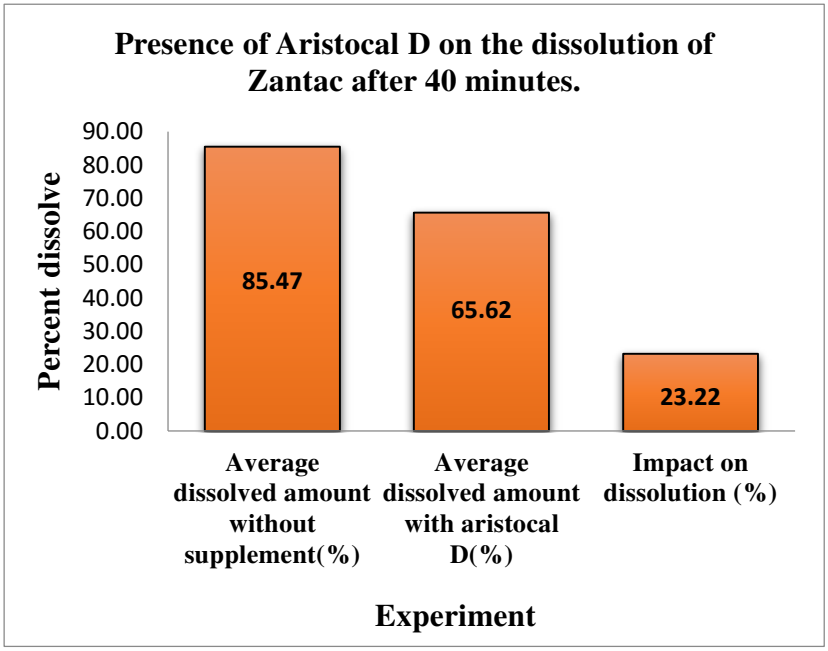

Figure 4.6: Graph represents the presence of Aristocal D on the dissolution of Zantac after 40 minutes.

4.1.2.3.2.3 Impact of Aristocal D on the dissolution of Zantac after 60 minutes.

Table 4.13: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Aristocal D (Calcium and vitamin D supplement) and impact on dissolution calculation after 60 minutes.

Zantac without any supplement				Zantac with Aristocal D				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolve amount (%)	Impact on dissolution (%)
118.2		78.8		99.4		66.27		
136.4		90.93		110.8		73.87		
149.8	141.13	99.87	94.09	118.8	108.9	79.2	72.6	-22.83
146.4		97.6		103.2		68.8		
148.2		98.8		117.4		78.27		
147.8		98.53		103.8		69.2		

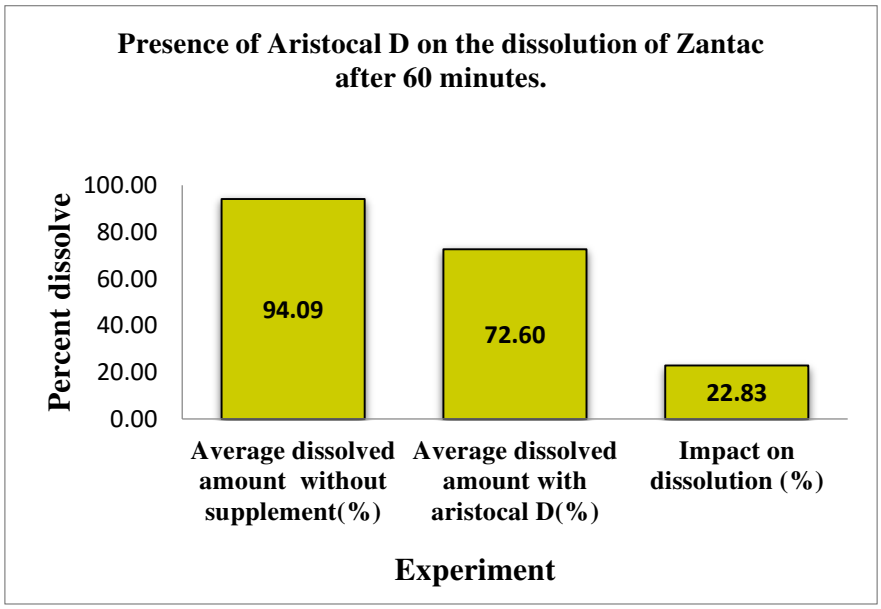

Figure 4.7: Graph represents the presence of Aristocal D on the dissolution of Zantac after 60 minutes.

4.1.2.4 Dissolution test of Zantac (ranitidine) with Acical-M (Calcium, vitamin D and multimineral supplement)

Table 4.14: UV absorbance of Zantac (Ranitidine) with Acical-M (Calcium, vitamin D and multimineral supplement).

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.145	0.237	0.327
2	0.217	0.316	0.413
3	0.316	0.325	0.347
4	0.266	0.398	0.401
5	0.253	0.321	0.353
6	0.322	0.406	0.412

4.1.2.4.1 Calculation for dissolved amount (mg) Zantac (ranitidine) with Acical-M (Calcium, vitamin D and multimineral supplement)

By using, Y= 0.045x + 0.012 equation dissolved amount of Zantac (ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) was calculated.

Table 4.15: Determination of Dissolved amount of Zantac (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement).

	After 20 minutes		**After 40 minutes**		**After 60 minutes**	
Serial number	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**
1	0.145	26.60	0.237	45.00	0.327	63.00
2	0.217	41.00	0.316	60.80	0.413	80.20
3	0.316	60.80	0.325	62.60	0.347	67.00
4	0.366	50.80	0.398	77.20	0.401	77.80
5	0.253	48.20	0.321	61.80	0.353	68.20
6	0.322	62.00	0.406	78.80	0.412	80.00

4.1.2.4.2 Comparison of dissolved amount and percent dissolved amount between Zantac (Ranitidine) and Zantac (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation 20, 40 and 60 minutes.

4.1.2.4.2.1 Impact of Acical M on the dissolution of Zantac after 20 minutes.

Table 4.16: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation after 20 minutes.

Zantac without any supplement				Zantac with Acical M				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
110.4		73.6		26.6		17.73		
80.6		53.73		41		27.33		
94.8	89.8	63.2	59.87	60.8	48.23	40.53	32.16	-46.28
82.4		54.93		50.8		33.87		
85.4		56.93		48.2		32.13		
85.2		56.8		62		41.33		

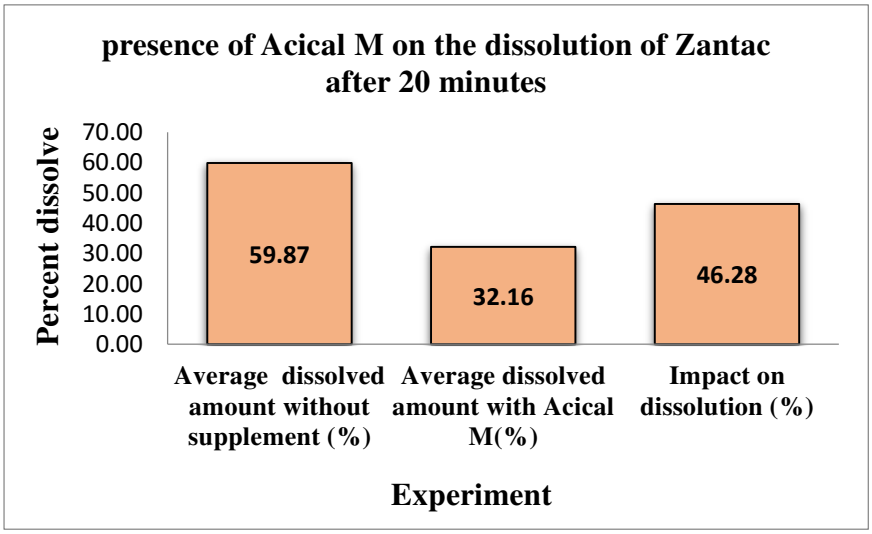

Figure 4.8: Graph represents the presence of Acical M on the dissolution of Zantac after 20 minutes.

4.1.2.4.2.2 Impact of Acical M on the dissolution of Zantac after 40 minutes.

Table 4.17: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation after 40 minutes.

Zantac without any supplement				Zantac with Acical M				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
128.2		85.47		45		30		
118.6		79.07		60.8		40.53		
139	128.2	92.67	85.47	62.6	64.37	41.73	42.91	-49.8
129.4		86.27		77.2		51.47		
126.2		84.13		61.8		41.2		
127.8		85.2		78.8		52.53		

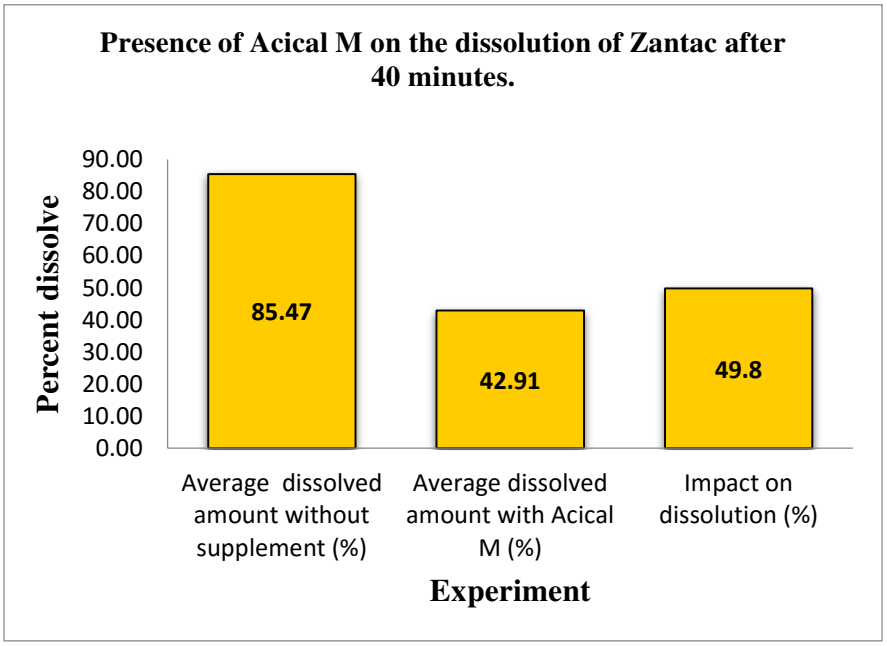

Figure 4.9: Graph represents the presence of Acical M on the dissolution of Zantac after 40 minutes.

4.1.2.4.2.2.3 Impact of Acical M on the dissolution of Zantac after 60 minutes.

Table 4.18: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation after 60 minutes.

Zantac without any supplement				Zantac with Acical M				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
118.2		78.8		63		42		
136.4		90.93		80.2		53.47		
149.8	141.13	99.87	94.09	67	72.7	44.67	48.47	-48.49
146.4		97.6		77.8		51.87		
148.2		98.8		68.2		45.47		
147.8		98.53		80		53.33		

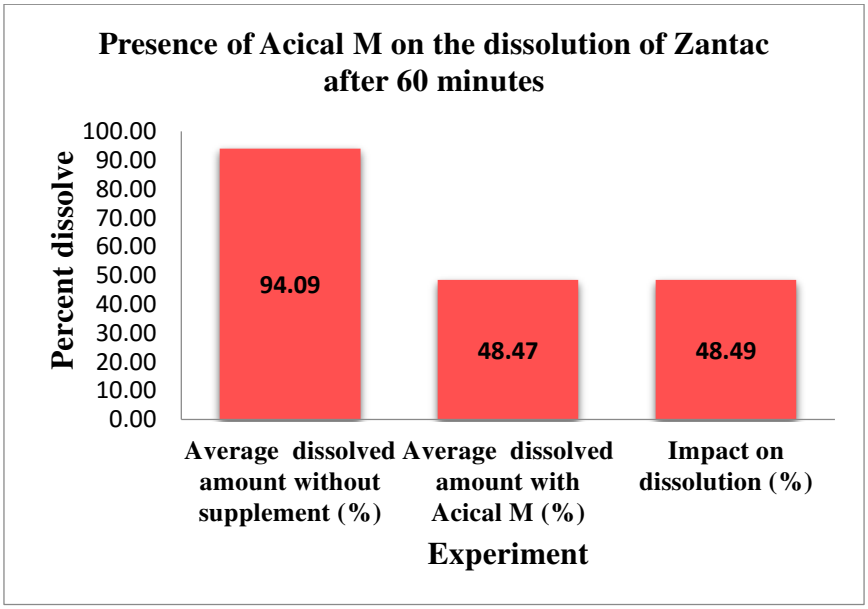

Figure 4.10: Graph represents the presence of Acical M on the dissolution of Zantac after 60 minutes.

4.1.2.5 Dissolution test of Zantac (ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement)

Table 4.19: UV absorbance of Zantac (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement).

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.352	0.589	0.654
2	0.387	0.577	0.712
3	0.366	0.509	0.679
4	0.321	0.615	0.764
5	0.639	0.822	0.738
6	0.654	0.815	0.767

4.1.2.5.1 Calculation for dissolved amount (mg) Zantac (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement).

By using, Y= 0.045x+0.012 equation dissolved amount of Zantac (ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) was calculated.

Table 4.20: Determination of Dissolved amount of Zantac (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement).

	After 20 minutes		**After 40 minutes**		**After 60 minutes**	
Serial number	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**
1	0.352	68	0.589	115.4	0.654	128.4
2	0.387	75	0.577	113	0.712	140
3	0.366	70.8	0.509	99.4	0.679	133.4
4	0.321	61.8	0.615	120.6	0.764	150.4
5	0.639	125.4	0.822	162	0.738	145.2
6	0.654	128.4	0.815	160.6	0.767	151

4.1.2.5.2 Comparison of dissolved amount and percent dissolved amount between Zantac (Ranitidine) and Zantac (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) and impact on dissolution calculation 20, 40 60 minutes.

4.1.2.5.2.1 Impact of Nutrum Gold on the dissolution of Zantac after 20 minutes.

Table 4.21: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) and impact on dissolution calculation after 20 minutes.

Zantac without any supplement				Zantac with Nutrum Gold				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolve amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
110.4		73.6		68		45.33		
80.6		53.73		75		50		
94.8	89.8	63.2	59.87	70.8	88.23	47.2	58.82	1.75
82.4		54.93		61.8		41.2		
85.4		56.93		125.4		83.6		
85.2		56.8		128.4		85.6		

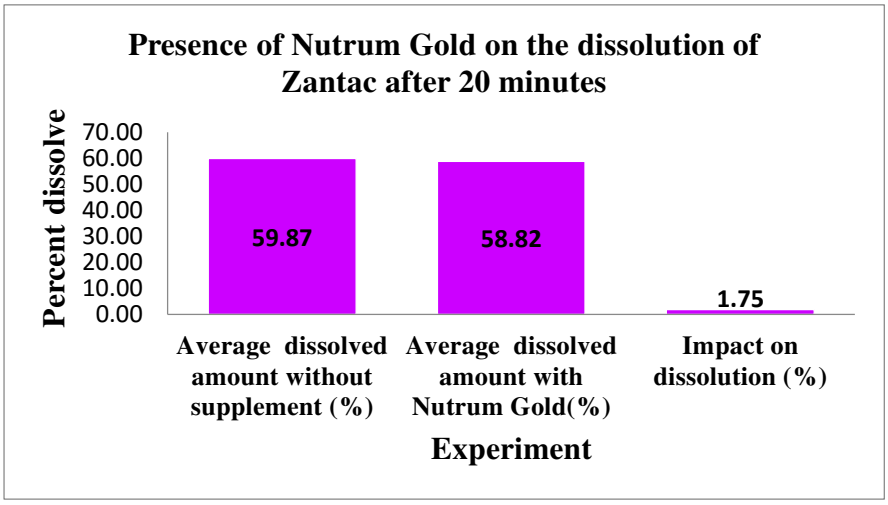

Figure 4.11: Graph represents the presence of Nutrum Gold on the dissolution of Zantac after 20 minutes.

4.1.2.5.2.2 Impact of Nutrum Gold on the dissolution of Zantac after 40 minutes.

Table 4.22: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) and impact on dissolution calculation after 20 minutes.

Zantac without any supplement				Zantac with Nutrum Gold				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
128.2		85.47		115.4		76.93		
118.6		79.07		113		75.33		
139	128.2	92.67	85.47	99.4	128.5	66.27	85.67	0.23
129.4		86.27		120.6		80.4		
126.2		84.13		162		108		
127.8		85.2		160.6		107.07		

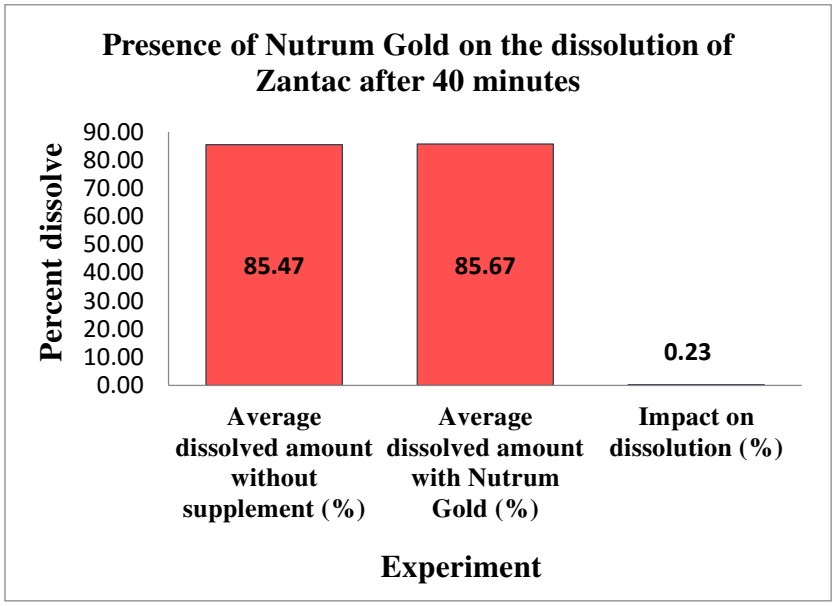

Figure 4.12: Graph represents the presence of Nutrum Gold on the dissolution of Zantac after 40 minutes.

4.1.2.5.2.3 Impact of Nutrum Gold on the dissolution of Zantac after 60 minutes.

Table 4.23: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) and impact on dissolution calculation after 60 minutes.

Zantac without any supplement				Zantac with Nutrum Gold				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
118.2		78.8		128.4		85.6		
136.4		90.93		140		93.33		
149.8	141.13	99.87	94.09	133.4	141.4	88.93	94.27	0.19
146.4		97.6		150.4		100.27		
148.2		98.8		145.2		96.8		
147.8		98.53		151		100.67		

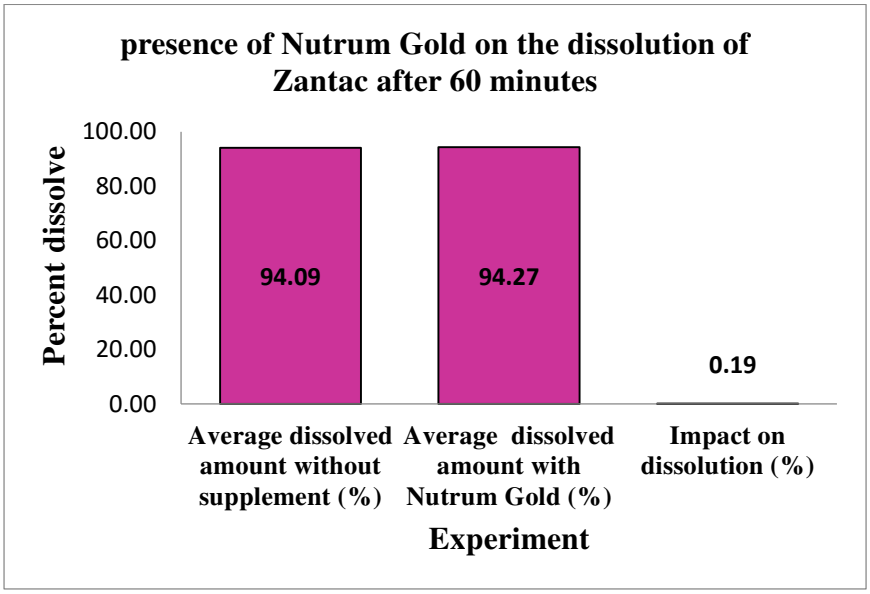

Figure 4.13: Graph represents the presence of Nutrum Gold on the dissolution of Zantac after 60 minutes.

4.1.2.6 Dissolution test of Zantac (ranitidine) with Filwel Silver (Multivitamin and multimineral supplement)

Table 4.24: UV absorbance of Zantac (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement)

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.472	0.712	0.835
2	0.469	0.627	0.737
3	0.563	0.825	0.857
4	0.494	0.598	0.657
5	0.432	0.602	0.658
6	0.474	0.653	0.703

4.1.6.1 Calculation for dissolved amount (mg) Zantac (ranitidine) with Filwel Silver (Multivitamin and multimineral supplement)

By using, Y= 0.045x+0.012 equation dissolved amount of Zantac (ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) was calculated

Table 4.25: Determination of Dissolved amount of Zantac (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement).

	After 20 minutes		After 40 minutes		After 60 minutes	
Serial number	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**
1	0.472	92	0.712	140	0.835	164.6
2	0.469	91.4	0.627	123	0.737	145
3	0.563	110.2	0.825	162.6	0.857	169
4	0.494	96.4	0.598	117.2	0.657	129
5	0.432	84	0.602	118	0.658	129.2
6	0.474	92.4	0.653	128.2	0.703	138.2

4.1.2.6.2 Comparison of dissolved amount and percent dissolved amount between Zantac (Ranitidine) and Zantac (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) and impact on dissolution calculation 20, 40 and 60 minutes.

4.1.2.6.2.1 Impact of Filwel Silver on the dissolution of Zantac after 20 minutes.

Table 4.26: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) and impact on dissolution calculation after 20 minutes.

Zantac without any supplement				Zantac with Filwel Silver				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
110.4		73.6		92		61.33		
80.6		53.73		91.4		60.93		
94.8	89.8	63.2	59.87	110.2	94.4	73.47	62.93	5.01
82.4		54.93		96.4		64.27		
85.4		56.93		84		56		
85.2		56.8		92.4		61.6		

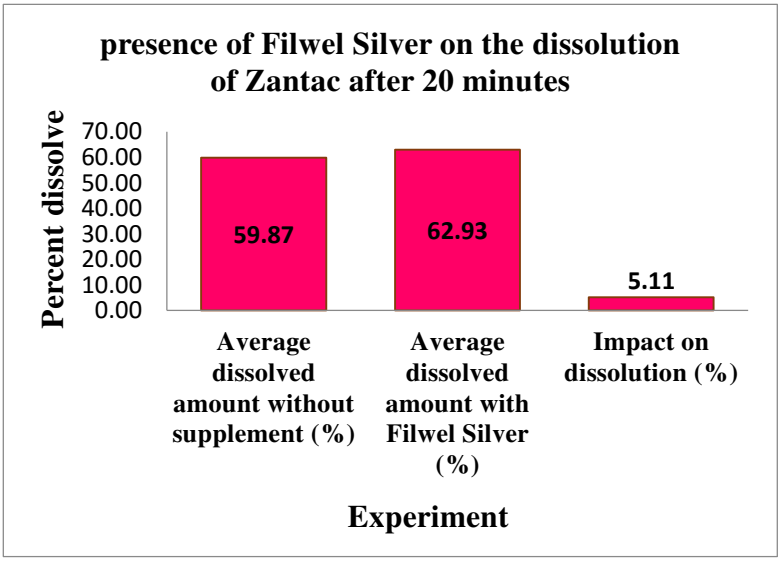

Figure 4.14: Graph represents the presence of Filwel Silver on the dissolution of Zantac after 20 minutes.

4.1.2.6.2.2 Impact of Filwel Silver on the dissolution of Zantac after 40 minutes.

Table 4.27.: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) and impact on dissolution calculation after 40 minutes.

Zantac without any supplement				Zantac with Filwel Silver				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
128.2		85.47		140		93.33		
118.6		79.07		123		82		
139	128.2	92.67	85.47	162.6	131.5	108.4	87.67	2.57
129.4		86.27		117.2		78.13		
126.2		84.13		118		78.67		
127.8		85.2		128.2		85.47		

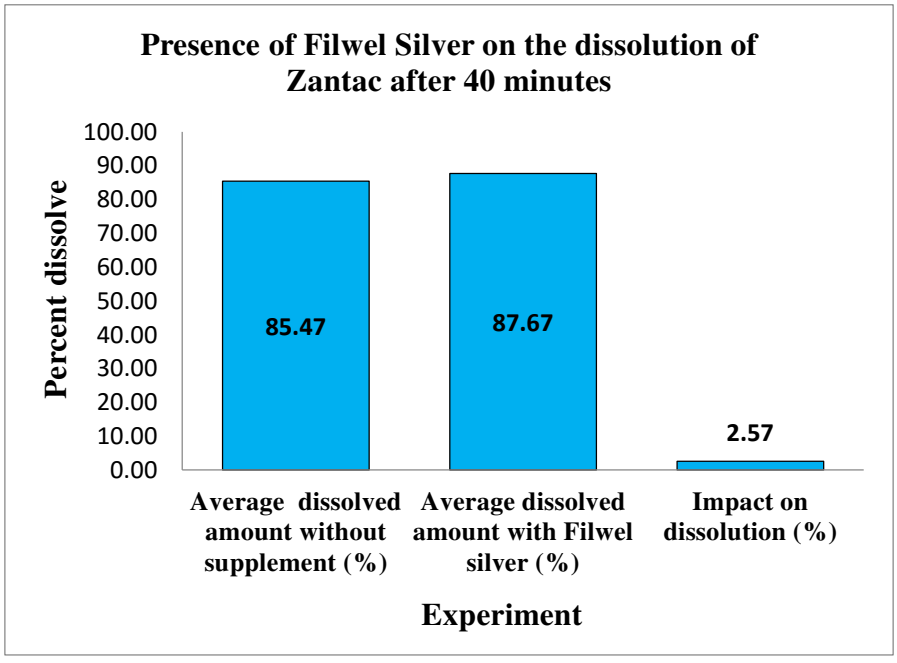

Figure 4.15: Graph represents the presence of Filwel Silver on the dissolution of Zantac after 40 minutes.

4.1.2.6.2.3 Impact of Filwel Silver on the dissolution of Zantac after 60 minutes.

Table 4.28: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) and impact on dissolution calculation after 60 minutes.

Zantac without any supplement				Zantac with Filwel Silver				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
118.2		78.8		164.6		109.73		
136.4		90.93		145		96.67		
149.8	141.13	99.87	94.09	169	145.83	112.67	97.22	3.33
146.4		97.6		129		86		
148.2		98.8		129.2		86.13		
147.8		98.53		138.2		92.13		

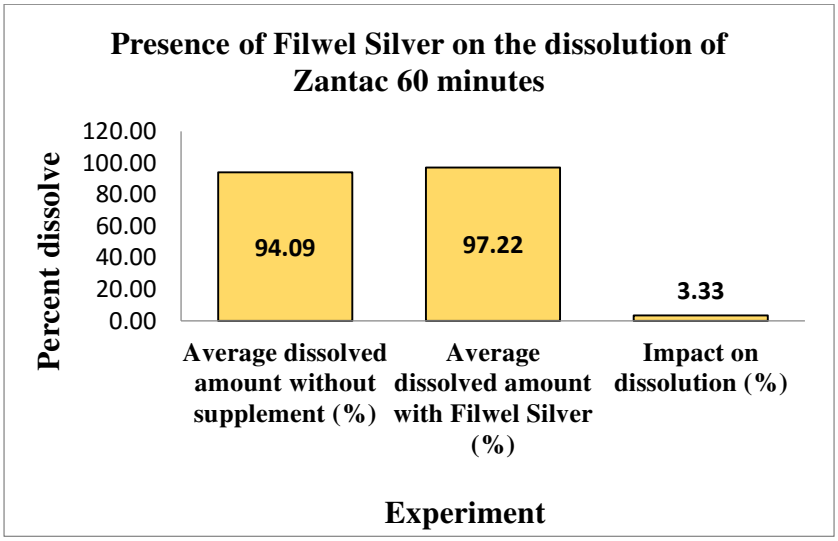

Figure 4.16: Graph represents the presence of Filwel Silver on the dissolution of Zantac 60 minutes.

4.1.2.7 Comparison among the average percent dissolved (%) amount of individual Zantac, Zantac with Calbo 500, Zantac with Aristocal D, Zantac with Acical M, and Zantac with Nutrum Gold and Zantac with Filwel silver after 20, 40 and 60 minutes.

Table 4.29: Table showing the differences among the average percent dissolve (%) amount of individual Zantac, Zantac with Calbo 500, Zantac with Aristocal D, Zantac with Acical M, Zantac with Nutrum Gold and Zantac with Filwel silver after 20 minute.

Average percent dissolved amount of Zantac without supplement (%)	Average percent dissolved amount of Zantac with calbo 500 (%)	Average percent dissolved amount of Zantac with Aristocal D (%)	Average percent dissolved amount of Zantac with Acical M (%)	Average percent dissolved amount of Zantac with Nutrum Gold (%)	Average percent dissolved amount of Zantac with Filwel Silver (%)
59.87	32.80	47.98	32.16	58.82	62.93

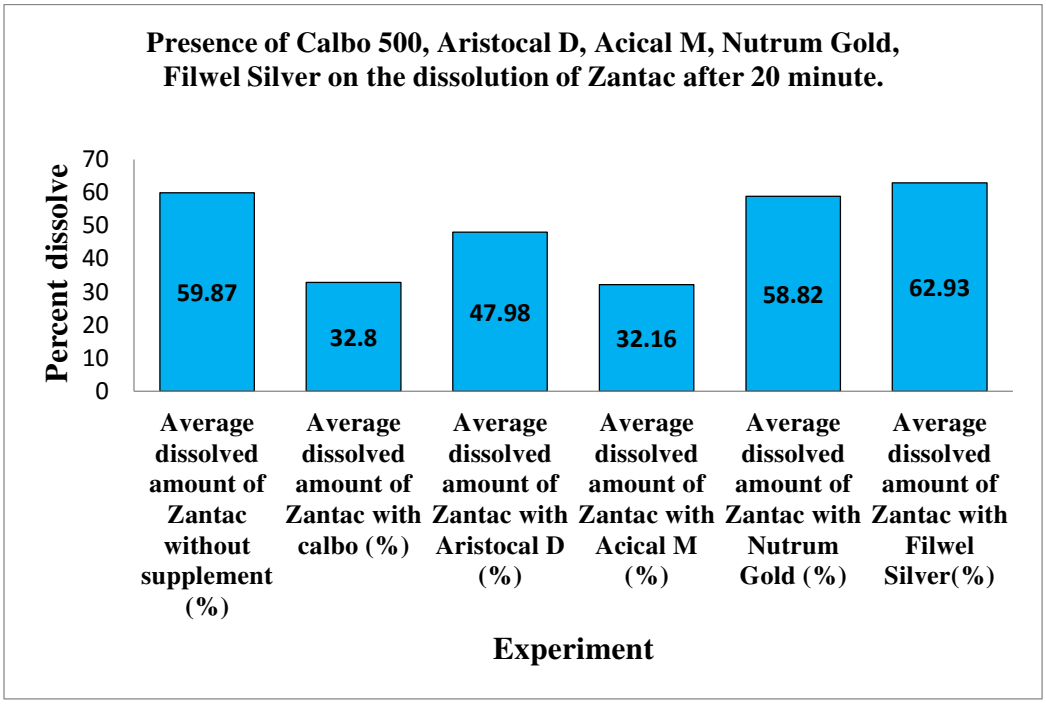

Figure 4.17: Graph represents the presence of Calbo 500, Aristocal D, Acical M, Nutrum Gold, and Filwel Silver on the dissolution of Zantac after 20 minute.

Table 4.30: Table showing the differences among the average percent dissolve (%) amount of individual Zantac, Zantac with Calbo 500, Zantac with Aristocal D, Zantac with Acical M, Zantac with Nutrum Gold and Zantac with Filwel silver after 40 minute.

Average percent dissolved amount of Zantac without supplement (%)	Average percent dissolved amount of Zantac with Calbo 500 (%)	Average percent dissolved amount of Zantac with Aristocal D (%)	Average percent dissolved amount of Zantac with Acical M (%)	Average percent dissolved amount of Zantac with Nutrum Gold (%)	Average percent dissolved amount of Zantac with Filwel Silver (%)
85.47	43.64	65.62	42.91	85.67	87.67

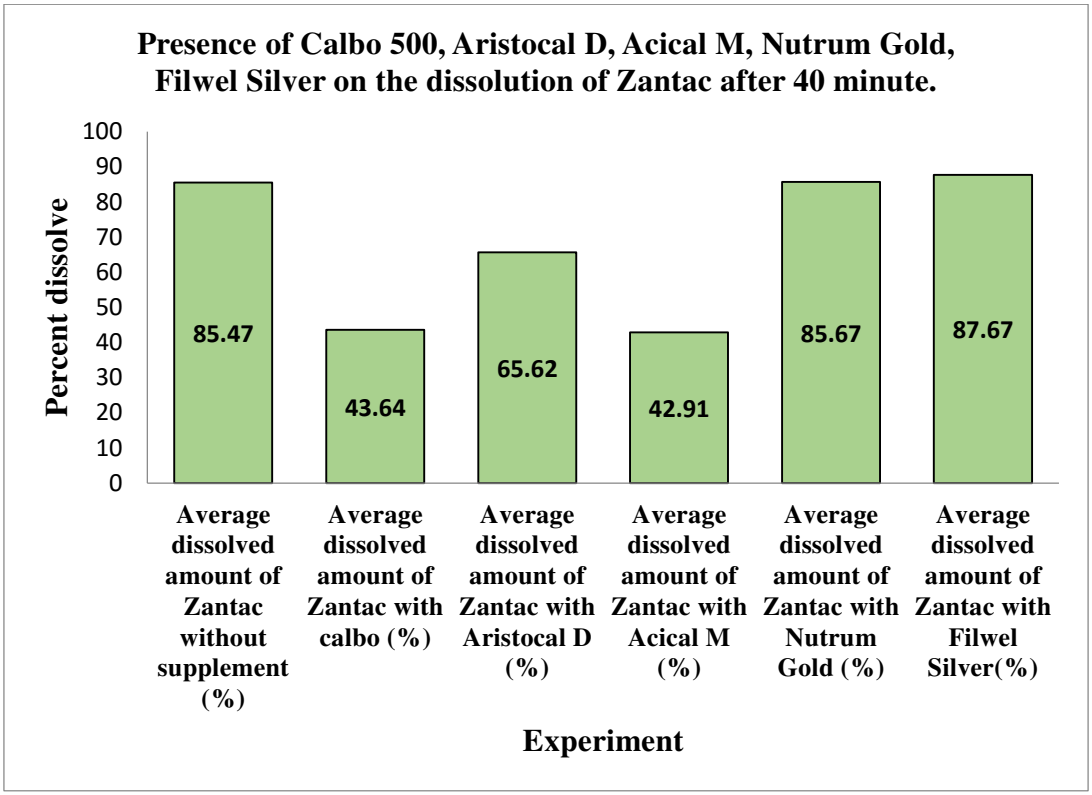

Figure 4.18: Graph represents the presence of Calbo 500, Aristocal D, Acical M, Nutrum Gold, and Filwel Silver on the dissolution of Zantac after 40 minute.

Table 4.31: Table showing the differences among the average percent dissolve (%) amount of individual Zantac, Zantac with Calbo 500, Zantac with Aristocal D, Zantac with Acical M, Zantac with Nutrum Gold and Zantac with Filwel silver after 60 minute.

Average percent dissolved amount of Zantac without supplement (%)	Average percent dissolved amount of Zantac with calbo 500 (%)	Average percent dissolved amount of Zantac with Aristocal D (%)	Average percent dissolved amount of Zantac with Acical M (%)	Average percent dissolved amount of Zantac with Nutrum Gold (%)	Average percent dissolved amount of Zantac with Filwel Silver (%)
94.09	47.84	72.6	48.47	94.27	97.22

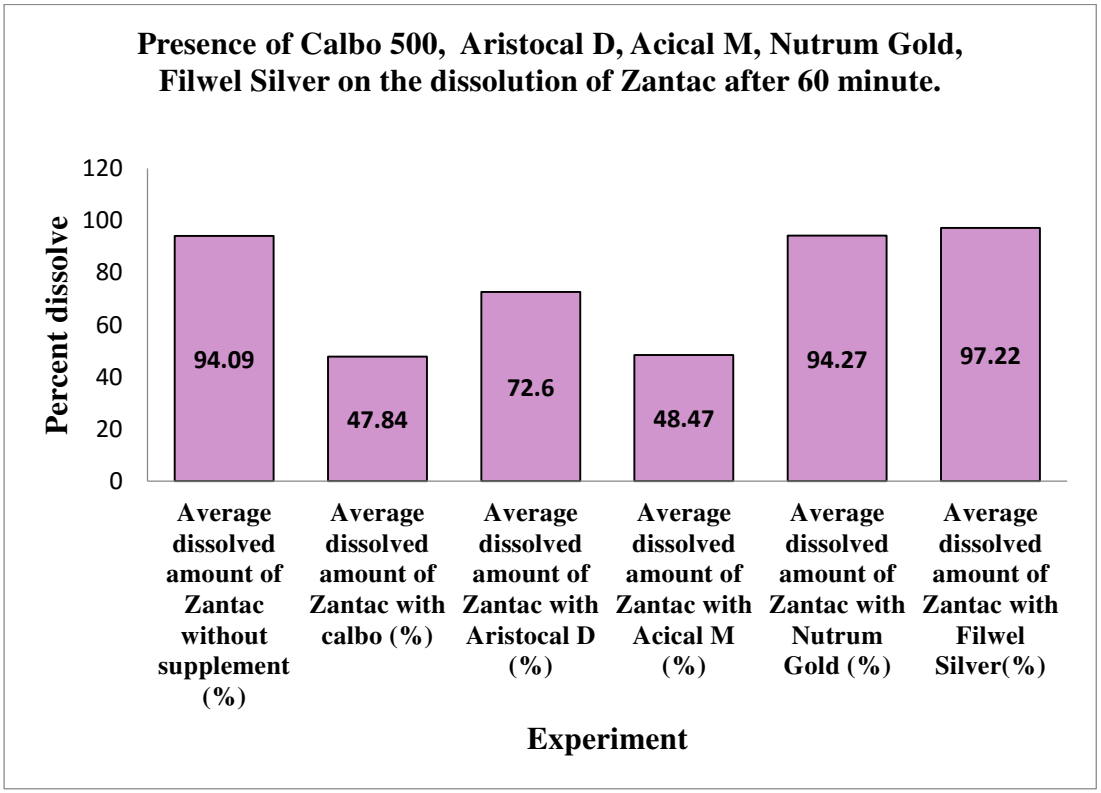

Figure 4.19: Graph represents the presence of Calbo 500, Aristocal D, Acical-M, Nutrum Gold, and Filwel Silver on the dissolution of Zantac after 60 minute.

4.1.3 Result of the dissolution test of individual Xantid and Xantid with Calbo 500, Aristocal D, Acical-M, Nutrum Gold and Filwel Silver.

4.1.3.1 Dissolution test of Xantid (Ranitidine) without any supplement.

Table 4.32: UV absorbance of Xantid (Ranitidine)

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.466	0.620	0.722
2	0.428	0.601	0.724
3	0.414	0.651	0.699
4	0.509	0.705	0.734
5	0.430	0.645	0.719
6	0.544	0.799	0.815

4.1.3.1.1 Calculation of dissolved amount for Xantid (Ranitidine):

By using, Y= 0.045x+0.012 equation dissolved amount of Xantid (ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) was calculated.

Table 4.33: Determination of Dissolved amount of Xantid (Ranitidine).

	After 20 minutes		After 40 minutes		After 60 minutes	
Serial number	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**
1	0.466	90.8	0.62	121.6	0.722	142
2	0.428	83.2	0.601	117.8	0.724	142.4
3	0.414	80.4	0.651	127.8	0.699	137.4
4	0.509	99.4	0.705	138.6	0.734	144.4
5	0.43	83.6	0.645	126.6	0.719	141.4
6	0.544	106.4	0.799	157.4	0.815	160.6

4.1.3.2 Dissolution test of Xantid (ranitidine) with Calbo 500 (Calcium supplement).

Table 4.34: UV absorbance of Xantid (Ranitidine) with Calbo 500 (Calcium supplement).

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.189	0.239	0.357
2	0.246	0.407	0.416
3	0.135	0.281	0.299
4	0.320	0.367	0.385
5	0.390	0.610	0.540
6	0.062	0.113	0.290

4.1.3.2.1 Calculation for dissolved amount (mg) of Xantid (ranitidine) with Calbo 500 (Calcium supplement).

By using, Y= 0.045x+0.012 equation dissolved amount of Xantid (ranitidine) with Calbo 500 (Calcium supplement) was calculated.

Table 4.35: Determination of Dissolved amount of Xantid (Ranitidine) with Calbo 500 (Calcium supplement).

	After 20 minutes		After 40 minutes		After 60 minutes	
Serial number	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**
1	0.189	35.4	0.239	45.4	0.357	69
2	0.246	46.8	0.407	79	0.416	80.8
3	0.135	24.6	0.281	53.8	0.299	57.4
4	0.32	61.6	0.367	71	0.385	74.6
5	0.39	75.6	0.61	119.6	0.54	105.6
6	0.062	10	0.113	20.2	0.29	55.6

4.1.3.2.2 Comparison of dissolved amount and percent dissolved amount between Xantid (Ranitidine) and Xantid (Ranitidine) with Calbo 500 (Calcium supplement) and impact on dissolution calculation after 20,40 and 60 minutes.

4.1.3.2.2.1 Impact of Calbo 500 on the dissolution of Xantid after 20 minutes.

Table 4.36: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Calbo 500 (Calcium supplement) and impact on dissolution calculation after 20 minutes.

Xantid without any supplement				Xantid with Calbo 500				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
90.8		60.53		35.4		23.6		
83.2		55.47		46.8		31.2		
80.4	90.63	53.6	60.42	24.6	42.33	16.4	28.22	-53.29
99.4		66.27		61.6		41.07		
83.6		55.73		75.6		50.4		
106.4		70.93		10		6.67		

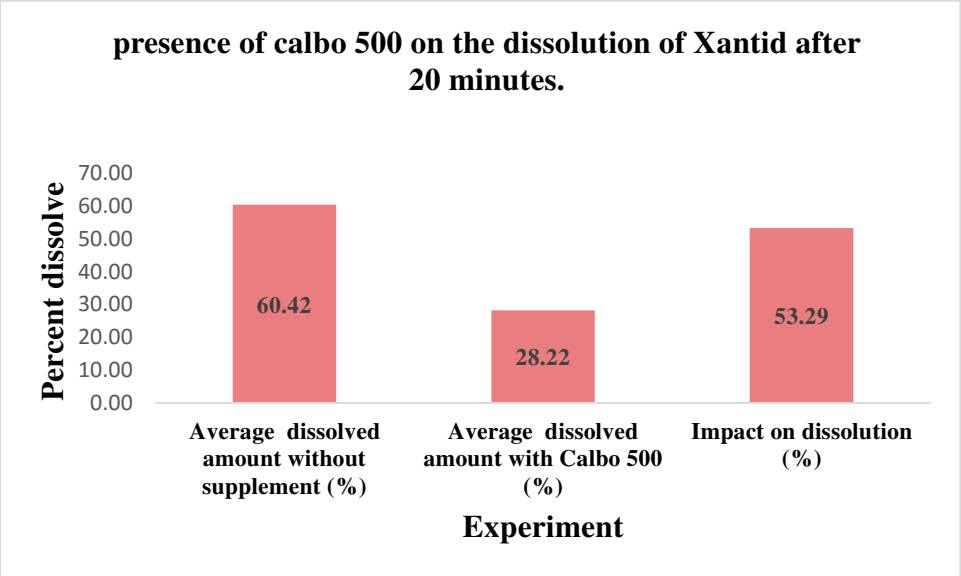

Figure 4.20: Graph represents the presence of calbo 500on the dissolution of Xantid after 20 minutes

4.1.3.2.2.2 Impact of Calbo 500 on the dissolution of Xantid after 40 minutes.

Table 4.37: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Calbo 500 (Calcium supplement) and impact on dissolution calculation after 40 minutes.

Xantid without any supplement				Xantid with Calbo 500				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
121.6		81.07		45.4		30.27		
117.8		78.53		79		52.67		
127.8	131.63	85.2	87.76	53.8	64.83	35.87	43.22	-50.75
138.6		92.4		71		47.33		
126.6		84.4		119.6		79.73		
157.4		104.93		20.2		13.47		

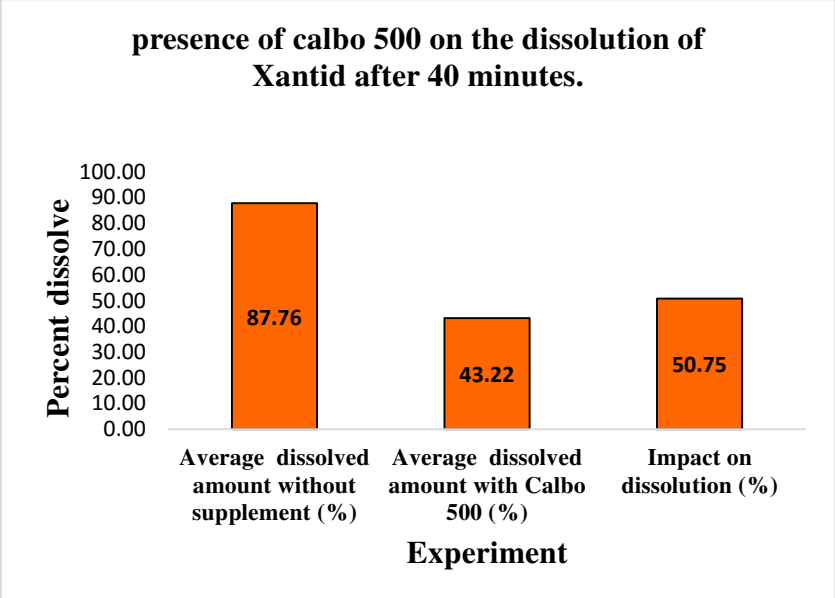

Figure 4.21: Graph represents the presence of calbo 500 on the dissolution of Xantid after 40 minutes.

4.1.3.2.2.3 Impact of Calbo 500 on the dissolution of Xantid after 60 minutes.

Table 4.38: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Calbo 500 (Calcium supplement) and impact on dissolution calculation after 60 minutes.

Xantid without any supplement				Xantid with Calbo 500				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
142		94.67		69		46		
142.4		94.93		80.8		53.87		
137.4	144.7	91.6	96.47	57.4	73.83	38.27	49.22	-48.98
144.4		96.27		74.6		49.73		
141.4		94.27		105.6		70.4		
160.6		107.07		55.6		37.07		

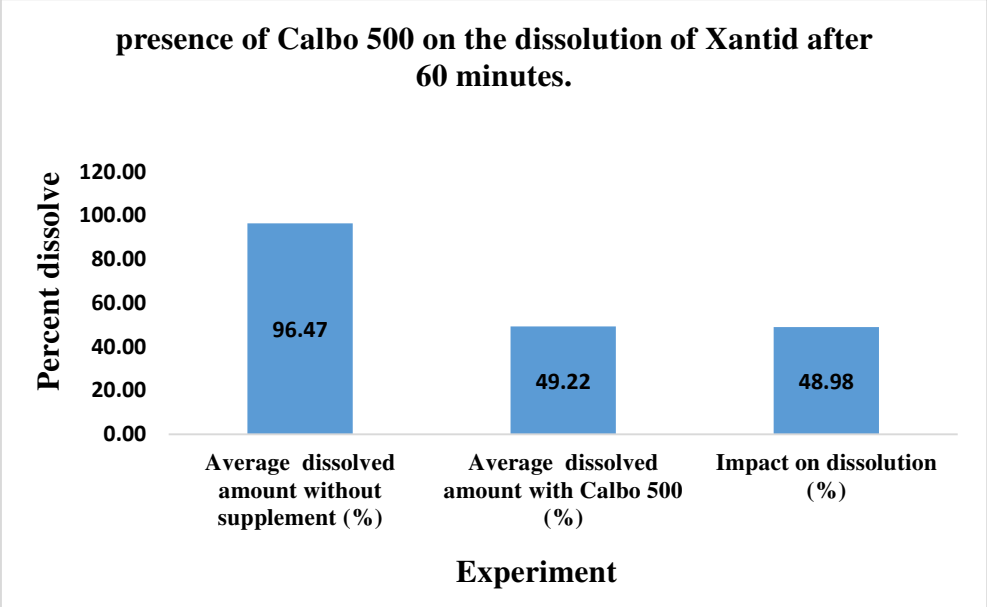

Figure 4.22: Graph represents the presence of calbo 500 on the dissolution of Xantid after 60 minutes.

4.1.3.3 Dissolution test of Xantid (ranitidine) with Aristocal D (Calcium and vitamin D supplement):

Table 4.39: UV absorbance of Xantid (Ranitidine) with Aristocal D (Calcium and vitamin D supplement.

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.245	0.350	0.620
2	0.345	0.488	0.467
3	0.432	0.422	0.635
4	0.437	0.560	0.550
5	0.478	0.450	0.490
6	0.421	0.510	0.590

4.1.3.3.1 Calculation for dissolved amount (mg) Xantid (ranitidine) with Aristocal D (Calcium and vitamin D supplement):

By using, Y= 0.045x+0.012 equation dissolved amount of Xantid (ranitidine) with Aristocal D (Calcium and vitamin D supplement) was calculated.

Table 4.40: Determination of Dissolved amount of Xantid (Ranitidine) with Aristocal D (Calcium and vitamin D supplement).

	After 20 minutes		**After 40 minutes**		**After 60 minutes**	
Serial number	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**
1	0.245	46.6	0.35	67.6	0.62	121.6
2	0.345	66.6	0.488	95.2	0.467	91
3	0.432	84	0.422	82	0.635	124.6
4	0.437	85	0.56	109.6	0.55	107.6
5	0.478	93.2	0.45	87.6	0.49	95.6
6	0.421	81.8	0.51	99.6	0.59	115.6

4.1.3.3.2 Comparison of dissolved amount and percent dissolved amount between Xantid (Ranitidine) and Xantid (Ranitidine) with Aristocal D (Calcium and vitamin D supplement) and impact on dissolution calculation after 20, 40 and 60 minutes.

4.1.3.3.2.1 Impact of Aristocal D on the dissolution of Xantid after 20 minutes.

Table 4.41: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Aristocal D (Calcium and vitamin D supplement) and impact on dissolution calculation after 20 minutes.

Xantid without any supplement				Xantid with Aristocal D				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
90.80		60.53		46.60		31.07		
83.20		55.47		66.60		44.40		
80.40	90.63	53.60	60.42	84.00	76.20	56.00	50.80	- 15.92
99.40		66.27		85.00		56.67		
83.60		55.73		93.20		62.13		
106.40		70.93		81.80		54.53		

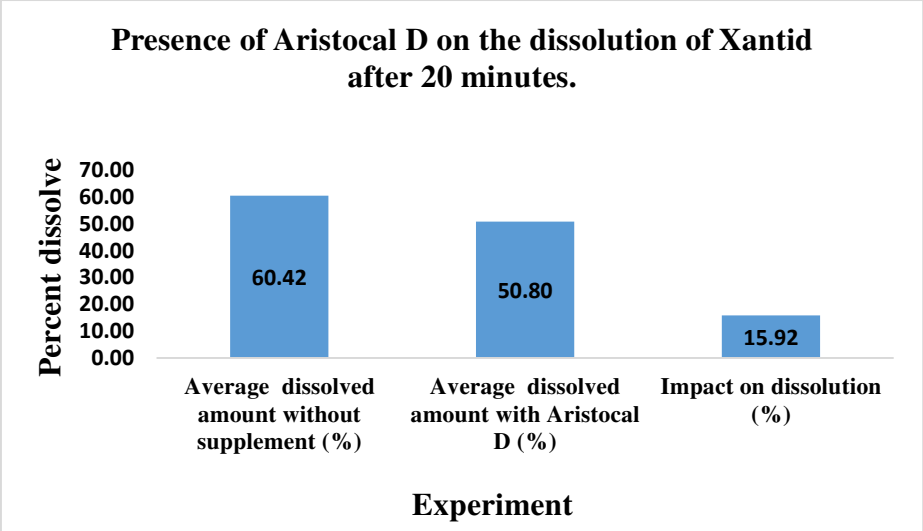

Figure 4.23: Graph represents the presence of Aristocal D on the dissolution of Xantid after 20 minutes.

4.1.3.3.2.2 Impact of Aristocal D on the dissolution of Xantid after 40 minutes.

Table 4.42: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Aristocal D (Calcium and vitamin D supplement) and impact on dissolution calculation after 40 minutes.

Xantid without any supplement				Xantid with Aristocal D				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
121.60		81.07		67.60		45.07		
117.80		78.53		95.20		63.47		
127.80	131.63	85.20	87.76	82.00	90.27	54.67	60.18	- 31.43
138.60		92.40		109.60		73.07		
126.60		84.40		87.60		58.40		
157.40		104.93		99.60		66.40		

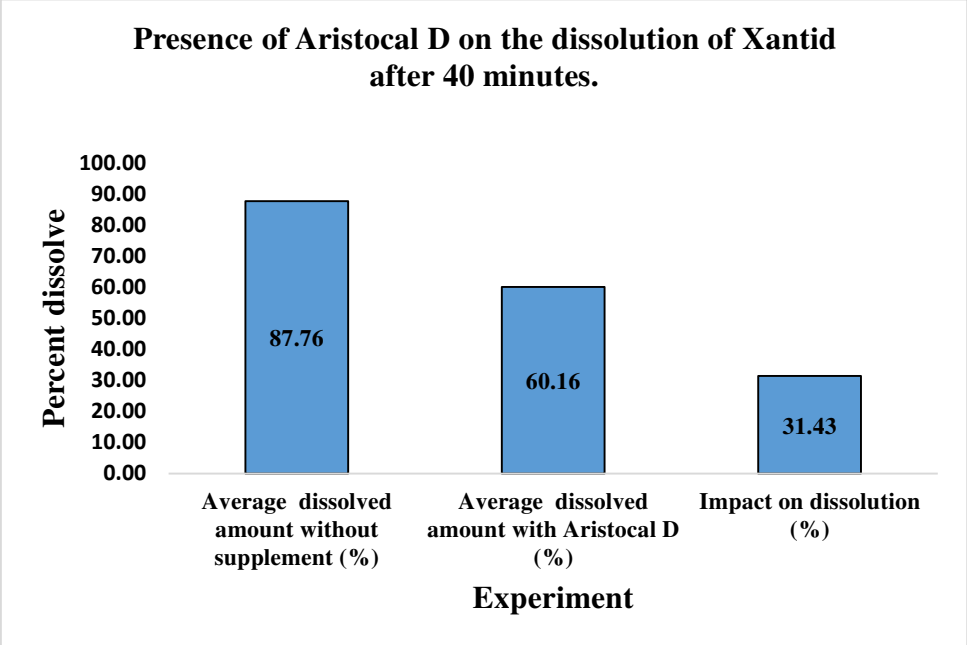

Figure 4.24: Graph represents the presence of Aristocal D on the dissolution of Xantid after 40 minutes.

4.1.3.3.2.3 Impact of Aristocal D on the dissolution of Xantid after 60 minutes.

Table 4.43: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Aristocal D (Calcium and vitamin D supplement) and impact on dissolution calculation after 60 minutes.

Xantid without any supplement				Xantid with Aristocal D				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
142.00		94.67		121.60		81.07		
142.40		94.93		91.00		60.67		
137.40	144.70	91.60	96.47	124.60	109.33	83.07	72.89	- 24.44
144.40		96.27		107.60		71.73		
141.40		94.27		95.60		63.73		
160.60		107.07		115.60		77.07		

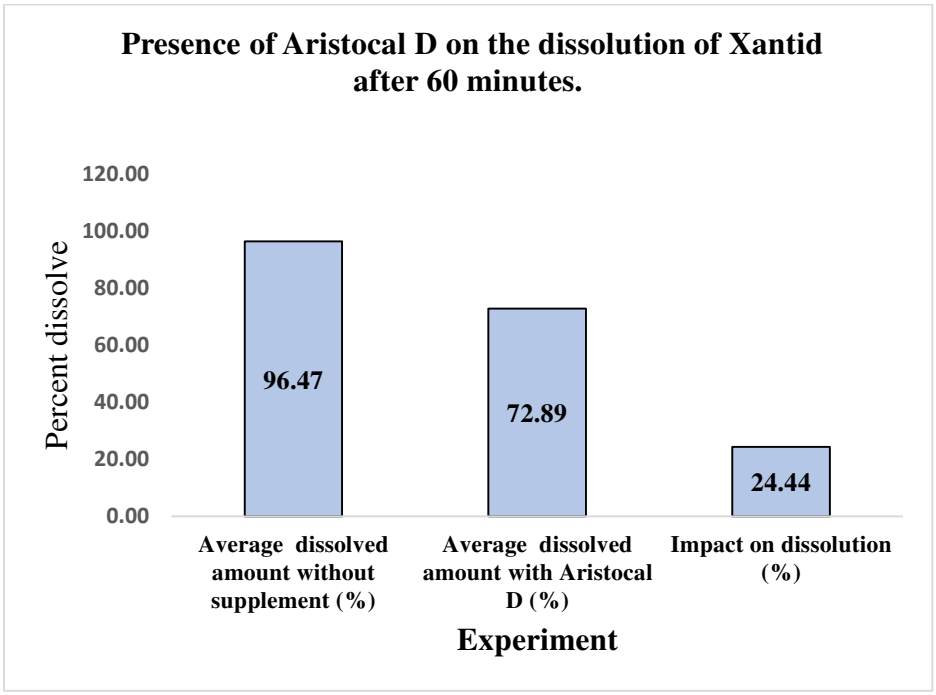

Figure 4.25: Graph represents the presence of Aristocal D on the dissolution of Xantid after 60 minutes.

4.1.3.4 Dissolution test of Xantid (ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement)

Table 4.44: UV absorbance of Xantid (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement).

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.137	0.189	0.210
2	0.394	0.422	0.467
3	0.105	0.129	0.378
4	0.135	0.489	0.366
5	0.380	0.441	0.461
6	0.220	0.322	0.388

4.1.3.4.1 Calculation for dissolved amount (mg) Xantid (ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement)

By using, Y= 0.045x+0.012 equation dissolved amount of Xantid (ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) was calculated.

Table 4.45: Determination of Dissolved amount of Xantid (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement).

	After 20 minutes		**After 40 minutes**		**After 60 minutes**	
Serial number	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**
1	0.137	25.00	0.189	35.40	0.210	39.60
2	0.394	76.40	0.422	82.00	0.467	91.00
3	0.105	18.60	0.129	23.40	0.378	73.20
4	0.135	24.60	0.489	95.40	0.366	70.80
5	0.380	73.60	0.441	85.80	0.461	89.80
6	0.220	41.60	0.322	62.00	0.388	75.20

4.1.3.4.2 Comparison of dissolved amount and percent dissolved amount between Xantid (Ranitidine) and Xantid (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation after 20, 40 and 60 minutes.

4.1.3.4.2.1 Impact of Acical M on the dissolution of Xantid after 20 minutes.

Table 4.46: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation after 20 minutes.

Xantid without any supplement				Xantid with Acical M				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
110.4		73.6		25		16.67		
80.6		53.73		76.4		50.93		
94.8	89.8	63.2	59.87	18.6	43.3	12.4	28.87	-52.21
82.4		54.93		24.6		16.4		
85.4		56.93		73.6		49.07		
85.2		56.8		41.6		27.73		

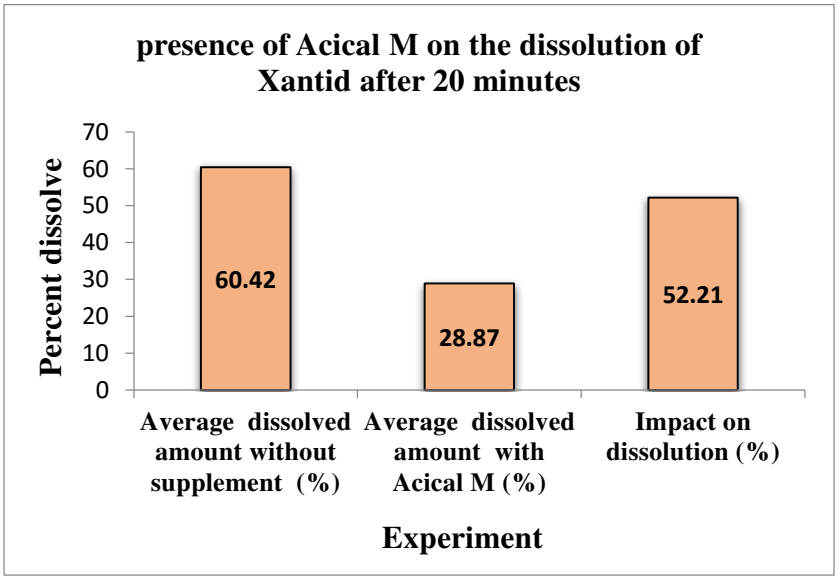

Figure 4.26: Graph represents the presence of Acical M on the dissolution of Xantid after 20 minutes.

4.1.3.4.2.2. Impact of Acical Mon the dissolution of Xantid after 40 minutes.

Table 4.47: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation after 40 minutes.

Xantid without any supplement				Xantid with Acical M				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
121.60		81.07		35.40		23.60		
117.80		78.53		82.00		54.67		
127.80	131.63	85.20	87.76	23.40	64.00	15.60	42.67	- 51.38
138.60		92.40		95.40		63.60		
126.60		84.40		85.80		57.20		
157.40		104.93		62.00		41.33		

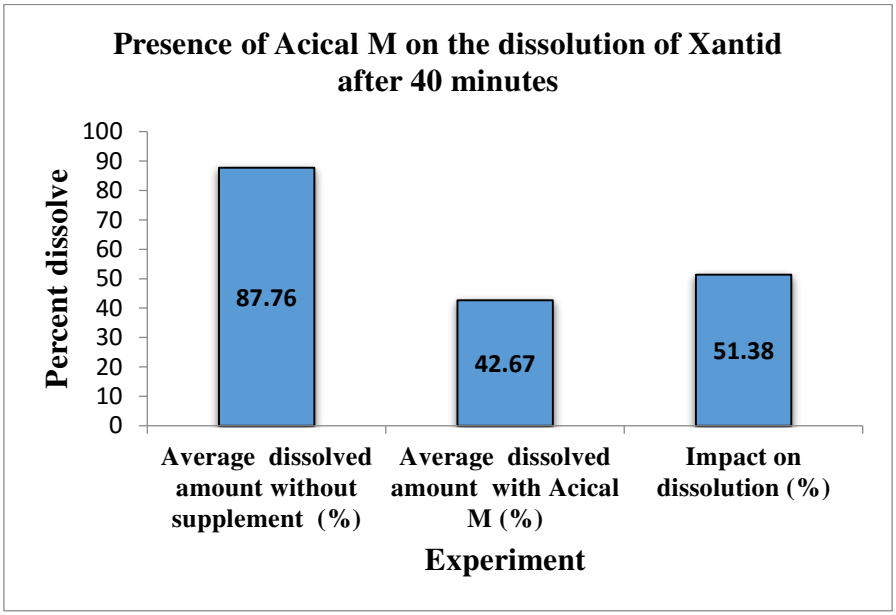

Figure 4.27: Graph represents the presence of Acical M on the dissolution of Xantid after 40 minutes.

4.1.3.4.2.3 Impact of Acical M on the dissolution of Xantid after 60 minutes.

Table 4.48: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation after 60 minutes.

Xantid without any supplement				Xantid with Acical M				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
142.00		94.67		39.60		26.40		
142.40		94.93		91.00		60.67		
137.40	144.70	91.60	96.47	73.20	73.27	48.80	48.84	- 49.89
144.40		96.27		70.80		47.20		
141.40		94.27		89.80		59.87		
160.60		107.07		75.20		50.13		

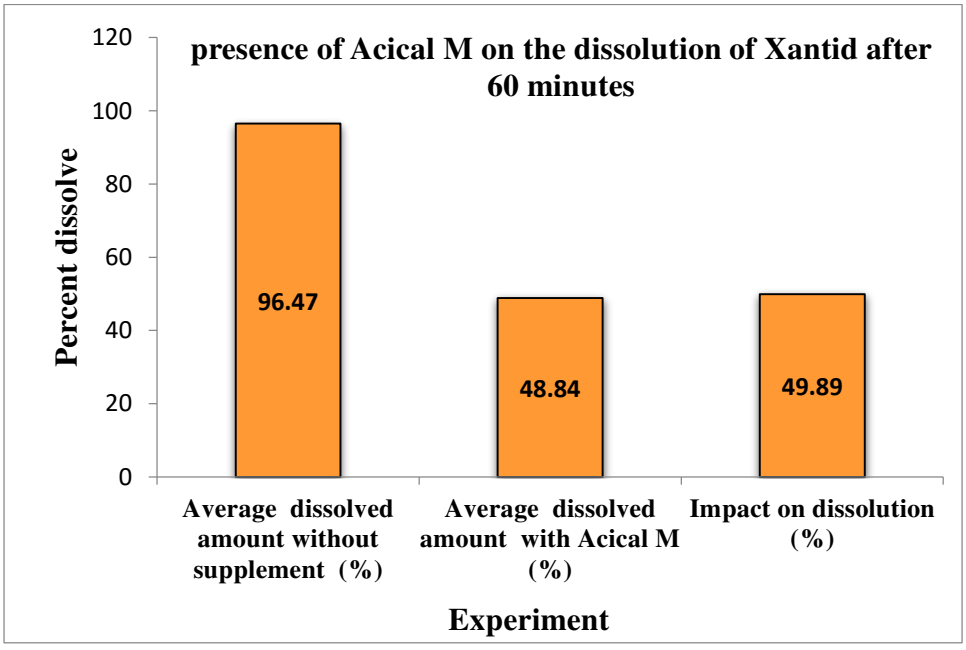

Figure 4.28: Graph represents the presence of Acical M on the dissolution of Xantid after 60 minutes.

4.1.3.5 Dissolution test of Xantid (ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement)

Table 4.49: UV absorbance of Xantid (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement).

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.412	0.589	0.612
2	0.447	0.605	0.754
3	0.460	0.685	0.698
4	0.501	0.729	0.740
5	0.527	0.721	0.810
6	0.616	0.752	0.823

4.1.3.5.1 Calculation for dissolved amount (mg) of Xantid (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement).

By using, Y= 0.045x+0.012 equation dissolved amount of Xantid (ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) was calculated.

Table 4.50: Determination of Dissolved amount of Xantid (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement).

	After 20 minutes		After 40 minutes		After 60 minutes	
Serial number	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**
1	0.412	80.00	0.589	115.40	0.612	120.00
2	0.447	87.00	0.605	118.60	0.754	148.40
3	0.460	89.60	0.685	134.60	0.698	137.20
4	0.501	97.80	0.729	143.40	0.740	145.60
5	0.527	103.00	0.721	141.80	0.810	159.60
6	0.616	120.80	0.752	148.00	0.823	162.20

4.1.3.5.2 Comparison of dissolved amount and percent dissolved amount between Xantid (Ranitidine) and Xantid (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) and impact on dissolution calculation after 20 40 and 60 minutes.

4.1.3.5.2.1 Impact of Nutrum Gold on the dissolution of Xantid after 20 minutes.

Table 4.51: Percentage calculation for dissolved amount of Xantid **(Ranitidine) and** Xantid **(Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) and impact on dissolution calculation after 20 minutes.**

Xantid without any supplement				Xantid with Nutrum Gold				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
90.8		60.53		80		53.33		
83.2		55.47		87		58		
80.4	90.63	53.6	60.42	89.6	96.37	59.73	64.24	6.32
99.4		66.27		97.8		65.2		
83.6		55.73		103		68.67		
106.4		70.93		120.8		80.53		

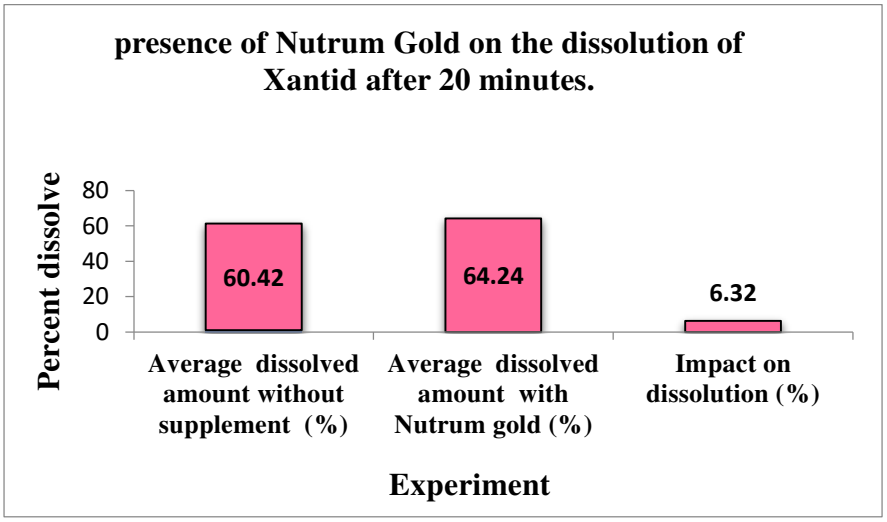

Figure 4.29: Graph represents the presence of Nutrum Gold on the dissolution of Xantid after 20 minutes.

4.1.3.5.2.2. Impact of Nutrum Gold on the dissolution of Xantid after 40 minutes.

Table 4.52: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) and impact on dissolution calculation after 40 minutes.

Xantid without any supplement				Xantid with Nutrum Gold				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
121.60		81.07		115.40		76.93		
117.80		78.53		118.60		79.07		
127.80	131.63	85.20	87.76	134.60	133.63	89.73	89.09	1.52
138.60		92.40		143.40		95.60		
126.60		84.40		141.80		94.53		
157.40		104.93		148.00		98.67		

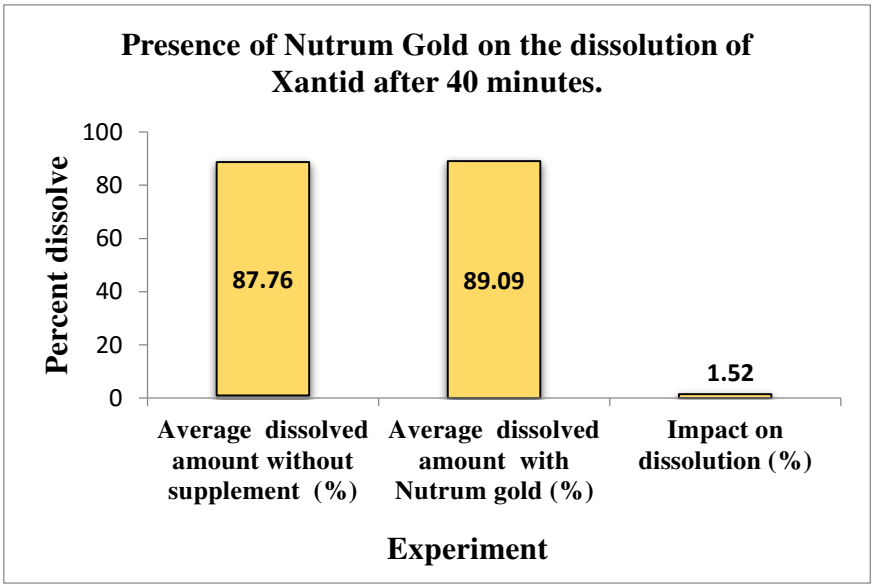

Figure 4.30: Graph represents the presence of Nutrum Gold on the dissolution of Xantid after 40 minutes.

4.1.3.5.2.3 Impact of Nutrum Gold on the dissolution of Xantid after 60 minutes.

Table 4.53: Percentage calculation for dissolved amount of Xantid **(Ranitidine) and** Xantid **(Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) and impact on dissolution calculation after 60 minutes.**

Xantid without any supplement				Xantid with Nutrum Gold				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
142.00		94.67		120.00		80.00		
142.40		94.93		148.40		98.93		
137.40	144.70	91.60	96.47	137.20	145.50	91.47	97.00	0.55
144.40		96.27		145.60		97.07		
141.40		94.27		159.60		106.40		
160.60		107.07		162.20		108.13		

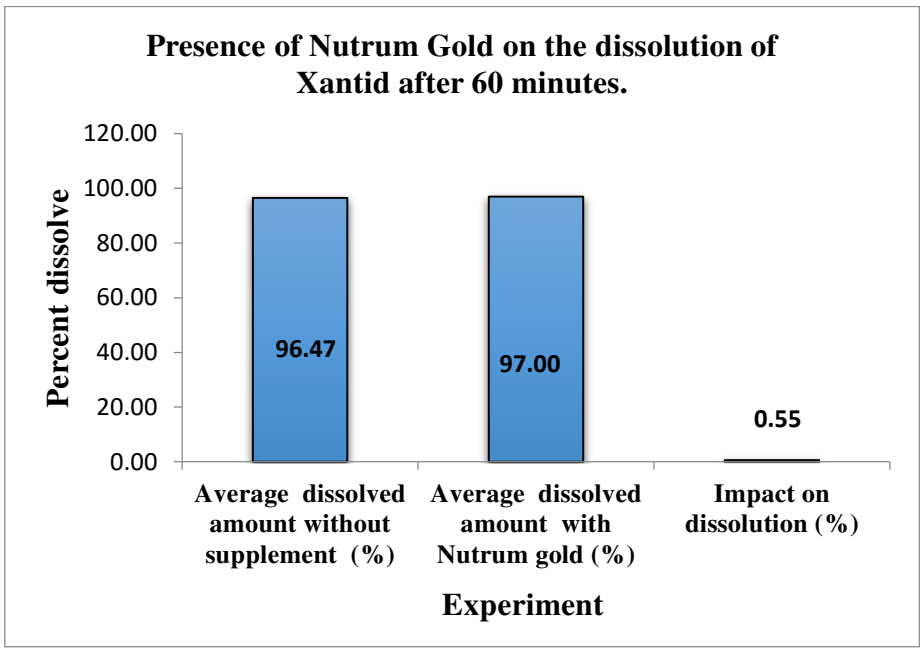

Figure 4.31: Graph represents the presence of Nutrum Gold on the dissolution of Xantid after 60 minutes

4.1.3.6 Dissolution test of Xantid (ranitidine) with Filwel Silver (Multivitamin and multimineral supplement).

Table 4.54: UV absorbance of Xantid (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement)

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.563	0.690	0.752
2	0.467	0.645	0.698
3	0.523	0.710	0.814
4	0.345	0.554	0.634
5	0.475	0.679	0.734
6	0.520	0.771	0.867

4.1.3.6.1 Calculation for dissolved amount (mg) of Xantid (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement).

By using, Y= 0.045x+0.012 equation dissolved amount of Xantid (ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) was calculated.

Table 4.55: Determination of Dissolved amount of Xantid (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement).

	After 20 minutes		After 40 minutes		After 60 minutes	
Serial number	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**	**Absorbance**	**Dissolved amount (mg)**
1	0.563	110.2	0.69	135.6	0.752	148
2	0.467	91	0.645	126.6	0.698	137.2
3	0.523	102.2	0.71	139.6	0.814	160.4
4	0.345	66.6	0.554	108.4	0.634	124.4
5	0.475	92.6	0.679	133.4	0.734	144.4
6	0.52	101.6	0.771	151.8	0.867	171

4.1.3.6.2 Comparison of dissolved amount and percent dissolved amount between Xantid (Ranitidine) and Xantid (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) and impact on dissolution calculation after 20, 40 and 60 minutes.

4.1.3.6.2.1 Impact of Filwel Silver on the dissolution of Xantid after 20 minutes.

Table 4.56: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) and impact on dissolution calculation after 20 minutes.

Xantid without any supplement				Xantid with Filwel Silver				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
90.80		60.53		110.20		73.47		
83.20		55.47		91.00		60.67		
80.40	90.63	53.60	60.42	102.20	94.03	68.13	62.69	3.75
99.40		66.27		66.60		44.40		
83.60		55.73		92.60		61.73		
106.40		70.93		101.60		67.73		

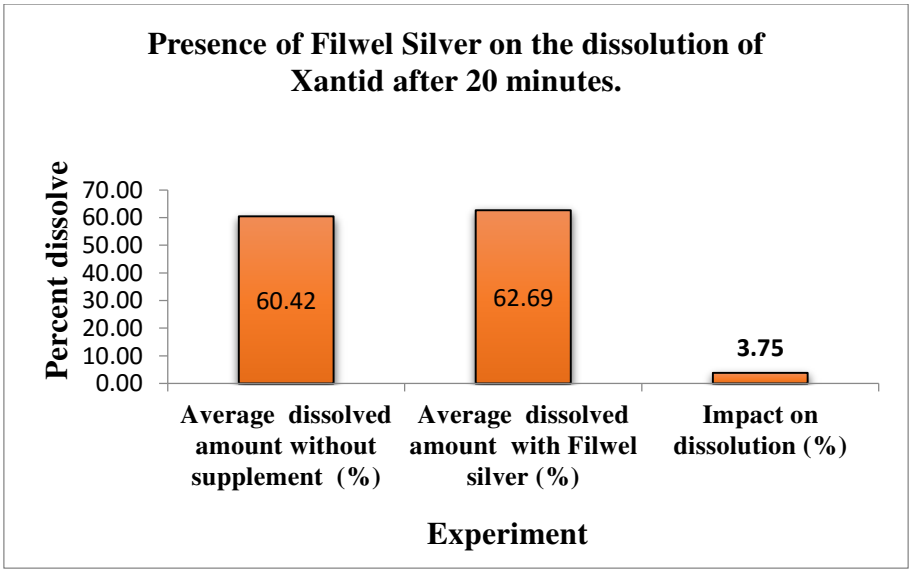

Figure 4.32: Graph represents the presence of Filwel Silver on the dissolution of Xantid after 20 minutes.

4.1.3.6.2.2 Impact of Filwel Silver on the dissolution of Xantid after 40 minutes.

Table 4.57: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) and impact on dissolution calculation after 40 minutes.

Xantid without any supplement				Xantid with Filwel Silver				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
121.60		81.07		135.60		90.40		
117.80		78.53		126.60		84.40		
127.80	131.63	85.20	87.76	139.60	132.57	93.07	88.38	0.71
138.60		92.40		108.40		72.27		
126.60		84.40		133.40		88.93		
157.40		104.93		151.80		101.20		

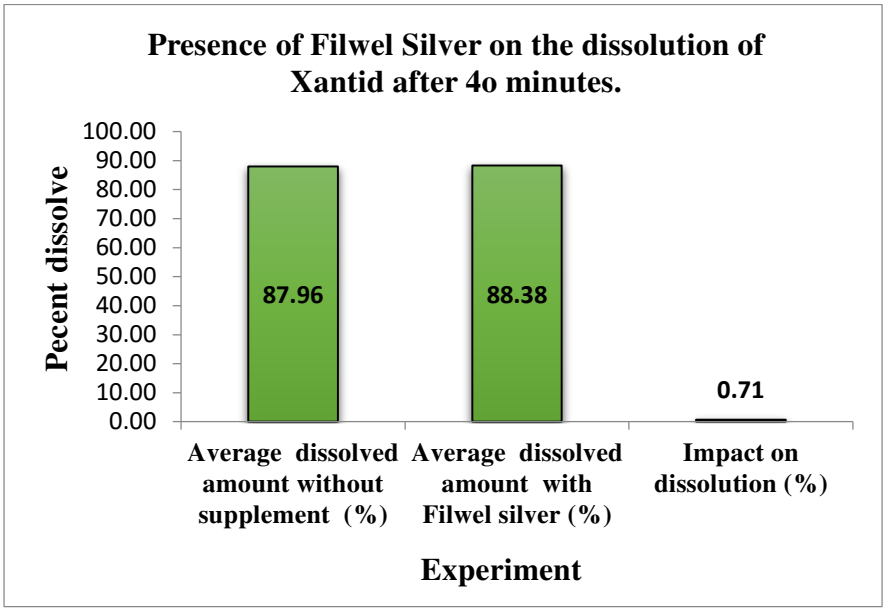

Figure 4.33: Graph represents the presence of Filwel Silver on the dissolution of Xantid after 4o minutes.

4.1.3.6.2.3 Impact of Filwel Silver on the dissolution of Xantid after 60 minutes.

Table 4.58: Percentage calculation for dissolved amount of Xantid (Ranitidine) and Xantid (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) and impact on dissolution calculation after 60 minutes.

Xantid without any supplement				Xantid with Filwel Silver				
Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Dissolved amount (mg)	Average dissolved amount (mg)	Percent dissolved amount (%)	Average percent dissolved amount (%)	Impact on dissolution (%)
142.00		94.67		148.00		98.67		
142.40		94.93		137.20		91.47		
137.40	144.70	91.60	96.47	160.40	147.57	106.93	98.38	1.97
144.40		96.27		124.40		82.93		
141.40		94.27		144.40		96.27		
160.60		107.07		171.00		114.00		

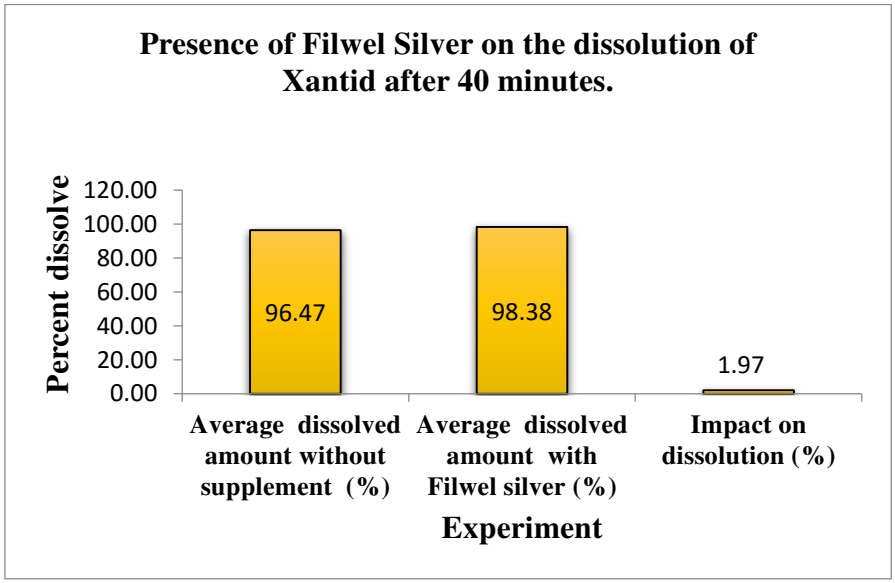

Figure 4.34: Graph represents the presence of Filwel Silver on the dissolution of Xantid after 60 minutes.

4.1.3.7 Comparison among the average percent dissolved (%) amount of individual Xantid, Xantid with Calbo, Xantid with Aristocal D, Xantid with Acical M, Xantid with Nutrum Gold and Xantid with Filwel silver after 20, 40, 60 minutes.

Table 4.59: Table showing the differences among the average percent dissolve (%) amount of individual Xantid, Xantid with Calbo 500, Xantid with Aristocal D, Xantid with Acical M, Xantid with Nutrum Gold and Xantid with Filwel silver after 20 minutes.

Average percent dissolved amount of Xnatid without supplement (%)	Average percent dissolved amount of Xnatid with calbo 500 (%)	Average percent dissolved amount of Xnatid with Aristocal D (%)	Average percent dissolved amount of Xnatid with Acical M (%)	Average percent dissolved amount of Xnatid with Nutrum Gold (%)	Average percent dissolved amount of Xnatid with Filwel Silver (%)
60.42	28.22	50.8	28.87	64.24	62.69

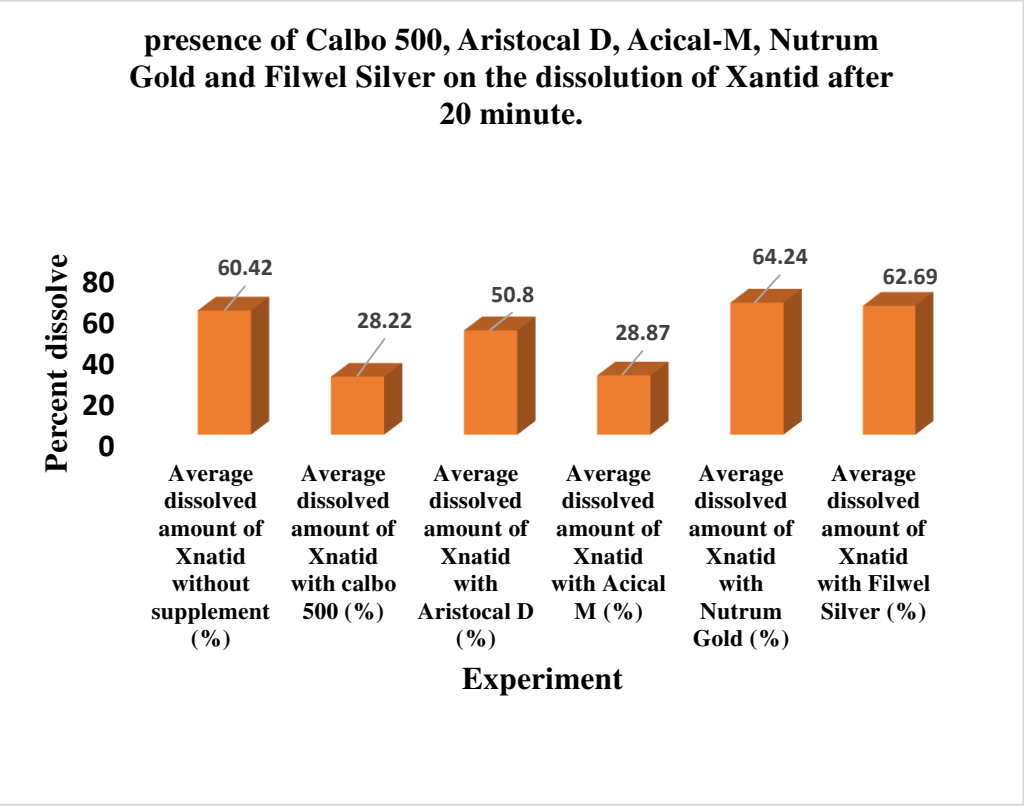

Figure 4.35: Graph represents the presence of Calbo 500, Aristocal D, Acical-M, Nutrum Gold and Filwel Silver on the dissolution of Xantid after 20 minute.

Table 4.60: Table showing the differences among the average percent dissolve (%) amount of individual Xantid, Xantid with Calbo 500, Xantid with Aristocal D, Xantid with Acical-M, Xantid with Nutrum Gold and Xantid with Filwel silver after 40 minutes.

Average percent dissolved amount of Xnatid without supplement (%)	Average percent dissolved amount of Xnatid with calbo 500 (%)	Average percent dissolved amount of Xnatid with Aristocal D (%)	Average percent dissolved amount of Xnatid with Acical M (%)	Average percent dissolved amount of Xnatid with Nutrum Gold (%)	Average percent dissolved amount of Xnatid with Filwel Silver (%)
87.76	43.22	60.18	42.67	89.09	88.38

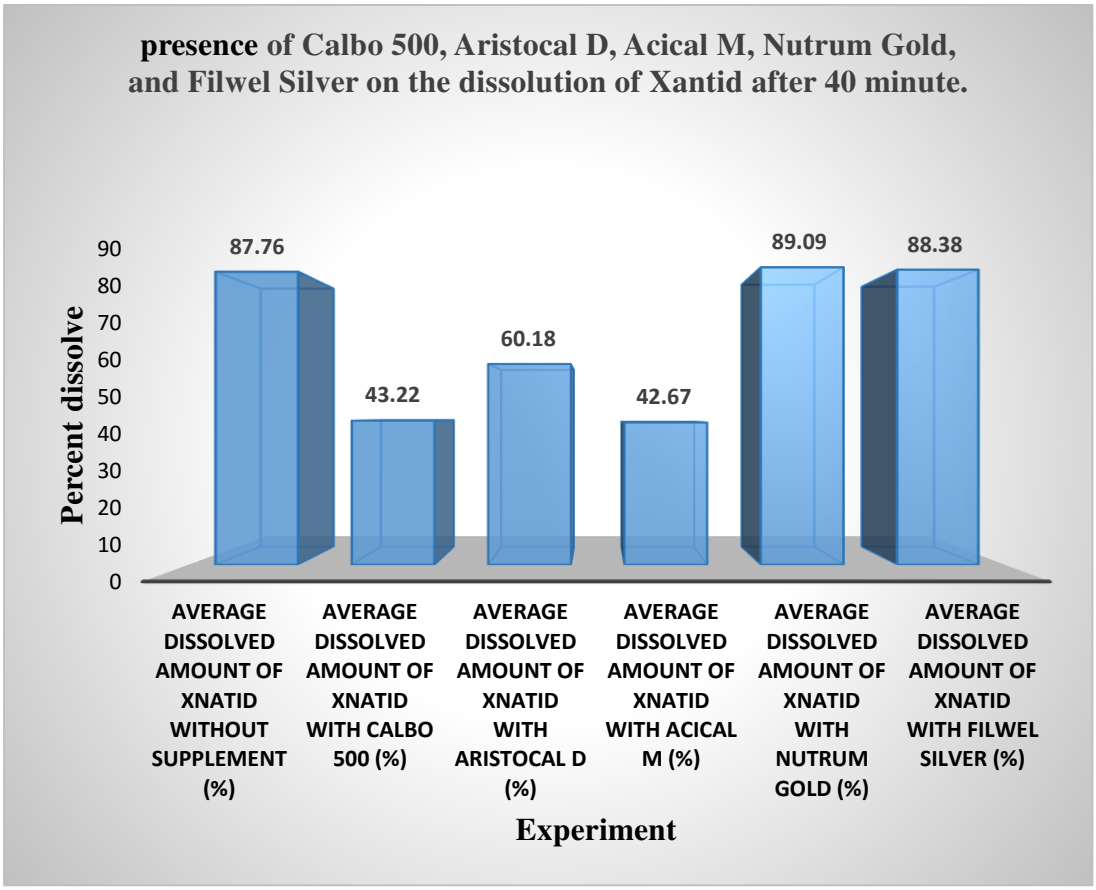

Figure 4.36: Graph represents the presence of Calbo 500, Aristocal D, Acical M, Nutrum Gold, and Filwel Silver on the dissolution of Xantid after 40 minute.

Table 4.61: Table showing the differences among the average percent dissolve (%) amount of individual Xantid, Xantid with Calbo 500, Xantid with Aristocal D, Xantid with Acical M, Xantid with Nutrum Gold and Xantid with Filwel silver after 60 minutes.

Average percent dissolved amount of Xnatid without supplement (%)	Average percent dissolved amount of Xnatid with calbo 500 (%)	Average percent dissolved amount of Xnatid with Aristocal D (%)	Average percent dissolved amount of Xnatid with Acical M (%)	Average percent dissolved amount of Xnatid with Nutrum Gold (%)	Average percent dissolved amount of Xnatid with Filwel Silver (%)
96.47	49.22	72.89	48.84	97	98.38

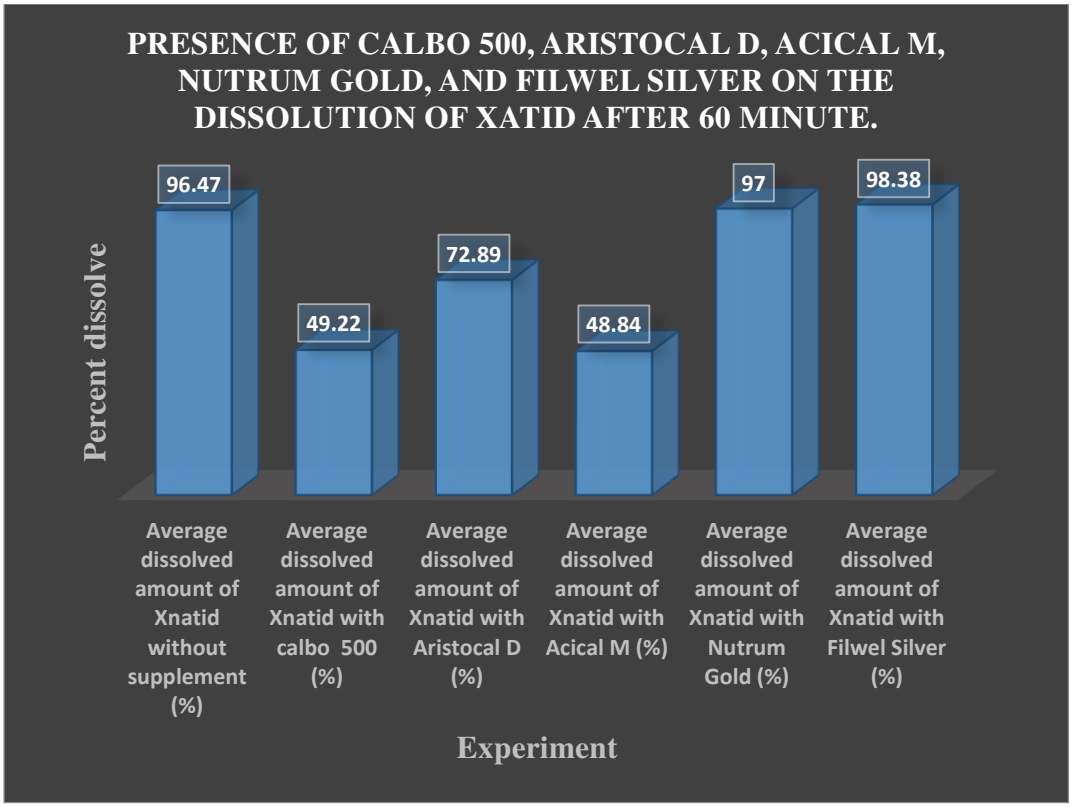

Figure 4.37: Graph represents the presence of Calbo 500, Aristocal D, Acical M, Nutrum Gold, and Filwel Silver on the dissolution of Xatid after 60 minute.

4.1.4 Result from weight variation test:

Table 4.62: Table showing weight variation test of Zantac tablets.

Tablet No.	Initial weight I (mg)	Average weight A (mg)	% Weight variation (A-I)/I *100
1	0.32		-4.06
2	0.31		-0.97
3	0.31		-0.97
4	0.31		-0.97
5	0.3	0.307	2.33
6	0.31		-0.97
7	0.3		2.33
8	0.31		-0.97
9	0.3		2.33
10	0.3		2.33

Table 4.63: Table showing weight variation test of Xantid tablets.

Tablet No.	Initial weight I (mg)	Average weight A (mg)	% Weight variation (A-I)/I *100
1	0.26		-2.69
2	0.27		-6.296
3	0.27		-6.296
4	0.26		-2.69
5	0.26	0.253	-2.69
6	0.23		10
7	0.22		15
8	0.26		-2.69
9	0.25		1.2
10	0.25		1.2

4.1.5 Results from thickness test:

Table 4.64: Table showing thickness test of Zantac Tablets.

Tablet No.	Main scale reading (cm), M	Vernier scale reading (cm), V	Thickness of the tablet (cm), (M+V)
1	0.3	0.06	0.36
2	0.3	0.07	0.37
3	0.3	0.05	0.35
4	0.3	0.07	0.37
5	0.3	0.06	0.36
6	0.3	0.04	0.34
7	0.3	0.08	0.38
8	0.3	0.02	0.32
9	0.3	0.08	0.38
10	0.3	0.06	0.36

Table 4.65: Table showing thickness test of Xantid Tablets.

Tablet No.	Main scale reading (cm), M	Vernier scale reading (cm), V	Thickness of the tablet (cm), (M+V)
1	0.4	0.03	0.43
2	0.4	0.06	0.46
3	0.4	0.03	0.43
4	0.4	0.03	0.43
5	0.4	0.02	0.42
6	0.4	0.03	0.43
7	0.4	0.02	0.42
8	0.4	0.02	0.42
9	0.4	0.02	0.42
10	0.4	0.02	0.42

4.1.6 Results from Hardness tests:

Table 4.66: Table showing harness test of Zantac Tablets.

Tablet No.	Hardness (Kg)	Average
1	10	
2	11	11
3	12	

Table 4.67: Table showing harness test of Xantid Tablets.

Tablet No.	Hardness (Kg)	Average
1	18.5	
2	19.2	18.9
3	19	

CHAPTER FIVE DISCUSSIONS

5.1 DISCUSSIONS

Weight variation test was run to ensure that all tablets in a batch are within the reasonable limits, of the same batch. All two batches of Zantac and Xantid showed a percentage weight variation within the range of ±7.5 and, therefore, comply with the specification of USP that is mentioned in Table 3.5 (Scribd, 2016). Hardness tests were done to observe the strength of the tablets. If tablet is too hard, it may not disintegrate in the required period of time and will fail dissolution test. If tablet is too soft it may not be able to withstand handling during subsequent processing such as coating or packaging and shipping operations (Don, 2011). All the tablets hardness were proper to be administered. Thickness is important parameter of a tablet because if thickness of the tablets of same batch varies then dissolution time will vary (Don, 2011).In this experiment the tablets of the same back showed thickness in the same range, so these tablets were proper to be administered.

After an hour the percent dissolved amount of Zantac with Calbo 500 (Calcium Supplement) and Acical-M (Calcium, vitamin D and Multimineral supplement) were extremely decreased by 49.87% (mentioned in table 4.4) and 48.49% (mentioned in table 4.10) respectively. After an hour the percent dissolved amount of Xantid with Calbo 500 and Acical-M were extremely decreased by 49.98% (mentioned in table 4.22) and 49.89% (mentioned in table 4.28) respectively. As the dissolution was affected, this indicates absorption will must be affected. So there is a chance of Zantac or Xantid not to reach to the Minimum Effective Concentration (MEC) (Guzman, 2016), and it will fail to give the therapeutic effect. So Zantac and Xantid should not be co-administered with Calbo 500 and Acical-M.

Experiment showed that after an hour the percent dissolved amount of Zantac and Xantid with Aristocal D (Calcium and vitamin D supplement) were 22.83% (mentioned in table 4.7) and 24.44% (mentioned in table 4.25) respectively. These results indicates that dissolution was moderately decreased in the presence Aristocal D. As the dissolution was affected, this indicates absorption can also be affected (Guzman, 2016). So the efficacy of Zantac and Xantid will decrease. So Zantac and Xantid should not be co-administered with Aristocal D.

Experiment showed that after an hour the dissolution of Zantac and Xantid was not significantly decreased in the presence of Nutrum Gold (Multivitamin and multimineral supplement) or Filwel Silver (Multivitamin and multimineral supplement). So absorption of Zantac and Xantid will not be affected in the presence of Nutrum Gold and Filwel Silver and efficacy will not be decreased. So Zantac and Xantid can be co-administered with Nutrum Gold and Filwel Silver.

CHAPTER SIX CONCLUSION

6.1 CONCLUSION

In this study it was observed that Calbo 500 (Calcium supplement) and Acical-M (Calcium, Vitamin D and Multimineral supplement) both has significant impact on the dissolution of Zantac and Xantid. Aristocal D (Calcium and vitamin D supplement) has moderate impact on the dissolution of Zantac and Xantid. But Nutrum Gold (multivitamin and multimineral supplement) and Filwel Silver (Multivitamin and multimineral supplement) does not have significant impact on the dissolution of Zantac and Xantid. So, Nutrum Gold and Filwel Silver can be co-administered Zantac and Xantid but Calbo 500, Acical-M and Aristocal D should not be co-administered with Zantac and Xantid because if Zantac and Xantid cannot reach to the therapeutic window, it will not be able to give the therapeutic effect.

CHAPTER SEVEN

REFERENCES

7.1 REFERENCES

Aci (2016) Acical – *M.* [Online] *Available* at: http://aci-bd.com/Brand/Acical-M.pdf [Accessed: 5 May 2016].

Aci (2016) Xantid. [Online] Available at: http://aci-bd.com/Brand/Xantid.pdf. [Accessed: 7 May 2016].

Acme (2014) *NUTRUM GOLD.* [Online] Available at: http://acmeglobal.com/acme/products/. [Accessed: 7 May 2016].

Beximcopharma (2014) Aristocal *D.* [Online] Available at: http://beximcopharma.com/component/sobipro/317.html?Itemid=913. [Accessed: 7 May 2016].

Adachi, K., Komazawa, Y., Fujishiro, H., Mihara, T., Kawamura, A., Amano, Y. (2003) Nocturnal gastric acid breakthrough during the administration of rabeprazole and ranitidine in Helicobacter pylori-negative subjects: effects of different regimens. *Journal of Gastroenterology,* 38(9), 830-835.

Aslani, A., Jahangiri, H. (2013) Formulation, characterization and physicochemical evaluation of ranitidine effervescent tablets. *Advanced pharmaceutical bulletin,* 3(2), 315-322.

Azad, A.K., Islam, M.A., Azizi, M.W. (2013) Appraisement of Ranitidine Hydrochloride Tablet (USP150mg) Preparations from Few Selected Companies in Bangladesh. *Pakistan Journal of Nutrition, 12*(11), 966-972.

Cappola, M.L. (2001) A better dissolution method for ranitidine tablets USP. *Pharmaceutical development and technology,* 6(1), 11-17.

Drug Bank (2005) *Ranitidine.* [Online] Available at: *http://www.drugbank.ca/drugs/DB00863*. [Accessed: 9 May 2016].

Caro, J.J., Salas, M., Ward, A. (2001) Healing and relapse rates in gastroesophageal reflux disease treated with the newer proton-pump inhibitors lansoprazole, rabeprazole, and pantoprazole compared with omeprazole, ranitidine, and placebo: evidence from randomized clinical trials. *Clinical Therapeutics,* 23(7), 998-1017.

Chen, M.L., Straughn, A.B., Sadrieh, N., Meyer, M., Faustino, P.J., Ciavarella, A.B., Meibohm, B., Yates, C.R., Hussain, A.S. (2007) A Modern View of Excipient Effects on Bioequivalence: Case Study of Sorbitol. *Pharmaceutical Research,* 24(1), 73-80.

Dagmar, K.M.D., Michael, B. Michael. Z.D., Mueck, W. (2006) Effect of Food, an Antacid, and the H2 Antagonist Ranitidine on the Absorption of BAY 59–7939 (Rivaroxaban), an Oral, Direct Factor Xa Inhibitor, in Healthy Subjects. *The Journal of Clinical Pharmacology,* 49(5), 549-558.

David, Y., Graham, M.D., Ginger, M., Peter, D., Saeed, Z.A., Hoda, M., Malaty, M.D. (1992) Effect of Treatment of Helicobacter pylori Infection on the Long-term Recurrence of Gastric or Duodenal Ulcer: A Randomized, Controlled Study. *Annals of Internal Medicine,* 116(9), 705-708.

Desechalliers, J.P., Galmiche, J.P., Touchais, Y.J., Denis, P., Colin, R. (1984) Ranitidine, cimetidine, antacids, and gastro-oesophageal reflux: results of a 20-hour oesophageal pH study. *International Journal of Clinical Pharmacology Research,* 4(3), 217-222.

Don, J. (2011) *Tablet friability, hardness and dissolution testing.* [Online] Available at: http://www.slideshare.net/donjacob81/tablet-friabilityharness-and-dissolution-testing?next_slideshow=2 [Accessed: 6 July 2016].

Drugs.com (2000) Ranitidine. [Online] Available at: http://www.drugs.com/ranitidine.html. [Accessed: 8 May 2016].

Drugs.com (2016) *Zantac.* [Online] Available at: http://www.drugs.com/pro/zantac.html. [Accessed: 8 May 2016].

Dyal, D.C., Garg, P., Fred, D.N., Eshelman, P., Donald, J. (1985) Pharmacokinetics of Ranitidine Following Oral Administration With Ascending Doses and With Multiple-Fixed Doses. *The Journal of Clinical Pharmacology,* 25(6), 437-443.

Ekstrom, T., Lindgren, B.R., Tibbling, L. (1989) Effects of ranitidine treatment on patients with asthma and a history of gastro-oesophageal reflux: a double blind crossover study. *Thorax,* 44(1), 19.

Farup, P.G., Larsen, S., Ulshagen, K., Osnes, M., (1991) Ranitidine for Non-Ulcer Dyspepsia: A Clinical Study of the Symptomatic Effect of Ranitidine and a Classification and Characterization of the Responders to Treatment. *Scandinavian Journal of Gastroenterology,* 26(11), 1209-1216.

Guzman, F.M.D. (2016) *pharmacokinetics (drug movement and absorption).* [Online] Available at: http://pharmacologycorner.com/usmle-like-pharmacology-quiz-part-2-pharmacokinetics-drug-movement-and-absorption. [Accessed: 29 June 2016].

Hallerback, B., Unge, P., Carling, L., Edwin, B., Glise, H., Havu, N., Lunberg, K. (1994) Omeprazole or ranitidine in long-term treatment of reflux esophagitis. *Gastroenterology,* 107(5), 1305-1311.

Jeffrey, R.B., Richard, W.H., Jaszewski, R.K., Mark, A., John, G. (1996) Misoprostol and Ranitidine in the Prevention of NSAID-Induced Ulcers: A Prospective, Double-Blind, Multicenter Study. *American Journal of Gastroenterology,* 91(2), 223-227.

Kamali, F., Howes, A., Thomas, S.H.L., Ford, G.A., Snoeck, E. (1997) A pharmacokinetic and pharmacodynamic interaction study between nebivolol and the H2-receptor antagonists cimetidine and ranitidine. *British Journal of Clinical Pharmacology,* 43(2), 201-204.

Kolkman, J.J., Groeneveld, A.B., Meuwissen, S.G. (1994) Effect of ranitidine on basal and bicarbonate enhanced intragastric PCO2: a tonometric study. *Gut,* 3(6), 737.

Kotagale, N.R., Parkhe, A.P., Jumde, A.B., Khandelwal, H.M., Umekar, M.J. (2011) Ranitidine Hydrochloride-loaded Ethyl Cellulose and Eudragit RS 100 Buoyant Microspheres: Effect of pH Modifiers. *Indian journal of pharmaceutical sciences,* 73 (6), 626-633.

Kuusela, A.L.M.D., Ruuska, T.M.D., Karikoski, R.M.D., Laippala, P., Ikonen, R.S.M.D., Janas, M.M.D., Maki, M.M.D. (1997) A randomized, controlled study of prophylactic ranitidine in preventing stress-induced gastric mucosal lesions in neonatal intensive care unit patients. *Critical Care Medicine,* 25(2), 346-351.

Labenz, J., Peitz, U., Leusing, C., Tillenburg, B., Blum, A.L., Borsc, G.H. (1997) Efficacy of primed infusions with high dose ranitidine and omeprazole to maintain high intragastric pH in patients with peptic ulcer bleeding: a prospective randomised controlled study. *Gut,* 40(1), 36.

Martin L.E., Janet, O., Tanner, R.J.N. (1982) Use of high-performance liquid chromatography-mass spectrometry for the study of the metabolism of ranitidine in man. *Journal of Chromatography A,* 251(2), 215-224.

Mayo Clinic (2016) *Histamine H2 Antagonist.* [Online] Available at: http://www.mayoclinic.org/drugs-supplements/histamine-h2-antagonist-oral-route-injection-route-intravenous-route/side-effects/drg-20068584. [Accessed: 8 May 2016].

Medbroadcast (2016) Zantac. [Online] Available at: http://www.medbroadcast.com/Drug/GetDrug/Zantac. [Accessed: 8 May 2016].

Mirmehrabia, M., Rohani, S., Murthy, K.S.K., Radatus, B. (2004) Solubility, dissolution rate and phase transition studies of ranitidine hydrochloride tautomeric forms. *International Journal of Pharmaceutics,* 282(1-2), 73-85.

Naurag, M., Agrawal, M.D., Donald, R., Campbell, M.D., Michael, A., Safdi, M.D., Nancy, L., Lukasik, B.S.N., Bidan, H., Marian, M., Haber, M.D. (2000) Superiority of Lansoprazole vs. Ranitidine in Healing Nonsteroidal Anti-inflammatory Drug–Associated Gastric Ulcers. *The Journal of the American Medical Association,* 160(10), 1455-1461.

Patient (2013) H2 *Blockers.* [Online] Available at: http://patient.info/health/h2-blockers. [Accessed: 8 May 2016].

Peghini, P.L., Katz, P.O., Castell, D.O. (1998) Ranitidine controls nocturnal gastric acid breakthrough on omeprazole: A controlled study in normal. *Gastroenterology,* 115(6), 1335–1339.

Peterson, W.L., Ciociola, A.A., Sykes, D.L., Sorley, D.L., Webb, D.D. (2006) Ranitidine bismuth citrate plus clarithromycin is effective for healing duodenal ulcers, eradicating H. pylori and reducing ulcer recurrence. RBC H. pylori Study Group. *Alimentary Pharmacology and Therapeutics*, 10(3), 251-261.

Postolache, L., Gafitanu, E. (2012) Comparative evaluation of the anionic superdisintegrant incorporation mode on the quality of ranitidine tablets. *Scandinavian Journal of Gastroenterology,* 116(1), 336-340.

Puscas, I., Puscas, C., Coltau, M., Pasca, R., Marquez, M., Herrero, E., Fillat, O., Ortiz, J.A. (1997) Comparative study of the safety and efficacy of ebrotidine versus ranitidine and placebo in the prevention of piroxicam-induced gastroduodenal lesions. *Arzneimittel-Forschung,* 47(4A), 568-572.

Sandmark, S., Carlsson, R.,Fausa, O., Lundell, L. (1988) Omeprazole or Ranitidine in the Treatment of Reflux Esophagitis: Results of a Double-Blind, Randomized, Scandinavian Multicenter Study. *Scandinavian Journal of Gastroenterology,* 23(5), 625-632.

Santos, A.D.F., Barbosa, I.S., Santos, V.L.D., Silva, R.L., Caetite, E. (2014) Test of dissolution and comparison of in vitro dissolution profiles of coated ranitidine tablets marketed in Bahia, Brazil. *Brazilian Journal of Pharmaceutical Sciences,* 50(1).

Scribd (2016) *Evaluation of Tablets*. [Online] Available at: *https://www.scribd.com/doc/59995285/11-Evaluation-of-Tablets*. [Accessed: 6 July 2016].

Smekhova, I.E., Moldaver, B.L., Perova, Y.M. (2009) Equivalence of ranitidine generic tablets studied using the in vitro dissolution test. *Pharmaceutical Chemistry Journal,* 43(11), 632-636.

Square (2016) *Calbo 500.* [Online] Available at: http://squarepharma.com.bd/products-details.php?pid=58. [Accessed: 7 May 2016].

Square (2016) *Filwel Silver.* [Online] Available at: http://squarepharma.com.bd/products-by-tradename.php?type=trade&char=F. [Accessed: 7 May 2016].

Thomas, N., Smedt, G.D., Vanaken, H., Bouche, M.P., Peeters, M., Woodfall, B., Richard, M., Hoetelmans, W. (2008) A pharmacokinetic study of etravirine (TMC125) co-administered with ranitidine and omeprazole in HIV–negative volunteers. *British Journal of Clinical Pharmacology,* 66(4), 508-516.

Villanueva, C., Balanzo, J., Torras, X., Sainz, S., Soriano, G., Gonzalez, D., Vilardell, F. (1995) Omeprazole versus ranitidine as adjunct therapy to endoscopic injection in actively bleeding ulcers: a prospective and randomized study. *Endoscopy,* 27(4), 308-312.

Wikipedia (2016) *Ranitidine.* [Online] Available at: https://en.wikipedia.org/wiki/Ranitidine. [Accessed: 10 May 2016].

Wiklund, L., Bardhan, K.D., Bigard, M.A., Bianchi, P.G., Ponce, J., Scott, M., Weir, D., Fulton, C., Gillon, K., Peacock, R. (1998) Quality of life during acute and intermittent treatment of gastro-oesophageal reflux disease with omeprazole compared with ranitidine. Results from a multicentre clinical trial. The European Study Group. *Italian Journal of Gastroenterology and Hepatology,* 30(1), 19-27.