IMPACT OF DIFFERENT SUPPLRMENT DRUGS ON DISSOLUTION PROFILE OF RANITIDINE (ZANTAC® AND NEOTACK®)

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.

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July 2016

DECLARATION BY THE CANDIDATE

I,Shoheba Akter, hereby declare that the dissertation entitled **"IMPACT OF DIFFERENT SUPPLRMENT DRUGS ON DISSOLUTION OF RANITIDINE (ZANTAC AND NEOTACK"** submitted to the Department of Pharmacy, East West University in the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy is a bona fied record of original research work carried out by me , under the supervision and guidance of **Md. Anisur Rahman,**Senior Lecturer, Department of Pharmacy, East West University. The research has not formed the basis for the award of any other degree/diploma/fellowship or other similar title to any candidate of any university.

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CERTIFICATE BY THE SUPERVISOR

This is to certify that the dissertation entitled "**IMPACT OF DIFFERENT SUPPLRMENT DRUGS ON DISSOLUTION OF RANITIDINE (ZANTAC AND NEOTACK)**", submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the Degree of Bachelor of Pharmacy, by Shoheba Akter (ID:2012-1-70-013) under my supervision. I further certify that it is a genuine research work and no part of the thesis has been submitted elsewhere for any other degree/diploma and all the resources of the information in thus connection are duly acknowledged.

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ENDORSEMENT BY THE CHAIRPERSON

This is to certify that the dissertation entitled "**IMPACT OF DIFFERENT SUPPLRMENT DRUGS ON DISSOLUTION OF RANITIDINE (ZANTAC AND NEOTACK)**", submitted by Shoheba Akter (ID:2012-1-70-013) is a genuine research work under the supervision of **Md. Anisur Rahman** (Senior Lecturer, Department of Pharmacy, East West University, Dhaka). I further certify that no part of the thesis has been submitted for any other degree and all the resources of the information in thus connection are duly acknowledged.

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Dedication

This paper is dedicated
to
my beloved parents and my teachers

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ABSTRACT

This work was proposed to determine the impact of different supplement drugs on the dissolution of Ranitidine. Here two brands of Ranitidine tablets were used, Zantac (GlasoSmithKine) and Neotack(Square). Weight variation test, hardness test, thickness test, dissolution of individual Ranitidine(Zantac and Neotack) and dissolution of Ranitidine(Zantac and Neotack) with different supplements were used as the parameters for the determination of impact on dissolution of different supplements on the dissolution of Ranitidine(Zantac and Neotack).The supplements used in this research work were Calbo (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 60 minutes the percent dissolved amount of individual Zantac, Zantac with Calbo , Aristocal D, Acical-M, Nutrum Gold and Filwel Silver were 94.09%, 47.84%, 72.6%, 48.47%, 94.27% and 97.22% respectively. The percent dissolved amount of individual Neotack, Calbo ,Aristocal D, Acical-M, Nutrum Gold and Filwel Silver were 97.4%, 46.09%, 50.22%,74.6%,98.31%,99.11% respectively after an hour. The study result showed that Calbo and Acical M has highly significant impact, Aristocal D has moderate impact and Filwel Silver and Nutrum Gold has less significant impact on the dissolution of Ranitidine(Zantac and Neotack).

Key words: Dissolution, Ranitidine, Zantac, Xantid, Calbo , Aristocal D, Acical-M, Nutrum Gold, Filwel Silver, Distilled water, UV spectroscopy, Absorbance, Percent dissolve,Standard curve,Impact.

Chapter one

INTRODUCTION

1.1 OVERALL OBJECTIVE OF THE RESEARCH

The objective of the research was to determine the dissolution impacts of different supplements on Ranitidine HCL. To determine the effects, I had used calcium supplements, calcium and vit-D,a combination of calcium, vit-D and multiminerals, multivitamin gold and multivitamin silver on the dissolution of Neotack, a product from Square Pharmaceuticals LTD, which contain 150mg Ranitidine HCL.

To do the research, I had performed some essential in-vitro test such as individual dissolution test of Ranitidine HCL(Neotack),dissolution test of Ranitidine HCL with calcium supplements, calcium and vit-D, a combination of calcium, vit-D and multiminerals , multivitamin gold and multivitamin silver. Besides this, some other important tests were also done such as weight variation test, thickness test, hardness test.

As Ranitidine HCL is dissolve in water, the dissolution test was performed by using distilled water. To perform this dissolution test, I had used the dissolution testing apparatus and the UV spectrophotometer was used to determine the absorbance of each of the samples taken from the dissolution chamber.

Other important tests(weight variation test,thickness and hardness test) were done to determine the physical properties of Ranitidine HCL.

1.2 H2 blockers

The H2 blockers (also called H2 antagonists) were the first effective drugs for peptic ulcer. In the 1980s, they were the only drug for the treatment of ulcers and gastro esophageal reflux disease (GERD). Now, antibiotics cure non-NSAID ulcers, and proton pump inhibitors (PPIs) are better for GERD. Therefore, H2 antagonists face an uncertain future as prescription drugs. Nonetheless, they are comparatively cheap, effective, and very safe for heartburn relief. Lower dose preparations are available over-the-counter to be used for mild heartburn and dyspepsia. (Thompson, 2009)

1.2.1 History and rationale of H2 blockers:

Histamine stimulates the parietal cells in the stomach lining to produce hydrochloric acid. Histamine also affects the H1 receptors on the nasal mucosa, bronchi, and skin that participate in allergic reactions such as hay fever and hives. These can be treated by antihistamines such as diphenhydramine (e.g., Benadryl, Siladryl) that block the H1 receptor. The British pharmacologist, Sir James Black noted that antihistamines block systemic histamine (H1) effects, but not stomach acid stimulation. He reasoned there must be a second histamine (H2) receptor in the stomach lining. He synthesized and tested histamine-like molecules searching for those that only inhibited acid secretion. The first commercially available H2 receptor antagonist, cimetidine was a great success helping Black to earn the 1988 Nobel Prize in Medicine. For the first time, doctors could heal peptic ulcers with a drug. (Thompson, 2009)

1.2.2 General mechanism of H2 blockers

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

In some people this barrier may have broken down allowing the acid to damage the stomach, causing an ulcer. In others there may be a problem with the muscular band at the top of the stomach (the sphincter) that keeps the stomach tightly closed.

This may allow the acid to escape and irritate the esophagus. This is called 'acid reflux', which can cause heartburn or inflammation of the esophagitis.

The letter H in their name stands for histamine. 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. H2 blockers stop the acid-making cells in the stomach lining from responding to histamine. This reduces the amount of acid produced by our 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, 2016)

1.3 INTRODUCTION OF RANITIDINE HCL

Ranitidine, a histamine H2-receptor antagonist similar to cimetidine and famotidine, is used to treat gastrointestinal disorders such as Helicobacter pylori-related peptic ulcer disease and for the treatment of peptic or duodenal ulcers.

(Pharmamanufactureindia.com,2016)

The chemical name of Ranitidine is dimethyl [(5-{[(2-{[(E)-1-(methylamino)-2-nitroethenyl]amino}ethyl)sulfanyl]methyl}furan-2-yl)methyl]amine. The chemical formula is $C_{13}H_{22}N_4O_3S$ and molecular weight is 314.404. (Drugbank , 2016)

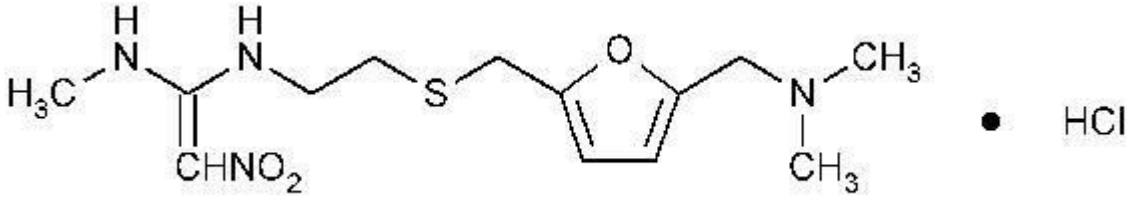

Figure 1.1 Structure of Ranitidine HCL (Drugbank , 2016)

1.3.1 Pharmacology of ranitidine HCL:

1.3.1.1 Therapeutic indication: It is used to treat-

- Duodenal ulcer
- Gastric ulcer
- Zollinger-Ellison syndrome (a pathological hypersecretory state resulting in excessive gastric pepsin & HCl)
- Gastroesophageal reflux disease
- Used prior to surgery in patients with GI obstruction to elevate gastric pH
- Reflux esophagitis (Lichtman, 2016)

1.3.1.2 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.(Drugbank ,2016)

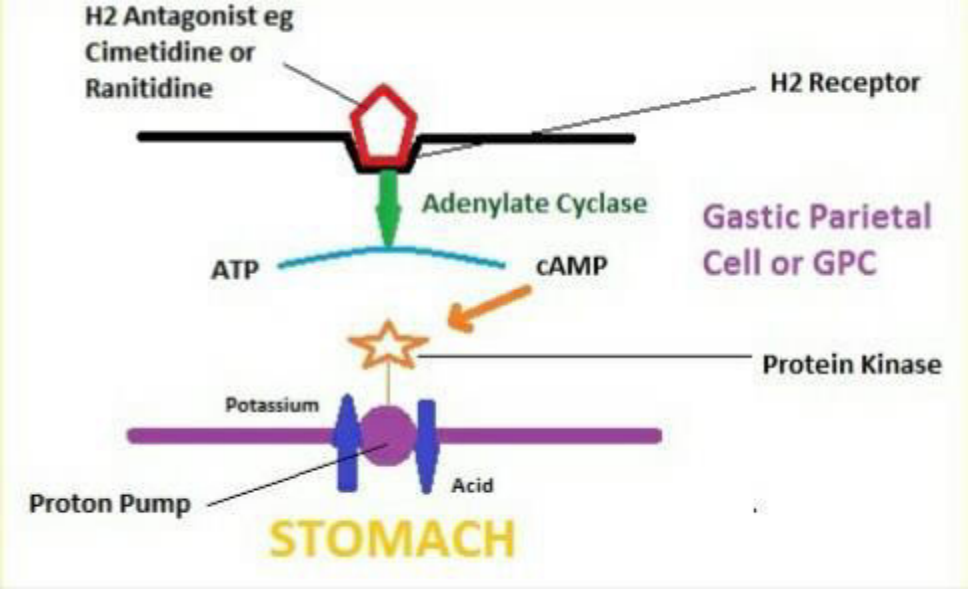

Figure 1.2 Mechanism of action of H2 antagonist.

1.3.1.3 Pharmacodynamics:

Ranitidine is a histamine H2-receptor antagonist similar to cimetidine and famotidine. An H2-receptor antagonist, often shortened to H2 antagonist, is a drug 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. (Drugbank,2016)

1.3.2 Pharmacokinetics:

1.3.2.1Absorption: Approximately 50% bioavailability orally.

1.3.2.2Volume of distribution:

- 1.14L/kg
- 1.76L/kg(clinically significant renal function impairment (creatinine clearance 25 to 35ml/min)

1.3.2.3Protein binding: 15%

1.3.2.4Metabolism: Hepatic metabolism. Ranitidine is metabolized to the N-oxide, S-oxide, and N-desmethyl metabolites, accounting for approximately 4%, 1%, and 1% of the dose, respectively.

1.3.2.5Route 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.

1.3.2.6Half life:2.8-3.1 hours

1.3.2.7Clearance:

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

1.3.3Toxicity:LD_{50}=77mg/kg (orally in mice). Symptoms of overdose include muscular tremors, vomiting, and rapid respiration.

1.3.4 Affected organisms: Humans and other mammals. (Drugbank.ca, 2016)

1.3.5 Ranitidine side effects:

One should stop taking ranitidine and call his/her doctor at once if they have a serious side effect such as:

- 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;
- nausea, stomach pain, low fever, loss of appetite, dark urine, clay-colored stools, jaundice (yellowing of the skin or eyes).

Less serious ranitidine side effects may include:

- headache (may be severe)
- drowsiness, dizziness
- sleep problems (insomnia)
- decreased sex drive, impotence, or difficulty having an orgasm
- swollen or tender breasts (in men)
- nausea, vomiting, stomach pain
- diarrhea or constipation.(Drugs.com,2016)

1.3.6 Dosage form: (Drugbank ,2016)

Form	Route	Strength
Capsule	Oral	150 mg/1
Capsule	Oral	300 mg/1
Capsule	Oral	150 mg
Capsule	Oral	300 mg
Injection	Intravenous, Intramuscular	25 mg/ml
Injection, Solution	Intravenous, Intramuscular	25 mg/ml
Liquid	Intravenous, Intramuscular	25 mg
Solution	Oral	15 mg/ml
Solution	Oral	150 mg/ml

Table 1.1 Table showing dosage form of Ranitidine HCL.

1.3.7 Dose schedule:(Drugbank,2016)

1.3.7.1Usual adult dose for duodenal ulcer

Oral: 150 mg 2 times a day, or 300 mg once a day after the evening meal or at bedtime.

Parenteral: 50 mg, IV or IM, every 6 to 8 hours. Alternatively, a continuous IV infusion may be administered at a rate of 6.25 mg/hour over 24 hours.

1.3.7.2Usual adult dose for dyspepsia

75 mg orally once daily (Over-the-counter) 30 to 60 minutes before meal. Dose may be increased to 75 mg twice daily. Maximum duration of therapy if self-medicating is 14 days.

1.3.7.3Usual adult dose for duodenal ulcer prophylaxis

150 mg orally once a day at bedtime.

1.3.7.4 Usual adult dose for gastric ulcer maintenance

150 mg orally once a day at bedtime.

1.3.7.5 Usual adult dose for erosive esophagitis

Oral:

Initial:150mg 4 times a day.

Maintenance:150mg twice daily.

Parenteral:50 mg, IV or IM, every 6 to 8 hours. Alternatively, a continuous IV infusion may be administered at a rate of 6.25 mg/hour over 24 hours.

1.3.7.6 Usual adult dose for stress ulcer prophylaxis

Parenteral: 50 mg IV or IM every 6 to 8 hours. Alternatively, a continuous IV infusion may be administered at a rate of 6.25 mg/hour over 24 hours titrated to gastric pH>= 4.

1.3.7.7 Usual adult dose for gastrointestinal hemorrhage

Parenteral: 50 mg IV loading dose, followed by 6.25 mg/hr continuous IV infusion titrated to gastric pH >7.0 for treatment.

1.3.7.8 Usual adult dose for zollinger-ellison syndrome

Oral: Initially 150mg twice a day. Doses up to 6gm per day have been used.

Parenteral: 1 mg/kg/hour administered as a continuous IV infusion to a maximum of 2.5 mg/kg/hour (infusion rates up to 220 mg/hour have been used).

1.3.7.9 Usual adult dose for pathological hypersecretory conditions

Oral: 150 mg 2 times a day initially. Adjust dose to control gastric acid secretion.Doses up to 6gm per day have been used.

Parenteral: 1 mg/kg/hour administered as a continuous IV infusion to a maximum of 2.5 mg/kg/hour (infusion rates up to 220 mg/hour have been used).

1.3.7.10 Usual adult dose for gastroesophageal reflux disease

Oral:150 mg twice daily.

Parenteral: 50 mg, IV or IM, every 6 to 8 hours.

1.3.7.11 Usual adult dose for gastric ulcer (Benign gastric ulcer)

Oral:150mg twice a day.

Parenteral: 50 mg, IV or IM, every 6 to 8 hours.

1.3.7.12 Usual pediatric dose for duodenal ulcer(1 month to 16 years)

IV: 2 to 4 mg/kg/day divided every 6 to 8 hours.

Maximum: 200mg/day.

Oral: 4 to 8 mg/kg divided twice daily, every 12 hours.

Maximum: 300mg/day orally.

Maintenance: 2 to 4 mg/kg/day orally once daily.

Maximum: 150mg/day orally.

1.3.7.13 Usual pediatric dose for duodenal ulcer prophylaxis(1 month to 16 years)

IV: 2 to 4 mg/kg/day divided every 6 to 8 hours.

Maximum: 200 mg/day.

Oral: 2 to 4 mg/kg once daily, not to exceed 150mg/24 hours.

1.3.7.14 Usual pediatric dose for gastric ulcer maintenance (1 month to 16 years)

IV: 2 to 4 mg/kg/day

Maximum: 200mg/day.

Oral: 2 to 4 mg/kg, not to exceed 150mg/24 hours.

1.3.7.15 Usual pediatric dose for gastro esophageal reflux disease

1.3.7.15.1 Neonatal

IV: 1.5 mg/kg IV as a loading dose followed 12 hours later with 1.5 to 2 mg/kg/day IV divided every 12 hours. Alternatively, a continuous IV infusion may be administered at a rate of 0.04 to0.08 mg/kg/hour (1 to 2 mg/kg/day) after a loading dose of 1.5 mg/kg has been given.

Continuous IV infusion: Loading dose: 1.5 mg/kg/dose, followed by 0.04 to 0.08 mg/kg/hour infusion(or 1 to 2 mg/kg/day)

Oral: 2 mg/kg/day divided into 2 doses, administered every 12 hours.

1.3.7.15.2 1 month to 16 years:

IV: 2 to 4 mg/kg/day divided every 6 to 8 hours.

Maximum: 200 mg/day. Alternatively, an initial IV bolus dose of 1 mg/kg given once, followed by a constant IV infusion at a rate of 0.08 to 0.17 mg/kg/hour (2 to 4 mg/kg/day) may be administered.

Oral: 4 to 10 mg/kg/day administered in 2 divided doses,every 12 hours. Maximum: 300 mg orally day

1.3.7.16 Usual pediatric dose for erosive esophagitis (1 month to 16 years)

IV: 2 to 4 mg/kg/day divided every 6 to 8 hours.

Maximum: 200 mg/day. Alternatively, an initial IV bolus dose of 1 mg/kg given once, followed by a constant IV infusion at a rate of 0.08 to 0.17 mg/kg/hour(2 to 4 mg/kg/day) may be administered.

Oral: 4 to 10 mg/kg/day administered in 2 divided doses, every 12 hours. Maximum: 300 mg orally day

1.3.7.17 Usual pediatric dose for dyspepsia (Children greater than or equal to 12 years)

Oral: 75ng orally once 30 to 60 minutes before eating food or drinking beverages which cause heartburn.

Maximum: 150 mg/24 hours.

Duration of therapy: Do not use for more than 14 days.

1.3.8Drug-drug interaction: (Drugbank , 2016)

Drug	Effects
Aripiprazole	The serum concentration of Aripiprazole can be increased when it is combined with Ranitidine.
Atazanavir	The serum concentration of Atazanavir can be decreased when it is combined with Ranitidine.
Bosutinib	The serum concentration of Bosutinib can be decreased when it is combined with Ranitidine
Bupropion	The serum concentration of Ranitidine can be increased when it is combined with Bupropion
Cefditoren	The serum concentration of Cefditoren can be decreased when it is combined with Ranitidine.
Cefpodoxime	Ranitidine can cause a decrease in the absorption of Cefpodoxime resulting in a reduced serum concentration and potentially a decrease in efficacy
Cefuroxime	Ranitidine can cause a decrease in the absorption of Cefuroxime resulting in a reduced serum concentration and potentially a decrease in efficacy
Chlorpropamide	The serum concentration of Chlorpropamide can be increased when it is combined with Ranitidine.
Cysteamine	The therapeutic efficacy of Cysteamine can be decreased when used in combination with Ranitidine.
Dabrafenib	The serum concentration of Dabrafenib can be decreased when it is combined with Ranitidine.

Figure 1.2 Table showing drug-drug interaction with Ranitidine.

1.3.9 Drug-Food interaction:

- Avoid alcohol.
- Avoid excessive quantities of coffee or tea (Caffeine
- Avoid milk, calcium containing dairy products, iron, antacids, or aluminum salts 2 hours before or 6 hours after using antacids while on this medication
- Take without regard to meal. (Drugbank ,2016)

1.3.10 Contraindication:

This medication should not be use if anyone is allergic to ranitidine.

Heartburn is often confused with the first symptoms of a heart attack. Seek emergency medical attention if anyone have chest pain or heavy feeling, pain spreading to the arm or shoulder, nausea, sweating, and a general ill feeling.

Incase of kidney disease or liver disease one should ask a doctor or pharmacist if it is safe for him/her to take ranitidine.

According to FDA pregnancy category B, Ranitidine is not expected to be harmful to an unborn baby. But patient should tell the doctor if anyone is pregnant or plan to become pregnant during treatment. Ranitidine passes into breast milk. One should not take ranitidine without telling her doctor if she has a breast-feeding baby.

Using ranitidine may increase the risk of developing pneumonia. Symptoms of pneumonia include chest pain, fever, feeling short of breath, and coughing up green or yellow mucus.

The ranitidine effervescent tablet may contain phenylalanine. One should talk to doctor before using this form of ranitidine if he/she have phenylketonuria (PKU).

(Drugs.com,2016)

Figure 1.3: Neotack 150mg tablet

Figure 1.4: Zantac 150 mg Tablet

1.4 INTRODUCTION OF ACICAL-M (CALCIUM+VITAMIND + MINERALS)

1.4.1 Acical-M:

Acical-M is the product from Advanced Chemical Industries(ACI) containing calcium,vitamin D and minerals.Calcium, magnesium and Vitamin D are the macro nutrients for bone. Without vitamin D very little calcium is absorbed. Like calcium, magnesium also increases bone strength and rigidity. Recent epidemiological studies show that some micro nutrients like copper, manganese, zinc and boron play an important rolein bone health. Deficiency of the micro nutrients is noticed in patients with osteoporosis.(ACIpharmaceuticals LTD., 2016)

14.2 Therapeutic indication:(ACI pharmaceuticals LTD., 2016)

- 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 and boron

1.4.3 Dose and administration:

2 tablets per day, preferably 1 tablet in the morning and 1 tablet in the evening.
(ACI pharmaceuticals LTD., 2016)

1.4.4 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 ofvitamin D supplements occasional skin rash has been reported. Hypercalciuria, and in rarecases hypocalcaemia have been seen with longterm treatment at high dosages. (ACI pharmaceuticals LTD., 2016)

1.4.5 Contraindications:

Hypersensitivity to any of the tablet ingredients. Absolute contraindications are hypercalcaemia resulting for example from myeloma, bone metastases or other malignant bone disease, sarcoidosis, primary hyperparathyroidism andvitamin D overdosage. Severe renal failure.(ACI pharmaceuticals LTD., 2016)

1.4.6 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 patientswith mild to moderate renal failure or mild hypercalciuria.(ACI pharmaceuticals LTD., 2016)

1.4.7 Drug interactions:

It has possible interaction with digoxin, antacids containing calcium, aluminium 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 pharmaceuticals LTD., 2016)

1.4.8 Overdose:

The most serious consequences of acute or chronic overdose is hypercalcaemia.

(ACI pharmaceuticals LTD., 2016)

1.4.9 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 theseagents from other sources.

(ACI pharmaceuticals LTD., 2016)

1.4.10 Presentation:

Acical-M tablet is light orange color, vanilla flavor, oblong film coated tablet,break line on one side & another side engraved with ACI. Each tablet contains Colecalciferol (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 pharmaceuticals LTD., 2016)

1.4.11 Package quantities:

Each container contains 30 tablets.(ACI pharmaceuticals LTD., 2016)

Figure 1.5: Acical M tablet

1.5 INTRODUCTION OF ARISTOCAL D (CALCIUM+VITAMIN D)

1.5.1 Aristocal D:

Aristocal D is a product of Beximco Pharma is a combined preparation of Calcium and Vitamin D (Cholecalciferol) specially designed to promote bone health and to sequester phosphorous in the intestine to reduce total body phosphate accumulation in chronic renal failure.(Baximcopharmaceuticals LTD.,2016)

1.5.2 Therapeutic indication:(Baximcopharmaceuticals LTD.,2016)

- 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 as a phosphate binder.

1.5.3 Dosage and Administration:(Baximcopharmaceuticals LTD.,2016)

For adults and elderly:

Dietary deficiency: 2 to 3 tablets daily.

As phosphate binder: Requirement of the dose depends on the serum calcium and phosphate levels.

Adjunct to osteoporosis therapy: 2 to 3 tablets daily

1.5.4 Contraindications:(Baximcopharmaceuticals LTD.,2016)

- Hypercalcaemia
- Hyperparathyroidism
- Renal calculi
- Nephrolythiasis
- Zollinger Ellision Syndrom
- Gastric acid hypersecretion

1.5.5 Precautions:(Baximcopharmaceuticals LTD.,2016)

Caution should be taken in patients with-

- Renal impairment
- Sarcoidosis
- Hypercalcemia and
- Hypercalciuria

1.5.6 Adverse Reactions:(Baximcopharmaceuticals LTD.,2016)

Aristocal is well tolerated. Mild gastrointestinal disturbances may occur.

1.5.7 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 efficacyof calcium supplements. Calcium salts reduce the absorption of a number of other drugs such as biphosphonates, fluoride, some fluoroquinolones and tetracyclines.

(Baximcopharmaceuticals LTD.,2016)

1.5.8 Side effects:(Baximcopharmaceuticals LTD.,2016)

- Flatulance
- Abdominal pain
- Constipation
- Hypercalcaemia
- Alkalosis

1.5.9 Pregnancy and lactating mother:

Calcium supplement is safe for pregnant and lactating mother. It is commonly used as oral tabletfor them.(Baximcopharmaceuticals LTD.,2016)

1.5.10 Commercial pack:

Box containing 100 tablets in 10X10's blister strips. Each tablet contains 1250mg calcium carbonate BP equivalent to 500 mg elemental calcium.

(Baximcopharmaceuticals LTD.,2016)

Figure 1.6: Aristocal D

1.6 INTRODUCTION OF FILWEL SILVER (MULTIVITAMINS AND MULTIMINERALS)

1.6.1 Filwel silver:

Filwel silver is a product of Square Pharmaceutical which contain multivitamin and multiminerals. (Squarepharmaceuticals LTD.,2016)

1.6.2 Indication:

Treatment of vitamin and mineral deficiencies above the age of 45 years. (Squarepharmaceuticals LTD.,2016)

1.6.3 Dosage and administration: One tablet daily with food. Not formulated for use in children. (Squarepharmaceuticals LTD.,2016)

1.6.4Side Effects: (Square Pharmaceuticals Ltd.,2016)

This preparation is well tolerated. But occasionally may lead to-

- Diarrhea(when treat with beta carotene)
- Skin discoloration
- Vitamin A lead to reversible side effets
- Diarrhea may cause due to Vitamin C and vitamin E
- Also responsible for other gastrointestinal disturbances

1.6.5 Contraindication and Precaution:

The product is contraindicated while –

- Patients having hypersensitivity to any of the product ingredients.
- Receiving other vitamin A supplements.

When high levels of vitamin A is administered for longer period of time then it increase the chance of osteoporosis in postmenopausal women.

(Square Pharmaceuticals Ltd.,2016).

1.6.6 Use in Pregnancy and Lactation:

Recommended by the consultation with physician.(Square Pharmaceuticals Ltd.,2016).

Figure 1.7: Filwel®Silver Tablet

1.7 INTRODUCTION OF NUTRUM GOLD (MULTIVITAMIN AND MULTIMMINERALS)

1.7.1 Nutrum gold:

Nutrum gold is a product of Acme Laboratories, is a complete well balanced multivitamin and multimineral supplement designed for the adults.

(ACME Laboratories Ltd., 2014)

1.7.2 Therapeutic indication:

Nutrum Gold is indicated for adults for treatment & prevention of vitamins & minerals deficiencies.(ACME Laboratories Ltd., 2014)

1.7.3 Dosage and administration:

One tablet daily with food or as directed by the physician.(ACME Laboratories Ltd., 2014)

1.7.4Contraindications:

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

1.7.5 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 Laboratories Ltd., 2014)

1.7.6 Side effects:

Generally well tolerated. Allergic sensitization has been reported following oral administration of folic acid. Long term intake of high levels of vitamin A (excluding that sourced from beta -carotene) may increase the risk of osteoporosis in postmenopausal women.(ACME Laboratories Ltd., 2014)

1.7.7 Use in pregnancy and lactation:

As with any supplement, pregnant women or nursing mother should consult with a doctor. (ACME Laboratories Ltd., 2014)

1.7.8 Drug interaction:

No prominent drug interactions have been reported.(ACME Laboratories Ltd., 2014)

1.7.9Tablet Pack: Each airtight plastic container contains 30 and 15 tablets. (ACME Laboratories Ltd., 2014)

Figure1.8: Nutrum Gold

1.8 INTRODUCTION OF CALBO (CALCIUM CARBONATE)

1.8.1 Calbo:

Calbo is a product of Square Pharmaceuticals containing calcium carbonate which is called as bone calcium regulator. (Squarepharma,2016)

1.8.2 Therapeutic indication: For the treatment or prevention of calcium depletion. (Squarepharma,2016)

1.8.3 Dosage & Administration: Calbo (500-1500 mg calcium) daily is recommended.(Squarepharma,2016)

1.8.4 Preparation: Calbo500 mg box containing 3 X10 tablets in blister pack. (Squarepharma,2016)

Figure 1.9: Calbo(500mg) Tablet

Chapter Two

LITERATURE REVIEW

2.1 LILERATURE REVIEW

Ranitidine is an antisecretory drug with H_2 antagonist action useful in treating gastric and duodenal disorders. The dissolution test was used to obtain and compare dissolution profiles and establish similarities of pharmaceutical forms. The aim of this study was to compare the dissolution profiles of 150-mg coated ranitidine tablets of a reference drug (product A) and a generic (product B) and a similar (product C) drug marketed in Bahia, Brazil using a simple, fast and inexpensive ultraviolet method. Dissolution was determined using a USP type 2 apparatus at 50 rpm with 900 ml of distilled water at 37.0 ± 0.5 ^{o}C for 1h.Factors were calculated and showed that the profiles of products A, B and C were dissimilar. However, all the products released ranitidine satisfactorily, with at least 80% of the drug dissolved within 30 min. (Junior et al., 2014)

Understanding the polymorphic behavior of pharmaceutical solids during the crystallization process and further in post-processing units is crucial to meet medical and legal requirements. In this study, an analytical technique was developed for determining the composition of two solid forms of ranitidine hydrochloride using two peaks of fourier transform infrared (FTIR) spectra without the need to grind the samples. Dissolution rate found to be equally fast for both forms. The solubility data were modeled using the group contribution parameters and universal quasi-chemical (UNIQUAC) theory. There was a good agreement between the experimental solubility data of ranitidine hydrochloride and the results of UNIQUAC equation.(Mirmehrabi et al., 2004)

The aim of the study was to evaluate the pharmaceutical properties of few selected generic products of ranitidine hydrochloride tablets available in retail pharmacies of Bangladesh. They collected 10 nationally manufactured generic ranitidine HCl tablets from local market who followed USP specifications and examined their physical parameters and potency to check their compliance with the USP. The intention was to evaluate the quality of this pharmaceuticals after 20 years of implementing the National Drug Policy in 1982.All tested ranitidine tablet samples were selectively collected from local retail pharmacies in Savar, Dhaka-1344, Bangladesh. It was found that all ten selected products met the USP 27 specifications. However, all brands complied with USP 27. It could be concluded that the selected ranitidine HCl tablets met the required USP

specifications and are considered quality products in terms of the mentioned parameters.(Azad, Islam and Azizi, 2013)

The pharmaceutical equivalence of Zantac (reference drug) and 10 domestic and foreign generics of ranitidine hydrochloride as 150-mg coated tablets were 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. It was established that Zantac and generics of two manufacturers were rapidly soluble (according to the WHO classification). It was demonstrated that the in vitro dissolution test recommended by WHO could be used for determining the bioequivalence of ranitidine generics. (Smekhova, Moldaver and Perova, 2009)

The objective of this study was to find the serum levels of ranitidine using assay method .In the study twenty six healthy male volunteers participated and completed the study. The bioequivalence study was conducted under fasting conditions and had been found acceptable by the division of bioequivalence. The dissolution testing conducted on 12 units of the test and reference products were acceptable. Not less than 80% of the labled amount was dissolved in 45% minutes.(Mojaverian, 1996)

The aim of this study was to establish similarity among the different brands of ranitidine HCl tablets available in local market of Karachi, Pakistan. Four different brands of (150 mg) were selected for the study. Six quality control parameters: weight variation test, hardness test, thickness, friability, disintegration test and dissolution test were carried out specified by USP. Result revealed that all brands comply within limits for hardness, weight variation, thickness, friability, disintegration and dissolution.Disintegration time for all brands was within 15 minutes complying with the USP commendation. All brands showed Q-value more than 80% within 45 minutes. (Huma and Dilshad, 2014)

Although hemorrhage is the most common complication of duodenal ulcer disease, there are few controlled trials of maintenance therapy in patients with documented hemorrhage .One recent randomized, controlled trial in patients with a history of hemorrhage from duodenal ulcers found no difference in rates of recurrent hemorrhage between ranitidine and placebo. They compared the efficacy and safety of maintenance treatment with ranitidine with the effects of placebo for the prevention of recurrent bleeding from

duodenal ulcers. Also studied patients with a recent severe hemorrhage, the group most likely to benefit from maintenance treatment(Jensen et al., 1994)

A multicentre, randomized, double-blind, placebo-controlled study was conducted to evaluate the efficacy and safety of ranitidine 150 mg and 300 mg in 342 patients with erosive oesophagitis. Treatment was given four times daily, and continued for 12 weeks or until healing. Erosive oesophagitis healing rates, as determined by endoscopy, were significantly greater in ranitidine-treated patients by 4 weeks compared with those of placebo-treated patients.Heartburn frequency and severity, as well as antacid consumed per week, were reduced in both ranitidine groups in comparison with placebo. Healing rates and symptom relief were similar in the two ranitidine groups. Both dosages of ranitidine were well tolerated. Ranitidine (150 mg) given four times daily appears to be as effective as 300 mg ranitidine given four times daily in patients with moderate to severe oesophageal erosions.(Roufail et al., 2007)

Stress ulcer prophylaxis (SUP) using ranitidine, a histamine H2 receptor antagonist, has been associated with an increased risk of ventilator-associated pneumonia.. The objective of this study was to determine whether SUP with pantoprazole increases pneumonia risk compared with ranitidine in critically ill patients. The cardiothoracic surgery database at our institution was used to identify retrospectively all patients who had received SUP with pantoprazole or ranitidine. The use of pantoprazole for SUP was associated with a higher risk of nosocomial pneumonia compared with ranitidine. This relationship warrants further study in a randomized controlled trial. (Miano et al., 2009)

The study aimed to evaluate whether ranitidine and pantoprazole were able to maintain gastric pH >or=4 in septic patients. Twenty intensive care unit patients from a university teaching hospital with sepsis were included in this study.Endoscopy of the upper digestive tract, gastric biopsy, and investigation for Helicobacter pylori were carried out before and at the end of the study. Intravenous ranitidine was unable to maintain gastric pH above 4 in septic patients. All cases in the ranitidine group in whom pH remained above 4 had gastric hypotrophy or atrophy. Pantoprazole successfully maintained pH levels above 4. (Coelho et al., 2009)

The aim of this study was to reduce the deliquescent character of Ranitidine which ultimately help to formulate the drug. During their study they used Karl Fischer titration method to determine the moisture content.They were also used thermo gravimetric analysis and differential thermal analysis (TG - DTA) plots. After their study the result showed that the resonatesof ranitidine have less moisture uptake rate and moisture content than resin and ranitidine alone. So this form of Ranitidine can be used to minimize the hygroscopicity of that drug product (Mangesh et al., 2009).

The ranitidine hydrochloride residues on various surfaces in the manufacture of pharmaceuticals was described by using a liquid chromatographic method.The study was conducted by high-performance liquid chromatography and 320nm was used for the detection.The study was showed that ,the detection method was validated for the detection or the residues of ranitidine hydrochloride(Nozal et al., 2001).

Urea breath test (UBT) results could be false negative in patients taking antisecretory drugs. This effect would be prevented by citric acid administration during UBT. They prospectively investigated whether acidified 14C-urea capsule prevents false negative UBT results in patients taking antisecretory drugs and showed interference with the duration of medications. Sixty Helicobacter pylori positive patients were included. The use of acidified 14C-urea capsule did not prevent false negative UBT results in patients taking pantoprazole and ranitidine, and the duration of medication does not affect the test results.(Stermer et al., 1997)

Ranitidine, methylparaben (MP) and propylparaben (PP) in oral liquids was simultaneously determined by using an accurate and selective high-performance liquid chromatographic method.UV detection was done at 254 nm. All the parameters that examined during the study were fulfilled the current recommendations for bioanalytical method validation. So it was found that, the novel gradient HPLC method was applicable for the routine analysis (assays and stability tests) of active compound (ranitidine) and preservatives (MP and PP)(Kokoletsi, Kafkala and Tsiaganis, 2005).

The purpose of the study was evaluating the efficacy and safety of lansoprazole to prevent the relapse of erosive esophagitis (EE), healed after open-label treatment with lansoprazole 30 mg once daily for 8 weeks and received double-blind maintenance treatment with lansoprazole 15 mg once daily or ranitidine 150 mg twice daily for up to 1

year.Lansoprazole-treated patients experienced significantly greater symptom relief (P<0.001), and, if asymptomatic at entry into the maintenance phase, remained asymptomatic for significantly longer than ranitidine-treated patients (P<0.001). Symptom status correlated with healing (P=0.001), supporting the symptom-directed management of EE. Both treatments were well tolerated and no unexpected events occurred. Daily therapy with lansoprazole to prevent the relapse of EE is effective, well tolerated, and superior to ranitidine in the maintenance of healing and symptom relief.(Peura et al., 2009)

An investigation was done on the control of the production cycle of ranitidine hydrochloride tablets. During this investigation a near-infrared reflectance spectrometric method was applied.The result of this investigation was good for the detection of ranitidine hydrochloride drug substance, mixtures for tablets, cores and coated tablets (Dreassi et al., 1996).

The purpose of this research was to prepare a gastroretentive drug delivery system of ranitidine hydrochloride. The inhibitory effect of ranitidine and cimetidine on pentagastrin stimulated volume, acid and pepsin secretion had been studied in eight healthy volunteers. The results of the full factorial design indicated that a low amount of citric acid and a high amount of stearic acid favors sustained release of ranitidine hydrochloride from a gastroretentive formulation. A theoretical dissolution profile was generated using pharmacokinetic parameters of ranitidine hydrochloride. No significant difference was observed. These studies indicated that the proper balance between a release rate enhancer and a release rate retardant could produce a drug dissolution profile similar to a theoretical dissolution profile. (Sewing, Billian and Malchow, 1980).

In the present study, an anti-ulcer drug, ranitidine hydrochloride,was delivered through a gastroretentive ethyl cellulose-based microparticulate system capable of floating on simulated gastric fluid for > 12 h. Preparation of microparticles was done by solvent evaporation technique with modification by using an ethanol co-solvent system. Microspheres showed excellent buoyancy and a biphasic controlled release pattern with 12 h. The data obtained thus suggests that a microparticulate floating delivery system could be successfully designed to give controlled drug delivery, improved oral bioavailability and many other desirable characteristics.(Dave, Amin and Patel, 2004)

Ranitidine hydrochloride was determined in pure form and pharmaceutical formulations. During this determination purpose four simple spectrophotometric methods were used. The aim was to observe the application of azine dyes to the determination of ranitidine hydrochloride.The methods were tested with spectrophotometric reference method and all tests were provided the appreciable results. (Sastry et al., 1997) .

The objective of this study was to develop the rapid assay of ranitidine hydrochloride in dosage forms and samples from tablet dissolution testing using a HPLC method with photometric detection. This method also separated ranitidine from its related compound ranitidine S-oxide. Analyses were carried out on a Microsorb-MV C18 column, with a (1:1) mixture of methanol- 0.01 M Na_2HPO_4 (pH 7.0) as the mobile phase, and detection at 320 nm. The result of the study was the samples from tablet dissolution tests required no preliminary preparation. Assay values by the proposed method were found to agree closely with those obtained using methods in the USP XXII.(Lau-Cam, Rahman and Roos, 1994)

The objective of this investigation was to develop the hollow microspheres as a new dosage form of floating drug delivery systems with prolonged stomach retention time. Hollow microspheres containing ranitidine hydrochloride (RH) was prepared by a novel solvent diffusion-evaporation method using ethyl cellulose (EC) dissolved in a mixture of ethanol and ether (6:1.0, v/v). The in vitro release profiles showed that the drug release rate decreased with increasing viscosity of EC and the diameter of hollow microspheres, while increased with the increase of RH/EC weight ratio. Hollow microspheres could prolong drug release time (approximately 24 h) and float over the simulate gastric fluid for more than 24 h. Pharmacokinetic analysis showed that the bioavailability from RH-hollow microspheres alone was about 3.0-times that of common RH gelatin capsules, and it was about 2.8-times that of the solid microspheres. These results demonstrated that RH hollow microspheres were capable of sustained delivery of the drug for longer period with increased bioavailability.(Wei and Zhao, 2008)

The aim of this study was to investigate the effects of different doses of polyethylene glycol 400 (PEG 400) on the bioavailability of ranitidine in male and female subjects. For this study they selected 12 healthy human volunteers (six males and six females) in a randomized order. The cumulative amount of ranitidine and its metabolites excreted in urine over 24 h was determined for each treatment using a validated HPLC method. All

doses of PEG 400 enhanced the bioavailability of ranitidine in male subjects but not females, with the most pronounced effect in males noted with the 0.75 g dose of PEG 400.(Ashiru, Patel and Basit, 2008)

The purpose of the study was to establish the dissolution profile of the drug that shows similarity. In order to establish this, the bioavailability of two formulations that did not meet this similarity were compared. Twenty-five female volunteers received 150 mg ranitidine (Azantac® or Midaven) under fasting conditions in two separate sessions using a cross-over design. No statistically significant difference was obtained in the parameters evaluated.It indicates that the formulationstested was bioequivalent, despite the dissimilarity in the dissolution profile of the formulations. These results suggest that the comparative dissolution profile was not an adequate test to demonstrate the interchangeability of ranitidine formulations. (Murrieta et al., 2005)

The objective of this study is to see the pharmacokinetics of bismuth and ranitidine following multiple doses of ranitidine bismuth citrate.The pharmacokinetics of bismuth and ranitidine derived from oral doses of ranitidine bismuth citrate 800 mg given twice daily for 28 days were examined in this double-blind, placebo controlled, parallel-group study in 27 healthy subjects.The pharmacokinetics of ranitidine derived from ranitidine bismuth citrate were similar to those of ranitidine administered alone. Ranitidine did not appreciably accumulate in plasma.Ranitidine bismuth citrate was well tolerated during 28 days of repeated dosing.(Koch et al., 1996)

The study objective was to see the pharmacokinetics and bioavailability of ranitidine in humans.Ranitidine produces a blood concentration curve with a pronounced secondary peak when administered orally and parenterally. A pharmacokinetic model was proposed to describe this reabsorption phenomenon. The choice of a discontinuous cyclic transfer was justified on the basis of physiological considerations and the good agreement with data from oral and intravenous administration. It was proposed that ranitidine accumulates mainly from the systemic circulation into a depot from which drug and bioreversible drug were spontaneously released in response to food intake.(Miller, 1984)

The pharmaceutical equivalent of different brands of Ranitidine Hydrochloride tablets was evaluated by a study by using some important quality control test such as weight variation test, friability test, hardness test and disintegration test according to the USP.

The result was indicated that all the tablets in the three brands were pharmaceutically equivalent. (Mullaicharamet al., 2012)

The aim of this study was to see the effects of low doses of ranitidine on intragastric acidity in healthy men. Intragastric pH was measured for 9 h after lunch in five studies involving 24 healthy male volunteers. Antacid was given to all subjects on day 1. They then received single oral doses of a study drug 45 min after lunch on four separate occasions: placebo and either ranitidine 25 mg, 75 mg or 125 mg were given double-blind according to a predetermined randomization schedule.Results with the antacid were similar to placebo.Using low doses of ranitidine (25, 75 or 125 mg) there was a dose-related decrease in intragastric acidity for 9 h after dosing. A single dose of antacid did not decrease intragastric acidity significantly.(Wyeth et al., 1998)

The aim of this study was to evaluate the pharmacokinetics and pharmacodynamics of a single dose of the over-the-counter histamine-2 receptor antagonist, ranitidine, 75 mg, in children with symptoms of gastro-oesophageal reflux disease.Children aged between 4 and 11 years with symptoms of heartburn suspected to be due to gastro-oesophageal reflux disease were recruited at six clinical centres. Following a single dose of either oral ranitidine, 75 mg (n=19), or placebo (n=10), recording of intragastric pH and serial blood sampling were carried out for 6 h. Ranitidine, 75 mg, significantly increased the intragastric pH in children aged 4–11 years. The pharmacokinetic and pharmacodynamic profiles were similar to those in adults. Ranitidine, 75 mg, appears to be effective for the control of intragastric acidity for 5–6 h in children aged 4–11 years.(Orenstein et al., 2002)

The objective of this study was to evaluate the bioequivalence of ranitidine and bismuth derived from two compound preparations. The bioavailability was measured in 20 healthy male Chinese volunteers following a single oral dose of the test or reference products in the fasting state. Then blood samples were collected for 24 h. Plasma concentrations of ranitidine and bismuth were analyzed by high-performance liquid chromatography and inductively coupled plasma-mass spectrometry (ICP-MS), respectively. The non-compartmental method was used for pharmacokinetic analysis.Various pharmacokinetic parameters of ranitidine derived from the two compound preparations both ranitidine and bismuth were found within the bioequivalence acceptable range of 80%-125%. No

significant difference was found in T_{max} derived from both ranitidine and bismuth. (Zhou, 2006)

A study was conducted with Ranitidine hydrochloride where the purpose was to evaluate the effect of formulation variables on floating lag time, the release properties, and hardness, when developing floating tablets of Ranitidine hydrochloride.The study was done by the statistical optimization technique. The result of that study was encouraged the probability of the model in the development of floating tablets of Ranitidine hydrochloride (Jain et al., 2010).

The aim of the present study was to compare the bioavailability of ranitidine from two different ranitidine hydrochloride film tablets .The study was conducted according to an open-label, randomised two-period cross-over design with a wash-out phase of 9 days. Blood samples for pharmacokinetic profiling were taken up to 24 h post-dose, and ranitidine plasma concentrations were determined with a validated HPLC method with UV-detection. Bioequivalence between test and reference preparation was demonstrated since for both parameters AUC and Cmax the 90 % confidence intervals of the T/R ratios of logarithmically transformed data were in the generally accepted range of 80 %-125 %.(Gschwend et al., 2011)

The objective of this research work was to explain the variable intra and inter-lab dissolution results of Ranitidine tablets USP. Thepaddle apparatus andthe basket apparatus both were used during the study. To prevent tablets from sticking to the bottom of the dissolution vessel, Paddle apparatus tablet sinkers were used. All tablets showed more rapid and complete dissolution with sinker then tablets without sinkers.Finally, the result was confirmed that the dissolution artifacts for ranitidine tablets could be reduced by the use of baskets or tablet sinkers (Cappola, 2001).

The tablet and injection dosage forms of Ranitidine hydrochloride was determined. During this study the ultraviolet spectrophotometry (UVS) at 313 nm and the visible spectrophotometry (VISS) at 615 nm were used.This determination was done after the reaction with 3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) and ferric chloride.In the range of5.0-18.0 µg/mL the Beer's law was obyed.The precision and accuracy of the following two methods were compared (Orsine and Martins, 1993).

The objectives were to ascertain the stability of thiamine HCl and ranitidine HCl at room and refrigeration temperatures in a central vein formula of parenteral nutrition solution and to determine the effect of ranitidine on the stability of thiamine. High pressure liquid chromatography (HPLC) methods were developed to measure thiamine and ranitidine in the PN mixture. Stability studies were conducted in triplicate and each sample was assayed in duplicate using newly developed HPLC methods. This work suggests that the concentration of thiamine in this central vein PN formula, with or without ranitidine, falls below the 90% acceptable stability within 24 h. (Baumgartner et al., 1997)

The aim of this study was to assess the in vitro stability of ranitidine to colonic bacteria by utilising a batch culture fermentation system to simulate the conditions of the colon. UV and mass spectrometry analysis indicated that metabolism occurred via cleavage of an N–oxide bond within the molecule with the resultant loss of an oxygen atom, although further metabolic reactions are possible. Such metabolism may in part be responsible for the poor bioavailability of ranitidine from the colon.(Basit and Lacey, 2001)

Chapter Three

MATERIALS AND METHODS

3.1 MATERIALS

3.1.1 Sample collection:

To determine the impacts of different supplements on ranitidine HCL 50 tablets of Neotack 150mg,Zantac 150mg, Aristocal, Acical M, Calbo, Filwel silver, Nutrum gold were collected from the local drug store in Dhaka as a sample.

3.1.2 Samples:

Sample name	**Source(Supplier name)**
Neotack	Square Pharmaceuticals Limited
Aristocal D	Beximco Pharmaceuticals Limited
Calbo	Square Pharmaceuticals Limited
Acical M	ACI Pharmaceuticals Limited
Filwel silver	Square Pharmaceuticals Limited
Zantac	
Nutrum gold	Acme Laboratories Limited

Table:3.1 Samples used in the experiment including source.

3.1.3 Reagents:

Reagent name	**Source(Supplier name)**
Distilled water	Laboratory(East West University)

Table 3.2 Reagent used in the experiment including source.

3.1.4 Equipments and instruments:

Serial no.	Equipments	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	PrecisaXB120A	Switzerland
5	Friability tester	Veegoindia	India
6	Vernier caliper	China supplier	Shanghai,China
7	Hardness tester	Manually operated hardness tester	India

Table 3.3: Lists of equipments used for the experiment.

3.1.5 Images of instruments:

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

Figure 3.1 (From left to right) Electronic balance Figure 3.2 Hardness tester

Figure 3.3 Distilled water propagating apparatus

Figure 3.4 Vernier calipers

Figure3.5(From left to right) Dissolution apparatus Figure 3.6 UV-1800 double beam spectrophotometer

3.1.6 Apparatus:

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

Serial no.	Apparatus
1	Beaker
2	Test tube
3	Volumetric flask(25ml,50ml,100ml,1000ml)
4	Filter paper
5	Morter and pastle
6	Spatula
7	Glass rod
8	Pipette pumper
9	Pipette(1ml,5ml,10ml)
10	Funnel

Table 3.4 Apparatus used throughout the experiments.

3.2METHODS

3.2.1 Standard curve preparation:

3.2.2 Preparation of distilled water 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.

3.2.3 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 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 3.5 Concentration of Ranitidine

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

3.2.4 Preparation for dissolution test:

3.2.5 Preparation of distilled water for dissolution test:

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

3.2.6 Method for dissolution test of Zantac (Ranitidine) or Neotack (Ranitidine):

1. 6L (6000ml) of distilled water was prepared.
2. Each vessel of dissolution tester was filled with 900 ml of 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 Neotack 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.

3.2.7 Method for dissolution test of Zantac (Ranitidine) or Neotack (Ranitidine) with Calbo(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 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.
8. Same procedure was followed in the dissolution tests of Zantac or Neotack with Aristocal D, Acical M, Nutrum Gold and Filwel Silver.

3.3 Determination of Physical parameters:

3.3.1 Weight variation test

3.3.1.1 Procedure:

1. 10 tablets were taken and weighed.
2. The average was taken and considered as the standard weight of an individual tablet.
3. All the 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:

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

(Pharmatreasurers.blogspot.com,2012)

3.3.1.2 Equation for weight variation:

Folllowing equation was used to determine % weight variation of tablets

% Weight variation = (A – I / A) x 100

Where,

Initial weight of tablet, I gm
Average weight of tablet, A gm

3.3.2 Thickness test:

3.3.2.1 Procedure:

1. First the tablet was placed between the two jaws of vernier caliper.
2. Then the main scale reading was taken.
3. The vernier scale reading was taken also.
4. The two reading were added together by multiplying with the vernier constant 0.01cm.

3.3.2.2 Equation:

Following equation was used to determine the thickness of the tablets:

Thickness of tablet = Main scale reading + Verniar scale reading X Vernier constant(0.01) + Vernier error

3.3.3 Hardness test:

3.3.3.1 Procedure:

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

Chapter four

RESULTS

4.A Preparation of Standard Curve:

Table 4.1 Concentration and UVAbsorbance for Standard curve of Zantac(Ranitidine)

Serial no	Concentration(µg/ml)	Absorbance
1	5	0.247
2	10	0.471
3	15	0.698
4	20	0.937
5	25	1.132

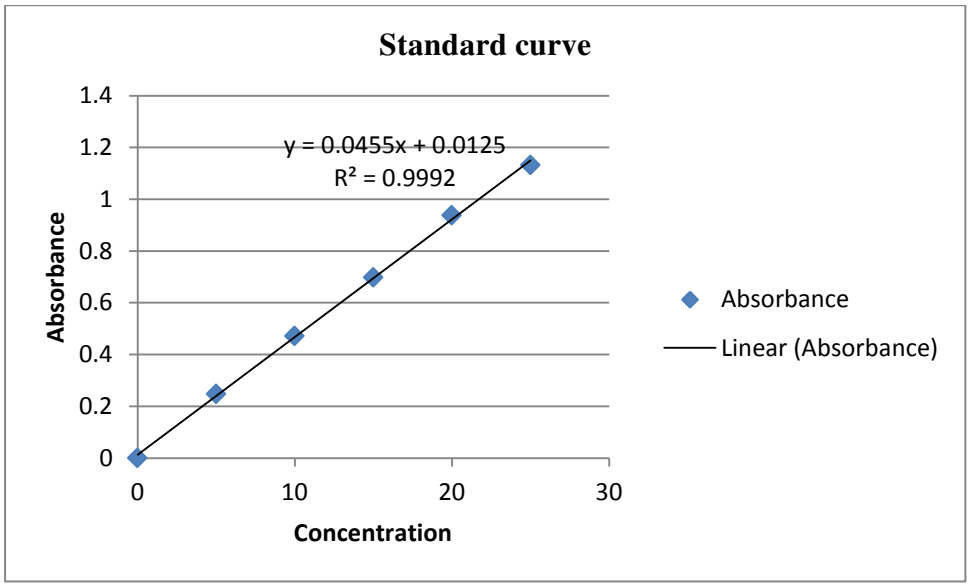

Figure 4.1 Graph showing straight line for absorbance with respect to concentration for ranitidine.

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

4.B.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.B.1.1 Calculation of dissolved amount for Zantac (Ranitidine):

From the standard curve a 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.B.2 Dissolution test of Zantac (Ranitidine) with Calbo (Calcium supplement):

Table 4.4: UV absorbance of Zantac(Ranitidine) with Calbo (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.B.2.1 Calculation for dissolved amount (mg) of Zantac (Ranitidine) with Calbo (Calcium supplement).

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

Table 4.5: Determination of Dissolved amount of Zantac (Ranitidine) with Calbo (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.B.2.2 Comparison of dissolved amount and percent dissolved amount between Zantac(Ranitidine) and Zantac(Ranitidine) with Calbo (Calcium supplement) and impact on dissolution calculation after 20,40 and 60 minutes.

4.B.2.2.1 Impact of Calbo on the dissolution of Zantac after 20 minutes.

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

Zantac without any supplement				**Zantac with Calbo**				
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		73.60		60.40		40.27		
80.60		53.73		39.80		26.53		
94.80	89.80	63.20	59.87	38.80	49.20	25.87	32.80	- 45.21
82.40		54.93		44.80		29.87		
85.40		56.93		60.20		40.13		
85.20		56.80		51.20		34.13		

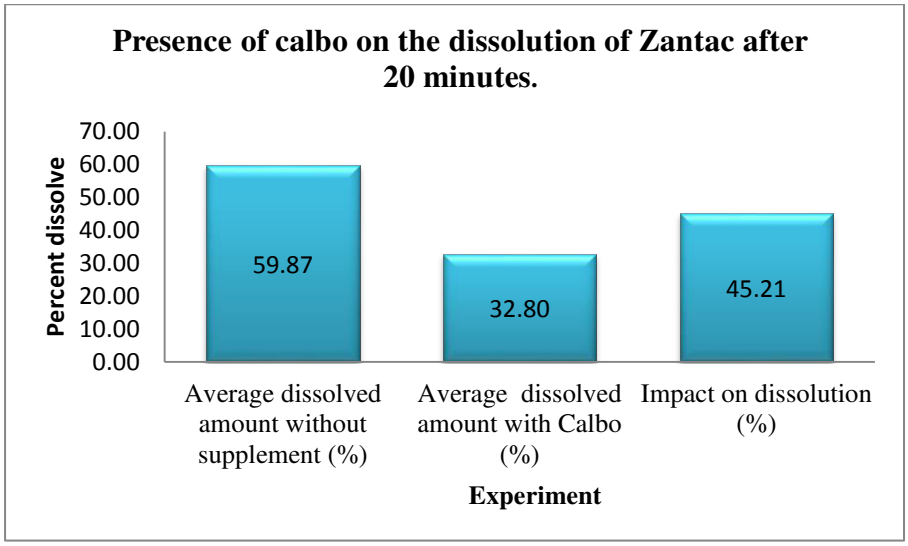

Figure 4.2: Graph represents the presence of calbo on the dissolution of Zantac after 20 minutes.

4.B.2.2.2 Impact of Calbo on the dissolution of Zantac after 40 minutes.

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

Zantac without any supplement				**Zantac with Calbo**				
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		63.80		42.53		
118.6		79.07		66.80		44.53		
139.0	128.20	92.67	85.47	67.60	65.47	45.07	43.64	- 48.94
129.4		86.27		69.80		46.53		
126.2		84.13		63.40		42.27		
127.8		85.20		61.40		40.93		

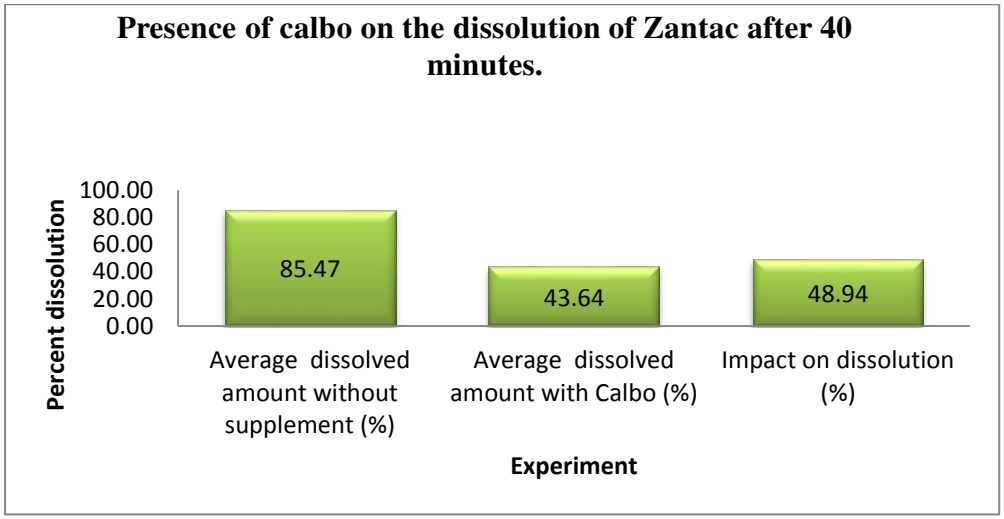

Figure 4.3: Graph represents the presence of calbo on the dissolution of Zantac after 40 minutes.

4.B.2.2.3 Impact of Calbo on the dissolution of Zantac after 60 minutes.

Table4.8 : Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Calbo and impact on dissolution calculation.

Zantac without any supplement				**Zantac with Calbo**				
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 (%)**
118.20		78.80		71.00		47.33		
136.40		90.93		72.00		48.00		
149.80	141.13	99.87	94.09	80.40	71.77	53.60	47.84	- 49.87
146.40		97.60		81.80		54.53		
148.20		98.80		63.60		42.40		
147.80		98.53		61.80		41.20		

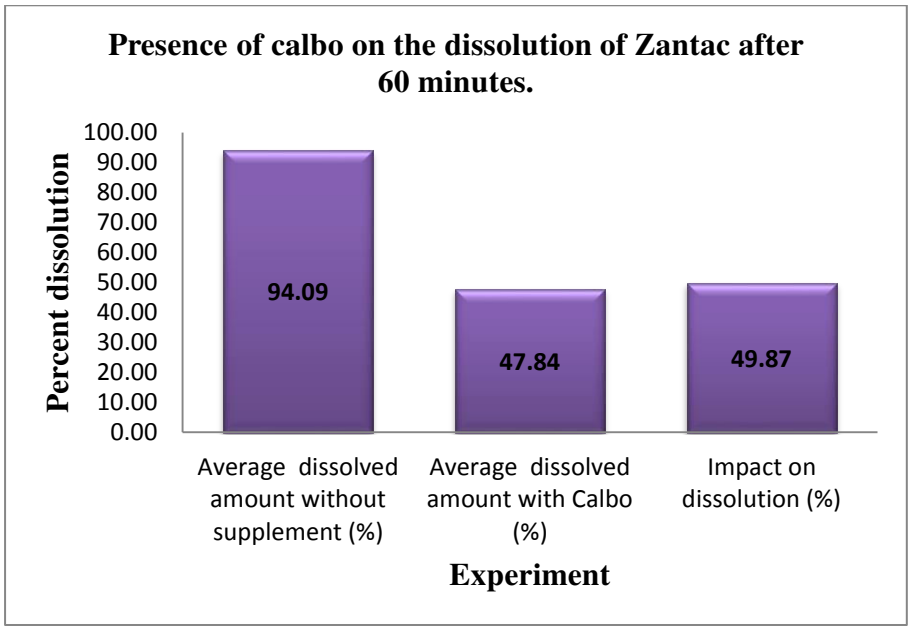

Figure 4.4: Graph represents the presence of Calbo on the dissolution of Zantac after 60 minutes.

4.B.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.B.3.1 Calculation 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	**Absorba Nce**	**Dissolved amount (mg)**	**Absorba nce**	**Dissolved amount (mg)**	**Absorba nce**	**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.B.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.B.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		73.60		60.60		40.40		
80.60		53.73		71.60		47.73		
94.80	89.80	63.20	59.87	92.80	71.97	61.87	47.98	- 19.86
82.40		54.93		69.40		46.27		
85.40		56.93		75.60		50.40		
85.20		56.80		61.80		41.20		

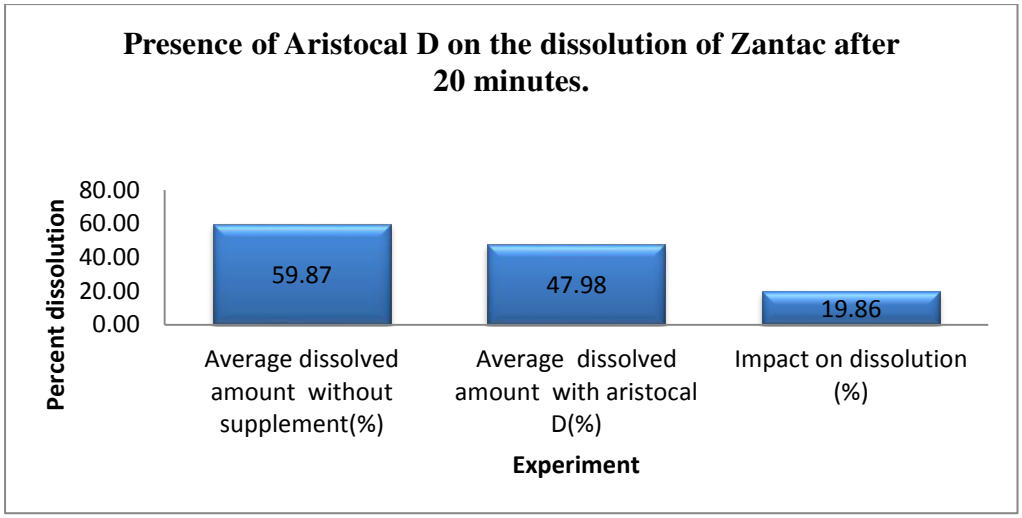

Figure 4.5: Graph represents the presence of Aristocal D on the dissolution of Zantac after 20 minutes.

4.B.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 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 (%)**
128.20		85.47		98.80		65.87		
118.60		79.07		97.20		64.80		
139.00	128.2	92.67	85.47	113.8	98.43	75.87	65.62	-23.22
129.40		86.27		94.60		63.07		
126.20		84.13		95.00		63.33		
127.80		85.20		91.20		60.80		

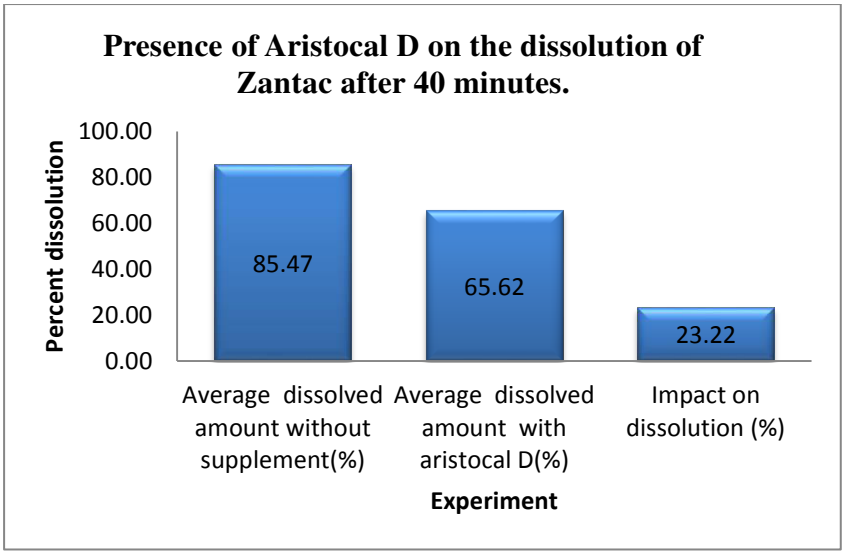

Figure 4.6: Graph represents the presence of Aristocal D on the dissolution of Zantac after 40 minutes.

4.B.3.2.3 Impact of Aristocal D on the dissolution of Zantac after 60 minutes.

4.13Table: Percentage calculation for dissolved amount of Zantac (Ranitidine) and Zantac (Ranitidine) with Aristocal D 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 dissolved amount (%)**	**Impact on dissolution (%)**
118.20		78.80		99.40		66.27		
136.40		90.93		110.80		73.87		
149.80	141.13	99.87	94.09	118.80	108.90	79.20	72.60	- 22.83
146.40		97.60		103.20		68.80		
148.20		98.80		117.40		78.27		
147.80		98.53		103.80		69.20		

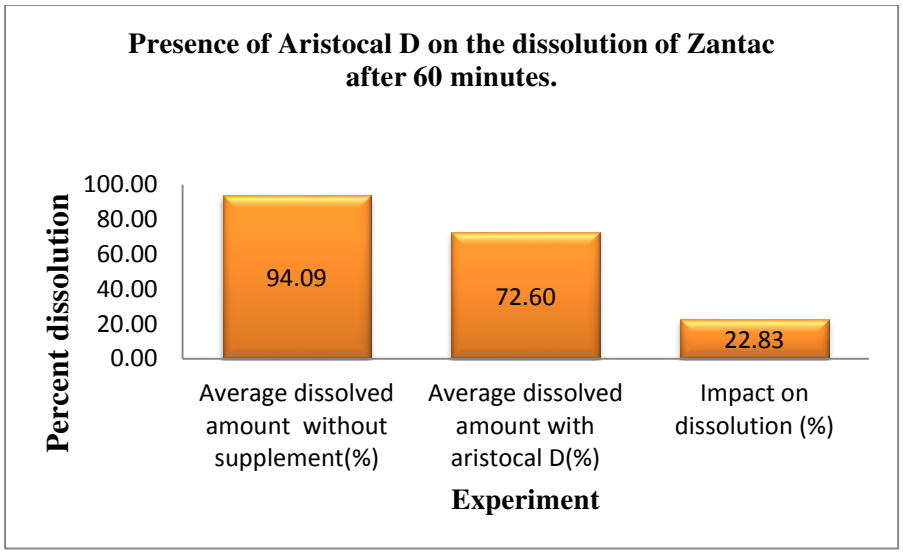

Figure 4.7: Graph represents the presence of Aristocal D on the dissolution of Zantac after 60 minutes.

4.B.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.B.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.B.4.2Comparison of dissolved amount and percent dissolved amount between Zantac (Ranitidine HCL) and Zantac (Ranitidine HCL) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation 20, 40 and 60 minutes.

4.B.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 (%)
110.40		73.60		26.60		17.73		
80.60		53.73		41.00		27.33		
94.80	89.80	63.20	59.87	60.80	48.23	40.53	32.16	- 46.28
82.40		54.93		50.80		33.87		
85.40		56.93		48.20		32.13		
85.20		56.80		62.00		41.33		

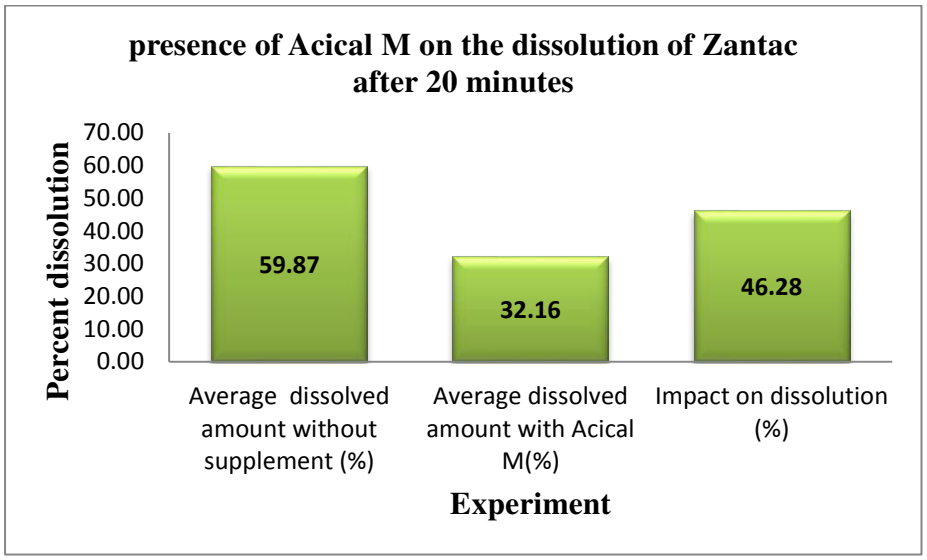

Figure4.8: Graph represents the presence of Acical M on the dissolution of Zantac after 20 minutes.

4.B.4.2.2 Impact of Acical M on the dissolution of Zantac after 40 minutes.

Table4.17: 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		45.00		30.00		
118.6		79.07		60.80		40.53		
139.0	128.2	92.67	85.47	62.60	64.37	41.73	42.91	- 49.80
129.4		86.27		77.20		51.47		
126.2		84.13		61.80		41.20		
127.8		85.20		78.80		52.53		

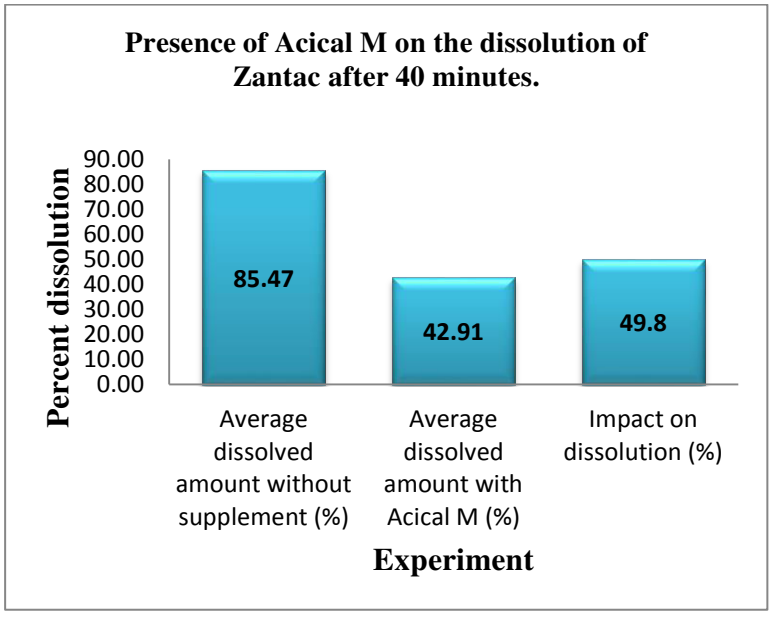

Figure 4.9: Graph represents the presence of Acical M on the dissolution of Zantac after 40 minutes.

4.B.4.2.3 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 (%)**
118.20		78.80		63.00		42.00		
136.40		90.93		80.20		53.47		
149.80	141.13	99.87	94.09	67.00	72.70	44.67	48.47	- 48.49
146.40		97.60		77.80		51.87		
148.20		98.80		68.20		45.47		
147.80		98.53		80.00		53.33		

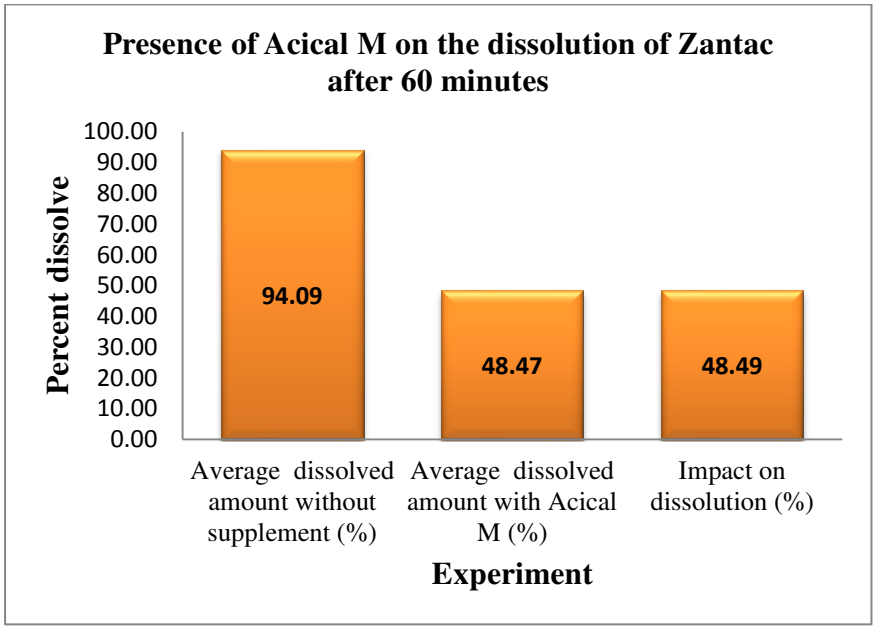

Figure 4.10: Graph represents the presence of Acical M on the dissolution of Zantac after 60 minutes.

4.B.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.B.5.1Calculation 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	68.00	0.589	115.40	0.654	128.40
2	0.387	75.00	0.577	113.00	0.712	140.00
3	0.366	70.80	0.509	99.40	0.679	133.40
4	0.321	61.80	0.615	120.60	0.764	150.40
5	0.639	125.40	0.822	162.00	0.738	145.20
6	0.654	128.40	0.815	160.60	0.767	151.00

4.B.5.2Comparison 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.B.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 dissolved amount (mg)**	**Percent dissolved amount (%)**	**Average percent dissolved amount (%)**	**Impact on dissolution (%)**
110.40		73.60		68.00		45.33		
80.60		53.73		75.00		50.00		
94.80	89.80	63.20	59.87	70.80	88.23	47.20	58.82	1.75
82.40		54.93		61.80		41.20		
85.40		56.93		125.40		83.60		
85.20		56.80		128.40		85.60		

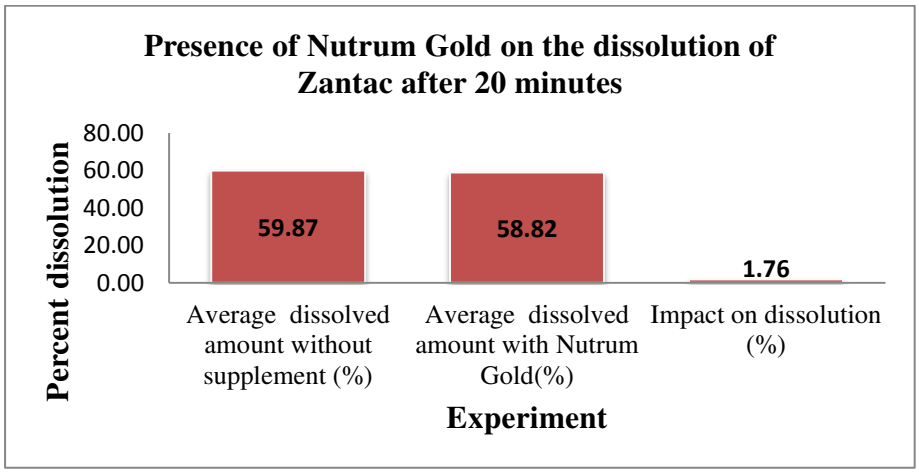

Figure 4.11: Graph represents the presence of Nutrum Gold on the dissolution of Zantac after 20 minutes.

4.B.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 and impact on dissolution calculation after 40 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		113.0		75.33		
139.0	128.2	92.67	85.47	99.40	128.50	66.27	85.67	0.23
129.4		86.27		120.6		80.40		
126.2		84.13		162.0		108.00		
127.8		85.20		160.6		107.07		

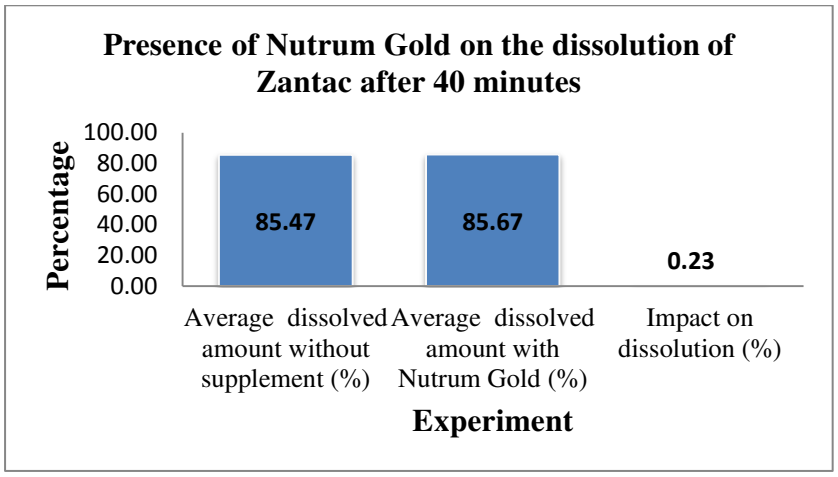

Figure 4.12: Graph represents the presence of Nutrum Gold on the dissolution of Zantac after 40 minutes.

4.B.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 and Zantac with Nutrum Gold 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 dissolvedamount (%)**	**Dissolved amount (mg)**	**Average dissolved amount (mg)**	**Percent dissolved amount (%)**	**Average percent dissolved amount (%)**	**Impact on dissolution (%)**
118.20		78.80		128.40		85.60		
136.40		90.93		140.00		93.33		
149.80	141.13	99.87	94.09	133.40	141.40	88.93	94.27	0.19
146.40		97.60		150.40		100.27		
148.20		98.80		145.20		96.80		
147.80		98.53		151.00		100.67		

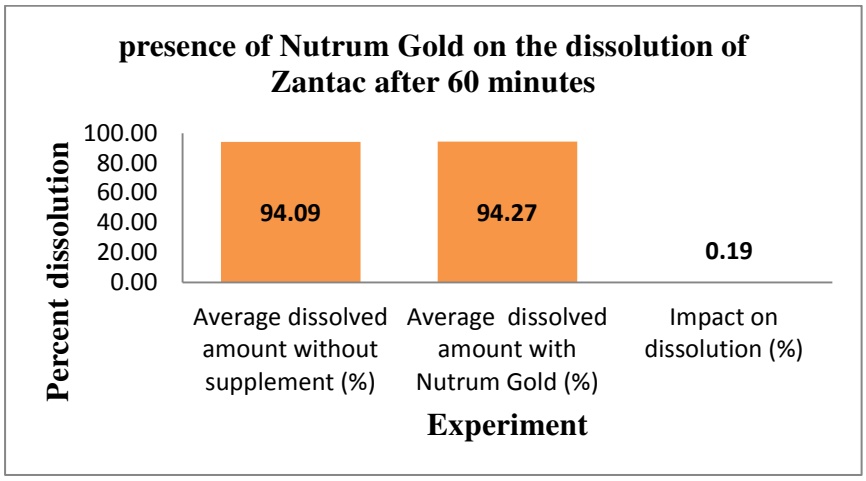

Figure 4.13: Graph represents the presence of Nutrum Gold on the dissolution of Zantac after 60 minutes.

4.B.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.B.6.1Calculation 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	92.00	0.712	140.00	0.835	164.60
2	0.469	91.40	0.627	123.00	0.737	145.00
3	0.563	110.20	0.825	162.60	0.857	169.00
4	0.494	96.40	0.598	117.20	0.657	129.00
5	0.432	84.00	0.602	118.00	0.658	129.20
6	0.474	92.40	0.653	128.20	0.703	138.20

4.B.6.2Comparison 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.B.6.2.1Impact 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 (%)**
110.40		73.60		92.00		61.33		
80.60		53.73		91.40		60.93		
94.80	89.80	63.20	59.87	110.20	94.40	73.47	62.93	5.01
82.40		54.93		96.40		64.27		
85.40		56.93		84.00		56.00		
85.20		56.80		92.40		61.60		

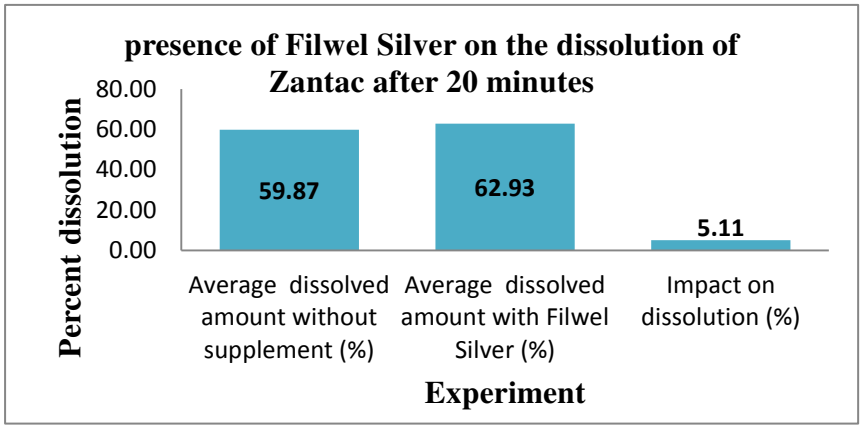

Figure 4.14: Graph represents the presence of Filwel Silver on the dissolution of Zantac after 20 minutes.

4.B.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		140.00		93.33		
118.6		79.07		123.00		82.00		
139.0	128.2	92.67	85.47	162.60	131.50	108.40	87.67	2.57
129.4		86.27		117.20		78.13		
126.2		84.13		118.00		78.67		
127.8		85.20		128.20		85.47		

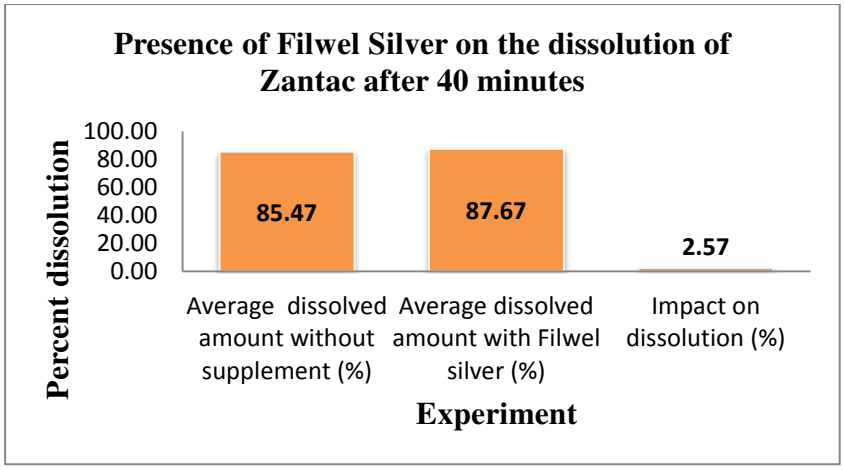

Figure 4.15: Graph represents the presence of Filwel Silver on the dissolution of Zantac after 40 minutes.

4.B.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.

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		78.80		164.6		109.73		
136.4		90.93		145.0		96.67		
149.8	141.13	99.87	94.09	169.0	145.83	112.67	97.22	3.33
146.4		97.60		129.0		86.00		
148.2		98.80		129.2		86.13		
147.8		98.53		138.2		92.13		

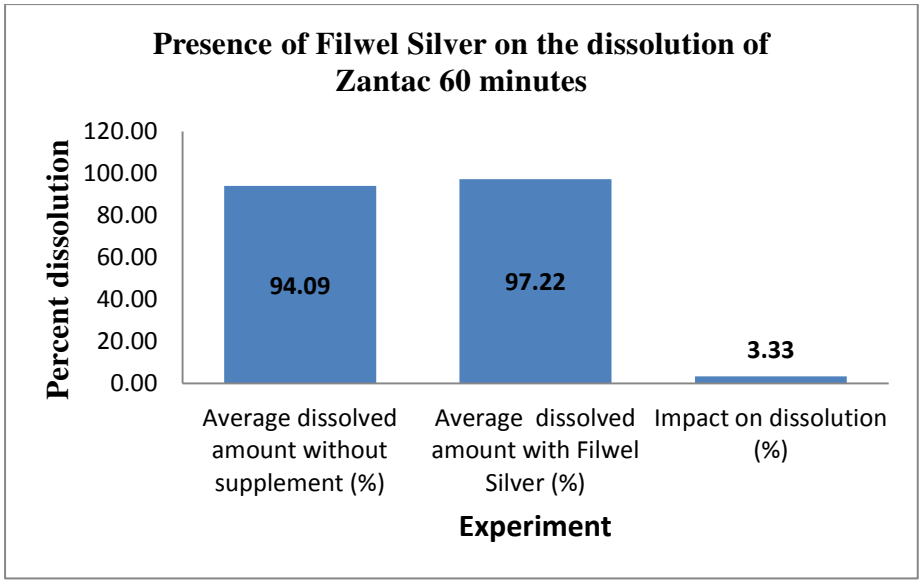

Figure4.16: Graph represents the presence of Filwel Silver on the dissolution of Zantac 60 minutes.

4.B.7 Comparison among the average percent dissolved (%) amount of individual Zantac, Zantac with Calbo, 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, 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 (%)	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

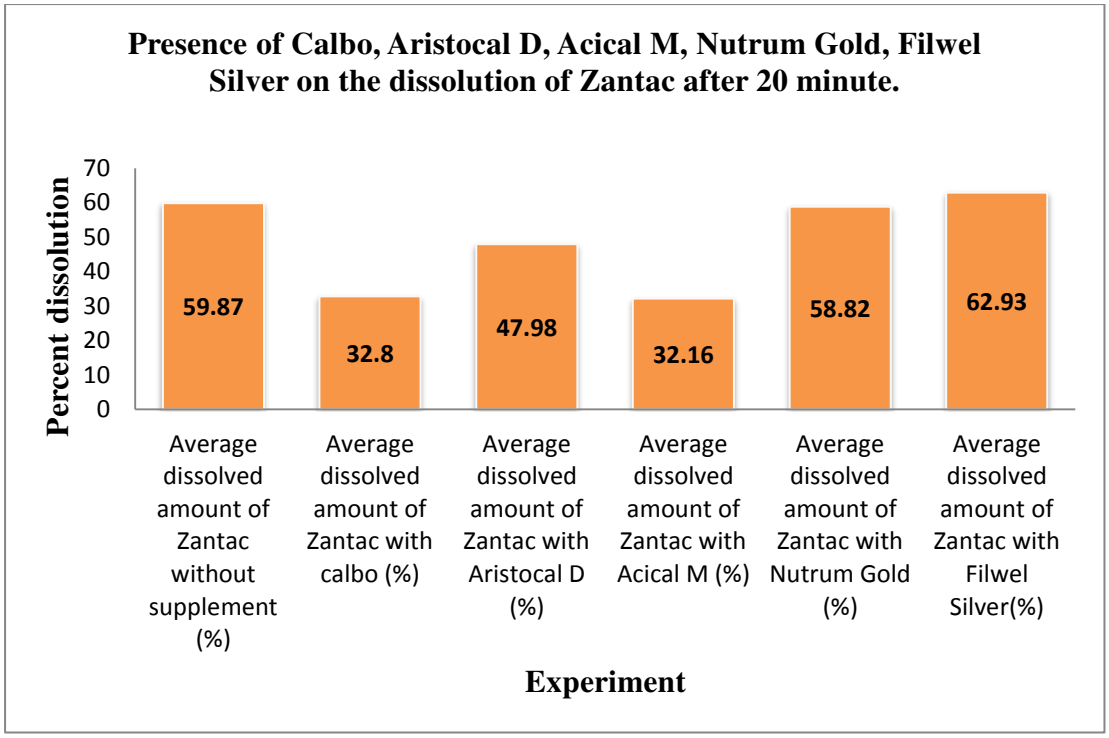

Figure 4.17: Graph represents the presence of Calbo, Aristocal D, Acical M, Nutrum Gold, and Filwel Silver on the dissolution of Zantac after 20 minute.

Table 4.30: Table showing the differences among the average percent dissolve (%) amount of individual Zantac, Zantac with Calbo, 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 (%)	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

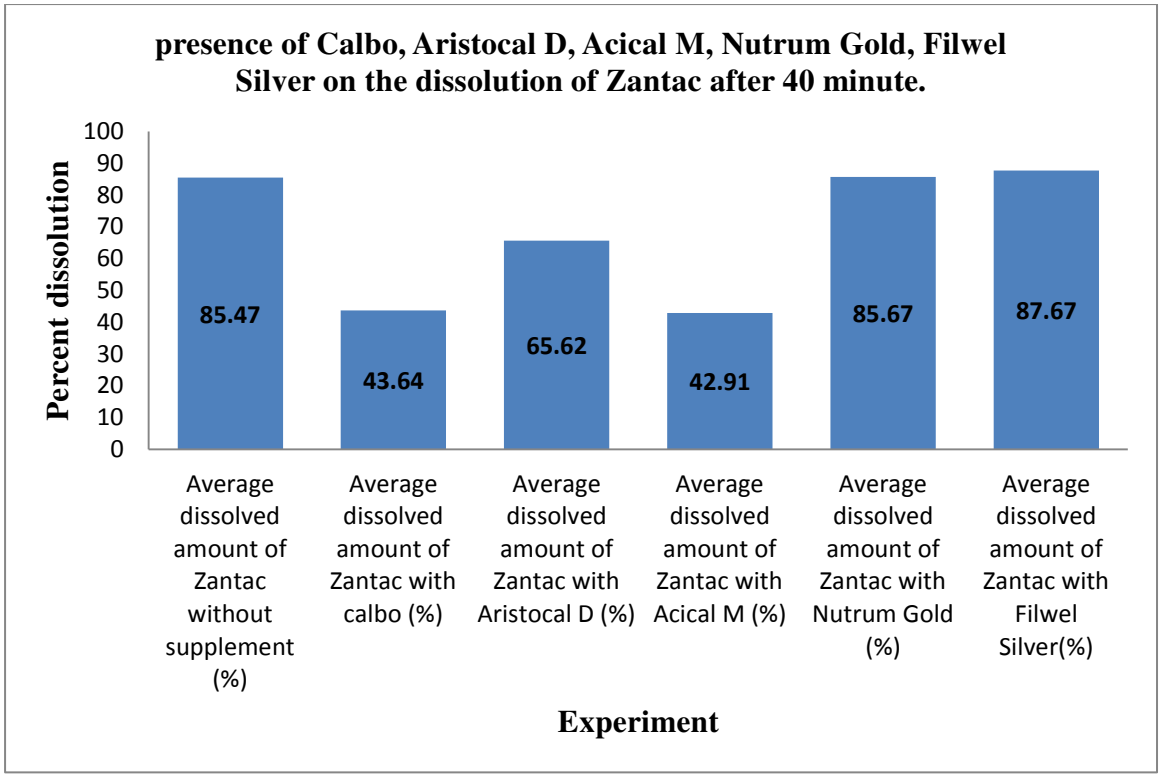

Figure 4.18: Graph represents the presence of Calbo, Aristocal D, Acical M, Nutrum Gold, and Filwel Silver on the dissolution of Zantac after 40 minute.

Table 4.31: Table showing the differences among the average percent dissolve (%) amount of individual Zantac, Zantac with Calbo, 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 (%)	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

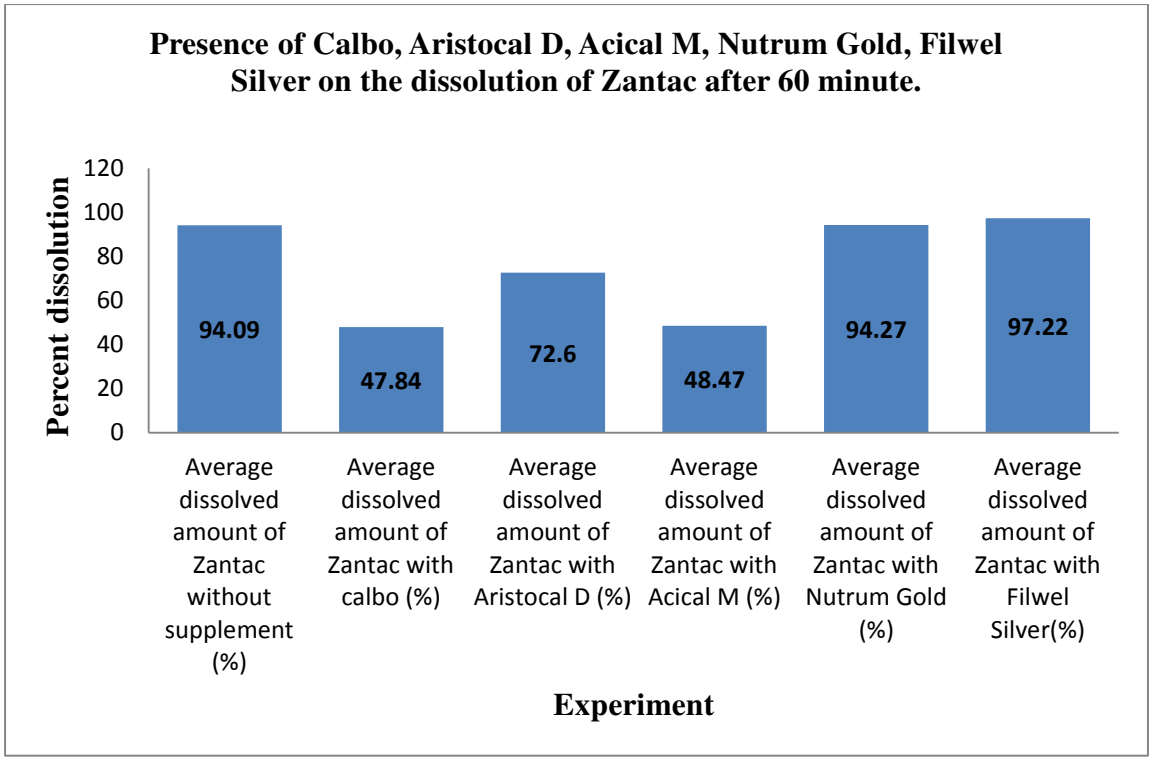

Figure 4.19: Graph represents the presence of Calbo, Aristocal D, Acical M, Nutrum Gold, and Filwel Silver on the dissolution of Zantac after 60 minute.

4.C Result of the dissolution test of individual Neotack and Neotack with Calbo, Aristocal D, Acical M, Nutrum Gold and Filwel Silver.

4.C.1 Dissolution test of Neotack (Ranitidine) without any supplement:

Table 4.32: UV absorbance of Neotack (Ranitidine)

	Absorbance		
Serial number	After 20 minutes	After 40 minutes	After 60 minutes
1	0.606	0.651	0.769
2	0.468	0.736	0.750
3	0.423	0.568	0.735
4	0.451	0.650	0.699
5	0.470	0.667	0.757
6	0.600	0.681	0.745

4.C.1.1 Calculation of dissolved amount for Neotack (Ranitidine):

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

Here, Y= Absorbance

X=concentration=?

Dilution factor=9000

If the absorbance is 0.606, then by putting the value in this equation,

0.606=0.045x + 0.012

0.045X=0.606-0.012

0.045x=0.594

X=0.594/0.045

X=13.2

Dissolve amount=13.2*9000/1000=118.8mg

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

Table 4.33: Determination of Dissolved amount of Neotack (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	0.606	118.80	0.651	127.80	0.769	149.40
2	0.468	91.20	0.736	144.80	0.750	147.60
3	0.423	82.20	0.568	111.20	0.735	144.60
4	0.451	87.8	0.650	127.60	0.699	137.40
5	0.470	91.6	0.667	131.00	0.757	149.00
6	0.600	117.6	0.681	133.80	0.745	146.60

4.C.2 Dissolution test of Neotack (Ranitidine) with Calbo (Calcium supplement)

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

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.313	0.320	0.358
2	0.236	0.388	0.372
3	0.212	0.341	0.361
4	0.308	0.358	0.404
5	0.221	0.247	0.287
6	0.239	0.343	0.364

4.C.2.1 Calculation for dissolved amount (mg) of Neotack (Ranitidine) with Calbo (Calcium supplement).

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

Table 4.35: Determination of Dissolved amount of Neotack (Ranitidine) with Calbo (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	0.313	60.20	0.320	61.60	0.358	69.20
2	0.236	44.80	0.388	75.20	0.372	72.00
3	0.212	40.00	0.341	65.80	0.361	69.80
4	0.308	59.20	0.358	69.20	0.404	78.40
5	0.221	41.80	0.247	47.00	0.287	55.00
6	0.239	45.40	0.343	66.20	0.364	70.40

4.C.2.2 Comparison of dissolved amount and percent dissolved amount between Neotack(Ranitidine) and Neotack(Ranitidine) with Calbo (Calcium supplement) and impact on dissolution calculation after 20,40 and 60 minutes.

4.C.2.2.1 Impact of Calbo on the dissolution of Neotack after 20 minutes.

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

Neotack without any supplement				**Neotack with Calbo**				
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 (%)**
118.8		79.20		60.20		40.13		
91.20		60.80		44.80		29.87		
82.20	98.20	54.80	65.47	40.00	48.57	26.67	32.38	-50.54
87.80		58.53		59.20		39.47		
91.60		61.07		41.80		27.87		
117.6		78.40		45.40		30.27		

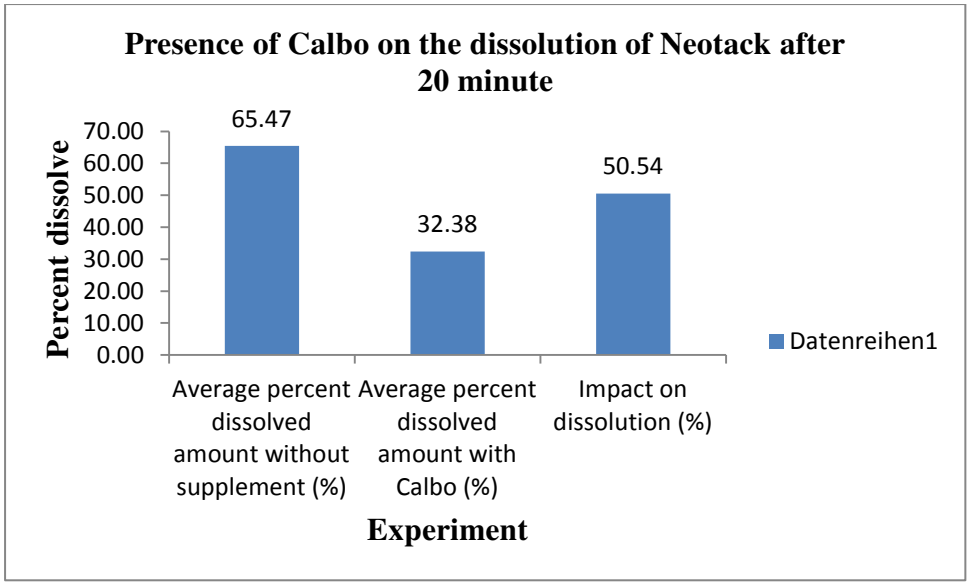

Figure 4.20: Graph represents the presence of calbo on the dissolution of Neotack after 20 minutes.

4.C.2.2.2 Impact of Calbo on the dissolution of Neotack after 40 minutes.

Table4.37 : Percentage calculation for dissolved amount of Neotack (Ranitidine) and Neotack (Ranitidine) with Calbo and impact on dissolution calculation after 40 minutes.

Neotack without any supplement				Neotack with Calbo				
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 (%)
127.80		85.20		61.60		41.07		
144.80		96.53		75.20		50.13		
111.20	129.37	74.13	86.24	65.80	67.32	43.87	42.78	-47.96
127.6		85.07		69.20		46.13		
131.00		87.33		47.00		31.33		
133.80		89.20		66.20		44.13		

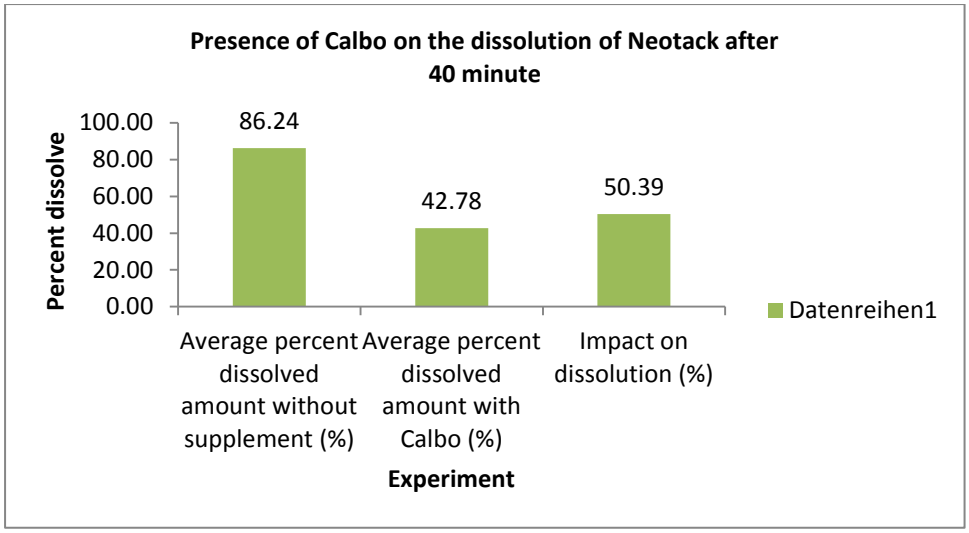

Figure 4.21: Graph represents the presence of calbo on the dissolution of Neotack after 40 minutes.

4.C.2.2.3 Impact of Calbo on the dissolution of Neotack after 60 minutes.

Table 4.38: Percentage calculation for dissolved amount of Neotack (Ranitidine) and Neotack (Ranitidine) with Calbo and impact on dissolution calculation.

Neotack without any supplement				**Neotack with Calbo**				
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 (%)**
151.4		100.93		69.20		46.13		
147.6		98.40		72.00		48.00		
144.6	146.1	96.40	97.40	69.80	69.13	45.53	46.09	-52.68
137.4		91.60		78.40		52.27		
149.0		99.33		55.00		36.67		
146.6		97.73		70.40		46.93		

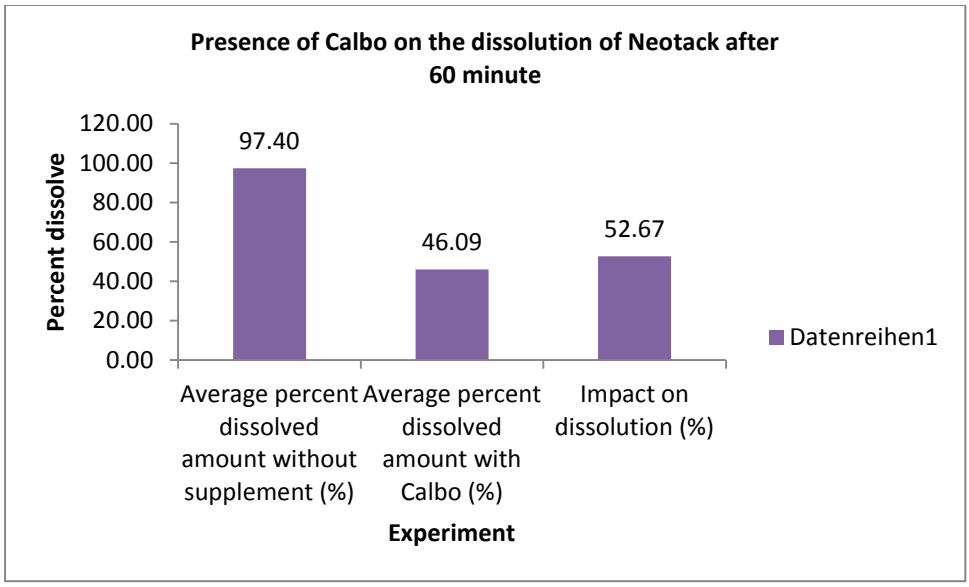

Figure 4.22: Graph represents the presence of Calbo on the dissolution of Neotack after 60 minutes.

4.C.3 Dissolution test of Neotack (Ranitidine) with Aristocal D (Calcium and vitamin D supplement):

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

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.383	0.468	0.539
2	0.428	0.513	0.579
3	0.433	0.453	0.544
4	0.512	0.554	0.575
5	0.398	0.530	0.595
6	0.457	0.485	0.597

4.C.3.1 Calculation for dissolved amount (mg) of Neotack (Ranitidine) with Aristocal D (Calcium and vitamin D supplement).

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

Table 4.40: Determination of Dissolved amount of Neotack (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	0.383	74.20	0.468	91.2	0.539	105.40
2	0.428	83.20	0.513	100.2	0.579	113.4
3	0.433	84.20	0.453	88.20	0.544	106.4
4	0.512	100.00	0.554	108.40	0.575	112.6
5	0.398	77.20	0.530	103.60	0.595	116.6
6	0.457	89.20	0.485	94.60	0.597	117.00

4.C.3.2 Comparison of dissolved amount and percent dissolved amount between Neotack (Ranitidine) and Neotack (Ranitidine) with Aristocal D (Calcium and vitamin D supplement) and impact on dissolution calculation after 20, 40 and 60 minutes.

4.C.3.2.1 Impact of Aristocal D on the dissolution of Neotack after 20 minutes.

Table 4.41: Percentage calculation for dissolved amount of Neotack (Ranitidine) and Neotack with Aristocal D and impact on dissolution calculation 20 minutes.

Neotack without any supplement				Neotack 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 (%)
118.80		79.20		74.20		49.47		
91.20		60.80		83.20		55.47		
82.20	98.20	54.80	65.47	84.20	84.63	56.13	56.42	-13.82
87.80		58.53		100.0		66.67		
91.60		61.07		77.20		51.46		
117.60		78.40		89.00		59.33		

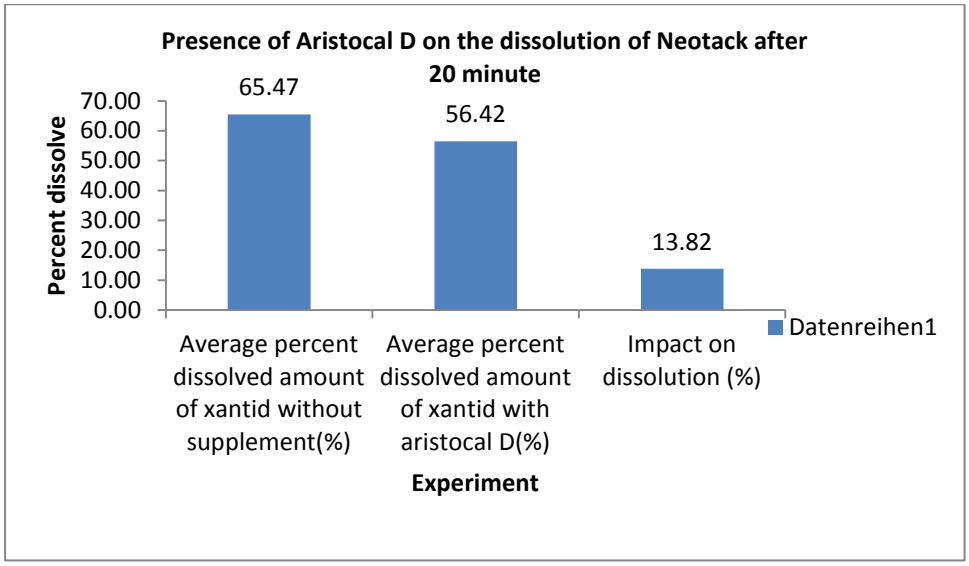

Figure 4.23: Graph represents the presence of Aristocal D on the dissolution of Neotack after 20 minutes.

4.C.3.2.2 Impact of Aristocal D on the dissolution of Neotack after 40 minutes.

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

Neotack without any supplement				Neotack 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 (%)
127.80		85.20		91.20		60.80		
144.80		96.53		100.20		66.80		
111.20	129.37	74.13	86.24	88.20	97.70	58.80	65.13	-24.47
127.6		85.07		108.40		72.27		
131.00		87.33		103.60		69.07		
133.80		89.20		94.60		63.07		

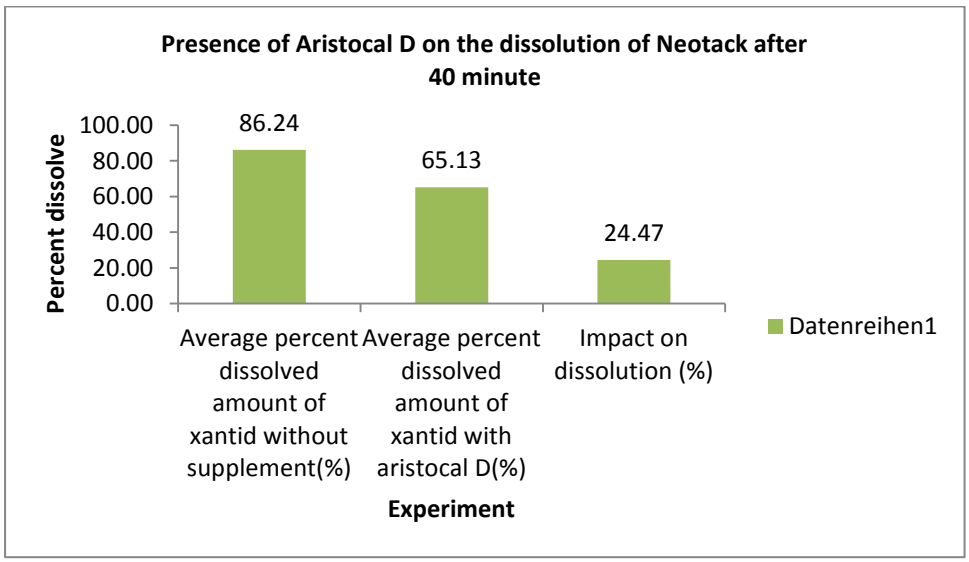

Figure 4.24: Graph represents the presence of Aristocal D on the dissolution of Neotack after 40 minutes.

4.C.3.2.3 Impact of Aristocal D on the dissolution of Neotack after 60 minutes.

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

Neotack without any supplement				**Neotack 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 (%)**
151.40		100.93		105.40		70.30		
147.6		98.40		113.40		75.60		
144.6	146.1	96.40	97.40	106.40	111.9	70.90	74.60	-23.40
137.4		91.60		112.60		75.10		
149.00		99.33		116.60		77.70		
146.60		97.73		117.00		78.00		

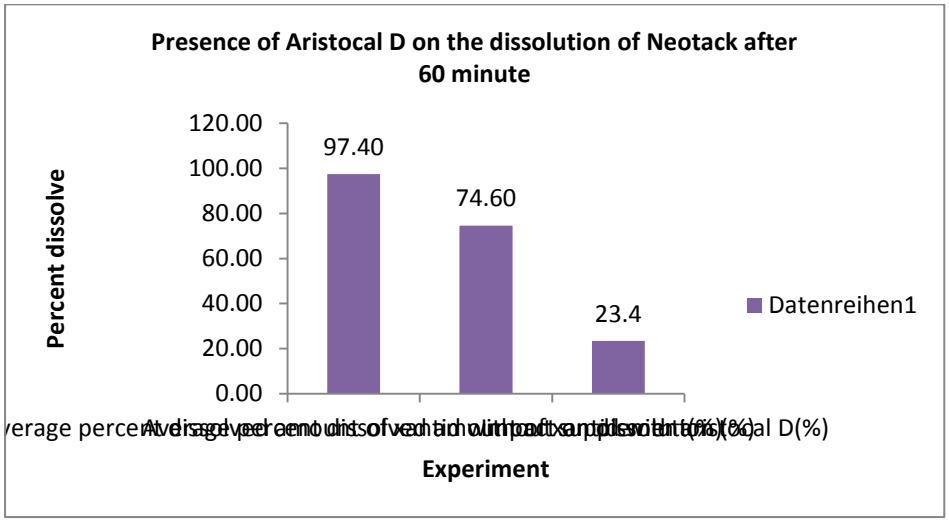

Figure 4.25: Graph represents the presence of Aristocal D on the dissolution of Neotack after 60 minutes.

4.C.4 Dissolution test of Neotack (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement)

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

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.241	0.368	0.427
2	0.239	0.316	0.413
3	0.300	0.251	0.353
4	0.224	0.401	0.434
5	0.247	0.317	0.330
6	0.303	0.355	0.375

4.C.4.1 Calculation for dissolved amount (mg) Neotack (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement)

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

Table 4.45: Determination of Dissolved amount of Neotack (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	0.241	45.80	0.368	71.20	0.427	83.00
2	0.239	45.40	0.316	60.80	0.413	80.20
3	0.300	57.60	0.251	47.80	0.353	68.20
4	0.224	42.40	0.401	77.80	0.434	84.40
5	0.247	47.00	0.317	61.00	0.330	63.60
6	0.303	58.20	0.355	68.60	0.375	72.60

4.C.4.2 Comparison of dissolved amount and percent dissolved amount between Neotack (Ranitidine) and Neotack (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation 20, 40 and 60 minutes.

4.C.4.2.1 Impact of Acical M on the dissolution of Neotack after 20 minutes.

Table 4.46: Percentage calculation for dissolved amount of Neotack (Ranitidine) and Neotack (Ranitidine) with Acical M and impact on dissolution calculation after 20 minute.

Neotack without any supplement				**Neotack 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 (%)**
118.8		79.20		45.80		30.53		
91.20		60.80		45.40		30.27		
82.20	98.20	54.80	65.47	57.60	49.40	38.40	32.93	-49.70
87.80		58.53		42.40		28.27		
91.60		61.07		47.00		31.33		
117.6		78.40		58.20		38.8		

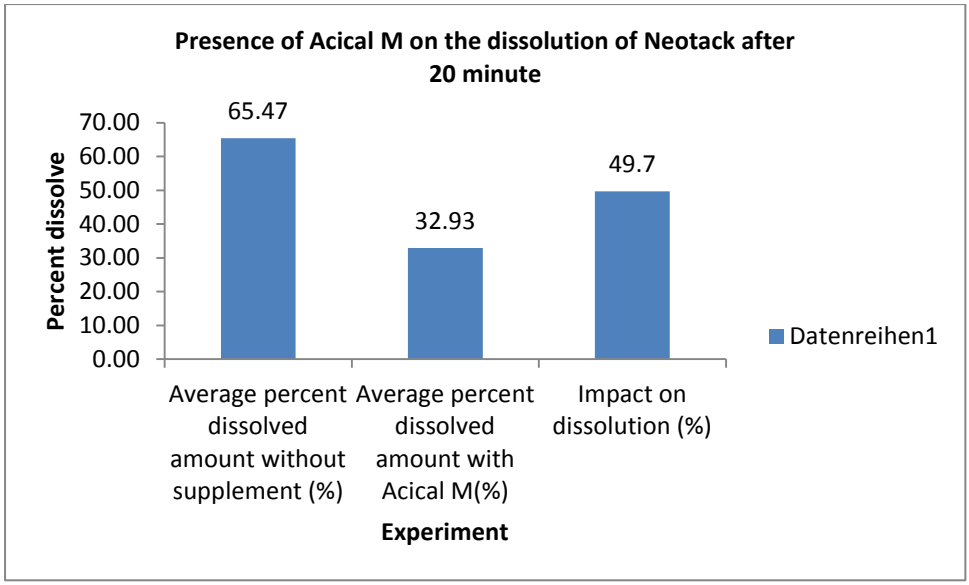

Figure4.26: Graph represents the presence of Acical M on the dissolution of Neotack after 20 minutes.

4.C.4.2.2Impact of Acical M on the dissolution of Neotack after 40 minutes.

Table4.47: Percentage calculation for dissolved amount of Neotack (Ranitidine) and Neotack (Ranitidine) with Acical M (Calcium, vitamin D and multimineral supplement) and impact on dissolution calculation after 40 minutes.

Neotack without any supplement				Neotack with Acical M				
Dissolved amount (mg)	Aver Age 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 (%)
127.8		85.20		71.20		47.47		
144.8		96.53		60.80		40.53		
111.2	129.37	74.13	86.24	47.80	67.49	31.87	42.91	-50.24
127.6		85.07		77.80		51.87		
131.0		87.33		61.00		40.67		
133.8		89.20		68.60		45.73		

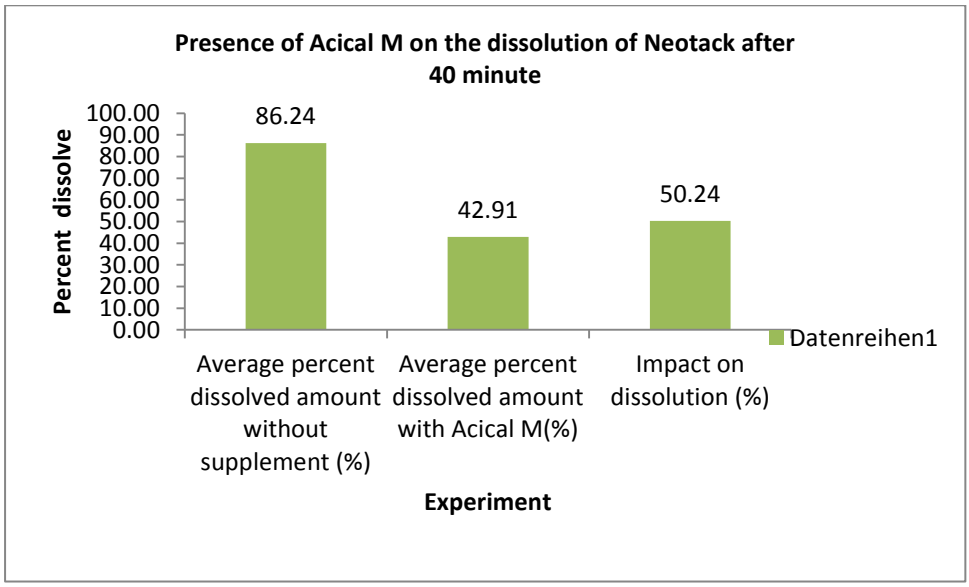

Figure 4.27: Graph represents the presence of Acical M on the dissolution of Neotack after 40 minutes.

4.C.4.2.3 Impact of Acical M on the dissolution of Neotack after 60 minutes.

Table 4.48: Percentage calculation for dissolved amount of Neotack(Ranitidine) and Neotack with Acical M and impact on dissolution calculation after 60 minutes.

Neotack without any supplement				**Neotack 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 (%)**
151.4		100.93		83.00		55.33		
147.6		98.40		80.20		53.47		
144.6	146.1	96.40	97.40	68.20	75.33	45.47	50.22	-48.43
137.4		91.60		84.40		56.27		
149.0		99.33		63.60		42.40		
146.6		97.73		72.60		48.40		

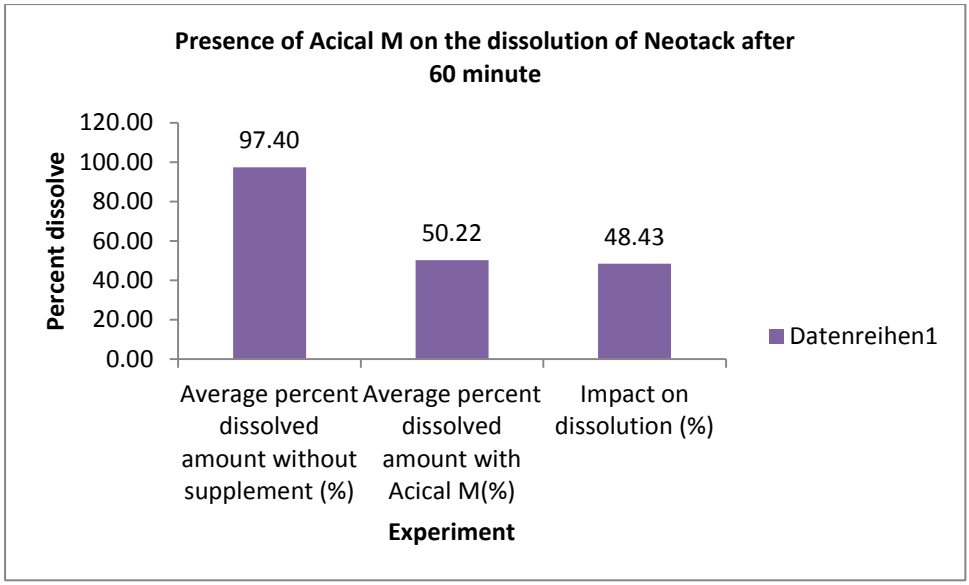

Figure 4.28: Graph represents the presence of Acical M on the dissolution of Neotack after 60 minutes.

4.C.5 Dissolution test of Neotack (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement)

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

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.450	0.650	0.733
2	0.560	0.731	0.748
3	0.463	0.757	0.760
4	0.501	0.583	0.803
5	0.595	0.621	0.752
6	0.525	0.675	0.736

4.C.5.1Calculation for dissolved amount (mg) Neotack (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement).

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

Table 4.50: Determination of Dissolved amount of Neotack (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	0.450	87.60	0.650	127.60	0.733	144.20
2	0.560	109.60	0.731	143.80	0.748	147.20
3	0.463	90.20	0.757	149.00	0.760	149.60
4	0.501	97.80	0.583	114.20	0.803	158.20
5	0.595	116.60	0.621	121.80	0.752	158.00
6	0.525	102.60	0.675	132.60	0.736	148.00

4.C.5.2Comparison of dissolved amount and percent dissolved amount between Neotack (Ranitidine) and Neotack (Ranitidine) with Nutrum Gold (Multivitamin and multimineral supplement) and impact on dissolution calculation 20, 40 60 minutes.

4.C.5.2.1 Impact of Nutrum Gold on the dissolution of Neotack after 20 minutes.

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

Neotack without any supplement				Neotack 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 (%)
118.8		79.20		87.60		58.60		
91.20		60.80		109.60		73.07		
82.20	98.20	54.80	65.47	90.20	100.73	60.01	67.16	2.58
87.80		58.53		97.80		65.20		
91.60		61.07		116.60		77.70		
117.6		78.40		102.60		68.40		

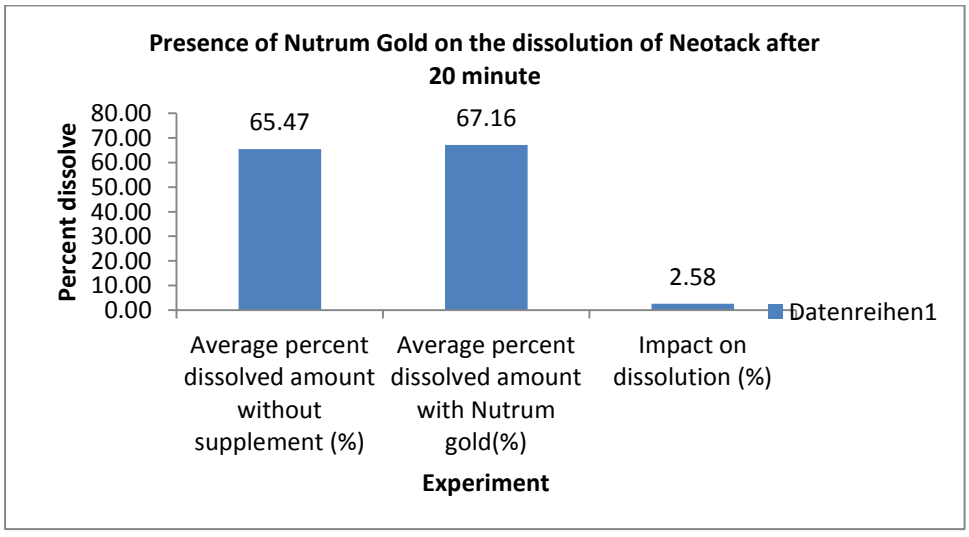

Figure 4.29: Graph represents the presence of Nutrum Gold on the dissolution of Neotack after 20 minutes.

4.C.5.2.2 Impact of Nutrum Gold on the dissolution of Neotack after 40 minutes.

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

Neotack without any supplement				Neotack 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 (%)
127.8		85.20		127.6		85.07		
144.8		96.53		143.8		95.90		
111.2	129.37	74.13	86.24	149.0	131.50	99.30	87.67	1.65
127.6		85.07		114.2		76.13		
131.0		87.33		121.8		81.20		
133.8		89.20		132.6		84.40		

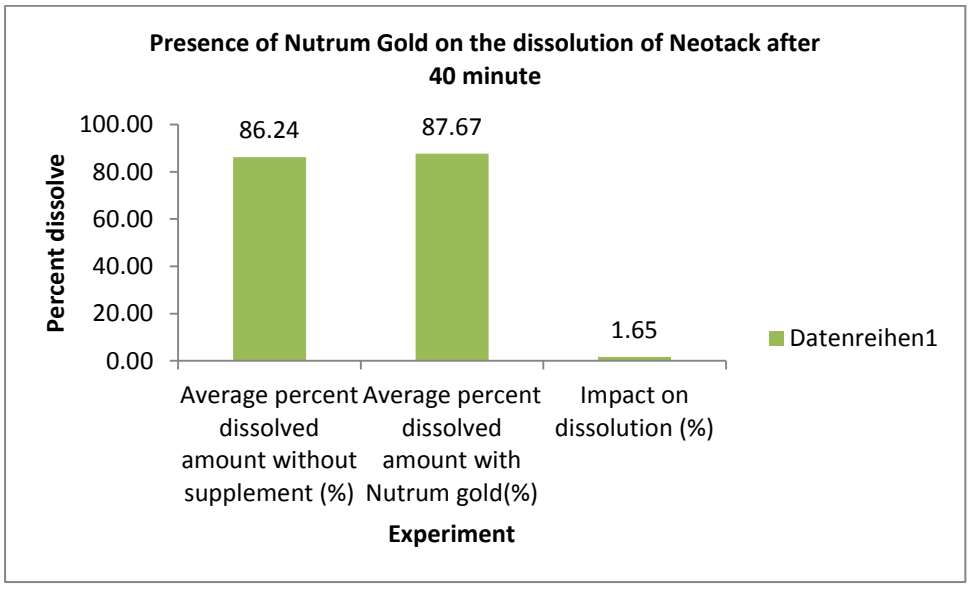

Figure 4.30: Graph represents the presence of Nutrum Gold on the dissolution of Zantac after 40 minutes.

4.C.5.2.3 Impact of Nutrum Gold on the dissolution of Neotack after 60 minutes.

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

Neotack without any supplement				**Neotack 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 (%)**
151.4		100.93		144.2		96.13		
147.6		98.40		147.2		98.13		
144.6	146.1	96.40	97.40	149.6	148.67	99.73	99.11	1.75
137.4		91.60		158.2		105.47		
149.0		99.33		148.0		98.67		
146.6		97.73		144.8		96.50		

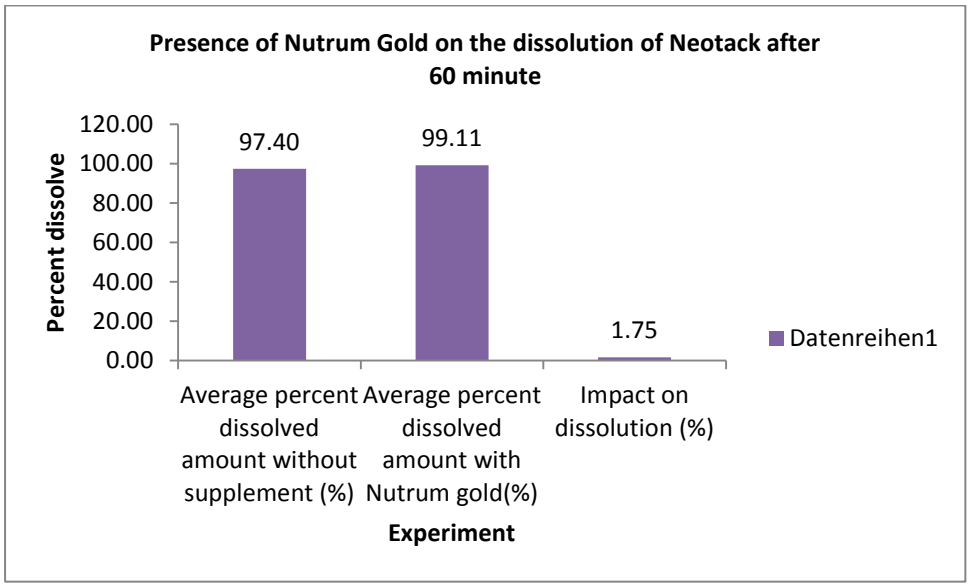

Figure 4.31: Graph represents the presence of Nutrum Gold on the dissolution of Neotack after 60 minutes.

4.C.6 Dissolution test of Neotack (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement)

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

	Absorbance		
Serial number	**After 20 minutes**	**After 40 minutes**	**After 60 minutes**
1	0.463	0.662	0.731
2	0.503	0.682	0.740
3	0.487	0.641	0.745
4	0.468	0.650	0.739
5	0.499	0.635	0.756
6	0.631	0.685	0.785

4.C.6.1 Calculation for dissolved amount (mg) Neotack (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement)

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

Table 4.55: Determination of Dissolved amount of Neotack (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	0.463	60.13	0.662	86.67	0.731	95.87
2	0.503	65.47	0.682	89.33	0.740	97.07
3	0.487	63.33	0.641	83.87	0.745	97.73
4	0.468	60.80	0.650	85.07	0.739	96.93
5	0.499	64.93	0.635	83.07	0.756	99.20
6	0.631	82.53	0.685	89.73	0.785	103.07

4.C.6.2 Comparison of dissolved amount and percent dissolved amount between Neotack (Ranitidine) and Neotack (Ranitidine) with Filwel Silver (Multivitamin and multimineral supplement) and impact on dissolution calculation 20, 40 and 60 minutes.

4.C.6.2.1Impact of Filwel Silver on the dissolution of Neotack after 20 minutes.

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

Neotack without any supplement				Neotack 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 (%)
118.8		79.20		90.20		60.13		
91.20		60.80		98.20		65.47		
82.20	98.20	54.80	65.47	95.00	99.30	63.33	66.20	1.11
87.80		58.53		91.20		60.80		
91.60		61.07		97.40		64.93		
117.6		78.40		123.8		82.53		

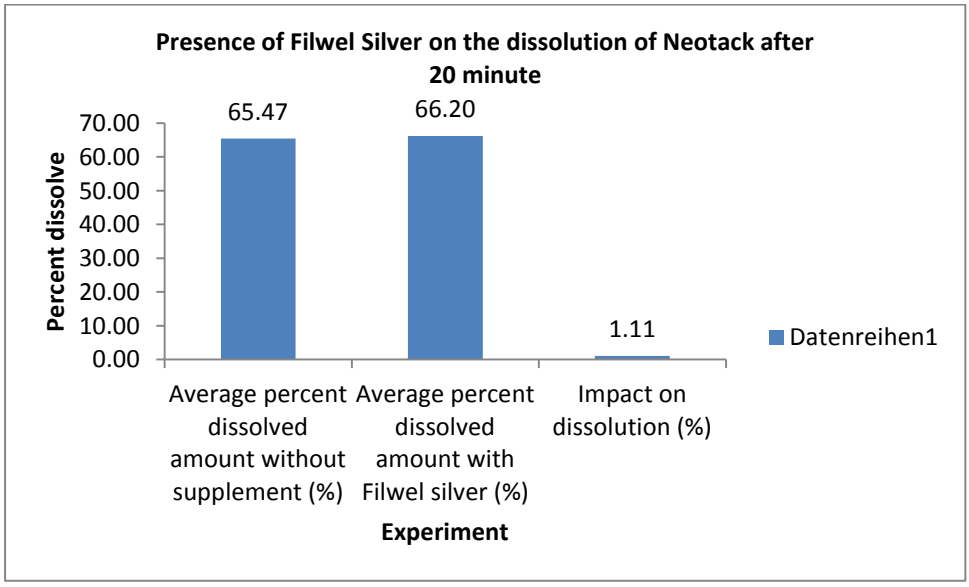

Figure 4.32: Graph represents the presence of Filwel Silver on the dissolution of Neotack after 20 minutes.

4.C.6.2.2 Impact of Filwel Silver on the dissolution of Neotack after 40 minutes.

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

Neotack without any supplement				Neotack 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 (%)
127.8		85.20		130.0		86.67		
144.8		96.53		134.0		89.33		
111.2	129.37	74.13	86.24	125.8	129.43	83.87	86.29	0.05
127.6		85.07		127.6		85.07		
131.0		87.33		124.6		83.07		
133.8		89.20		134.6		89.73		

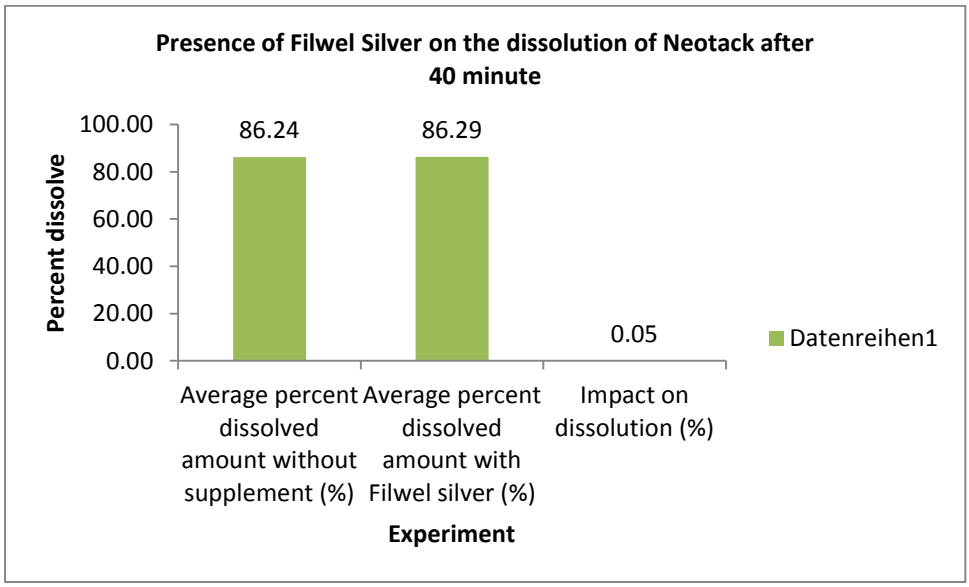

Figure 4.33: Graph represents the presence of Filwel Silver on the dissolution of Zantac after 40 minutes.

4.C.6.2.3 Impact of Filwel Silver on the dissolution of Neotack after 60 minutes.

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

Neotack without any supplement				Neotack 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 (%)
151.4		100.93		143.8		95.87		
147.6		98.40		145.6		97.07		
144.6	146.1	96.40	97.40	146.6	147.47	97.73	98.31	0.93
137.4		91.60		145.4		96.93		
149.0		99.33		148.8		99.20		
146.6		97.73		154.6		103.07		

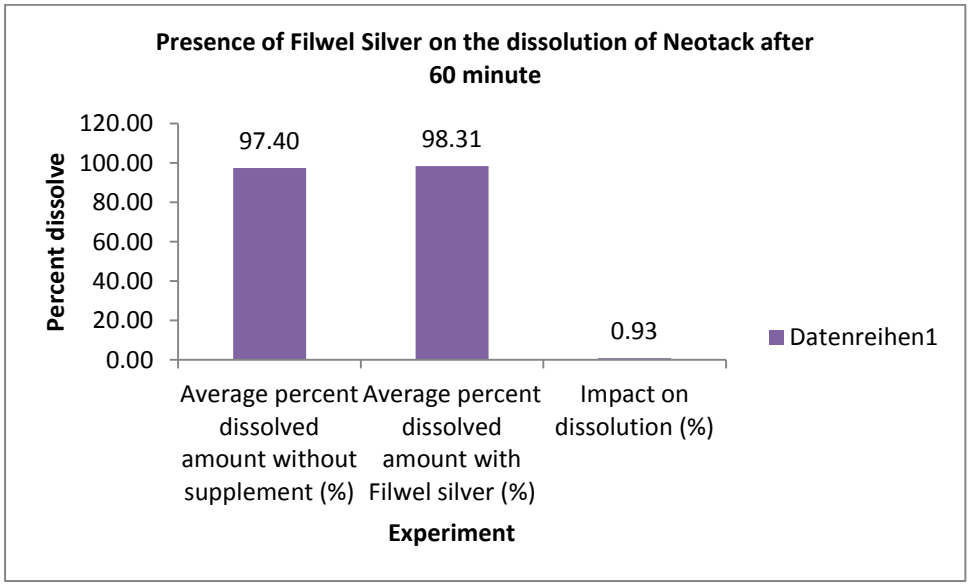

Figure4.34: Graph represents the presence of Filwel Silver on the dissolution of Zantac 60 minutes.

4.C.7 Comparison among the average percent dissolved (%) amount of individual Neotack,Neotack with Calbo,Neotack with Aristocal D,Neotack with Acical M, and Neotack with Nutrum Gold and Neotack with Filwel silver after 20, 40 and 60 minutes.

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

Average percent dissolved amount of Neotack without supplement (%)	Average percent dissolved amount of Neotack with calbo (%)	Average percent dissolved amount of Neotack with Aristocal D (%)	Average percent dissolved amount of Neotack with Acical M (%)	Average percent dissolved amount of Neotack with Nutrum Gold (%)	Average percent dissolved amount of Neotack with Filwel Silver (%)
65.47	32.38	56.42	32.93	67.16	66.2

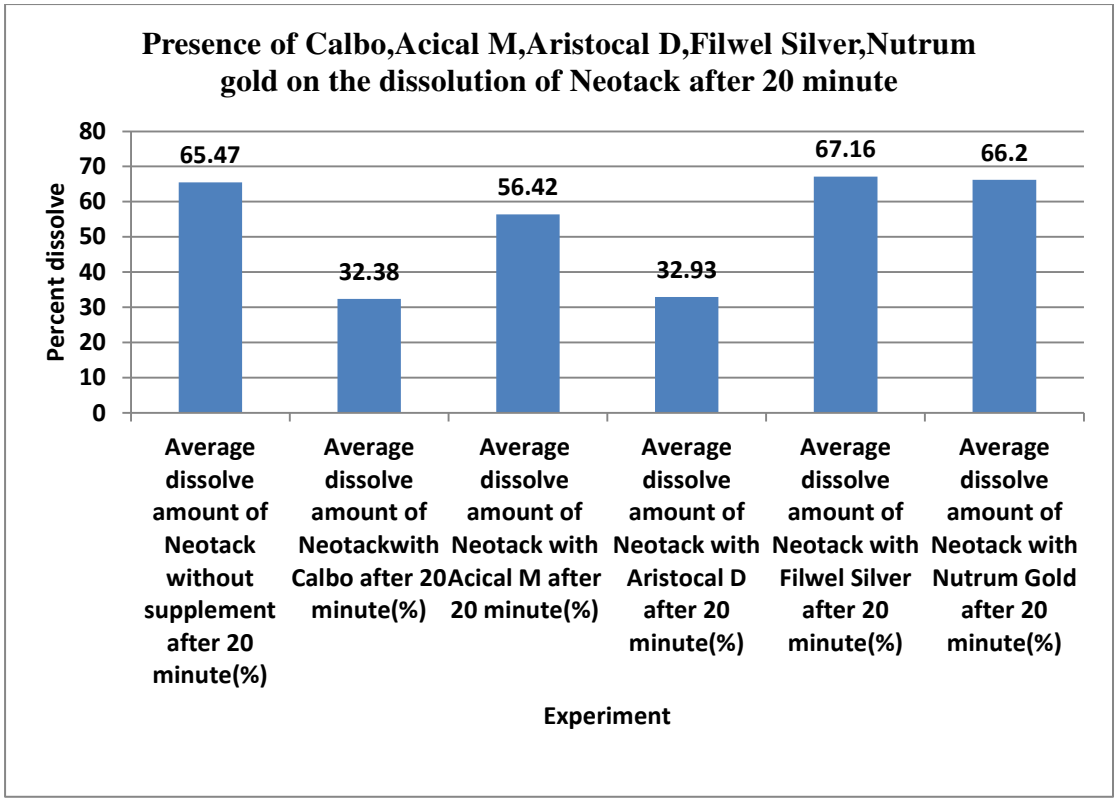

Figure 4.35: Graph represents the presence of Calbo, Aristocal D, Acical M, Nutrum Gold, and Filwel Silver on the dissolution of Neotack after 20 minute.

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

Average percent dissolved amount of Neotack without supplement (%)	Average percent dissolved amount of Neotack with calbo (%)	Average percent dissolved amount of Neotack with Aristocal D (%)	Average percent dissolved amount of Neotack with Acical M (%)	Average percent dissolved amount of Neotack with Nutrum Gold (%)	Average percent dissolved amount of Neotack with Filwel Silver (%)
86.24	42.47	65.13	42.91	87.67	86.29

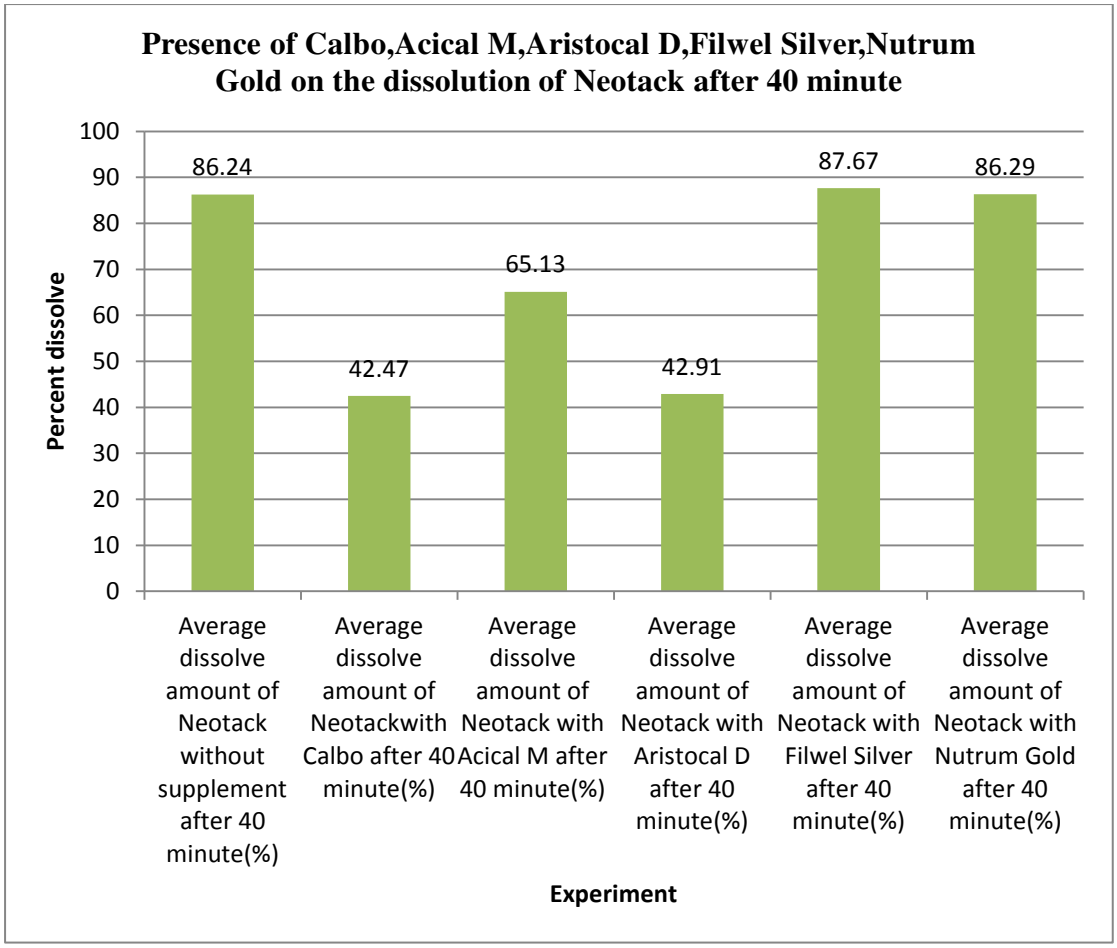

Figure 4.36: Graph represents the presence of Calbo, Aristocal D, Acical M, Nutrum Gold, and Filwel Silver on the dissolution of Neotack after 40 minute.

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

Average percent dissolved amount of Zantac without supplement (%)	Average percent dissolved amount of Zantac with calbo (%)	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 (%)
97.40	46.09	74.60	50.22	99.11	98.31

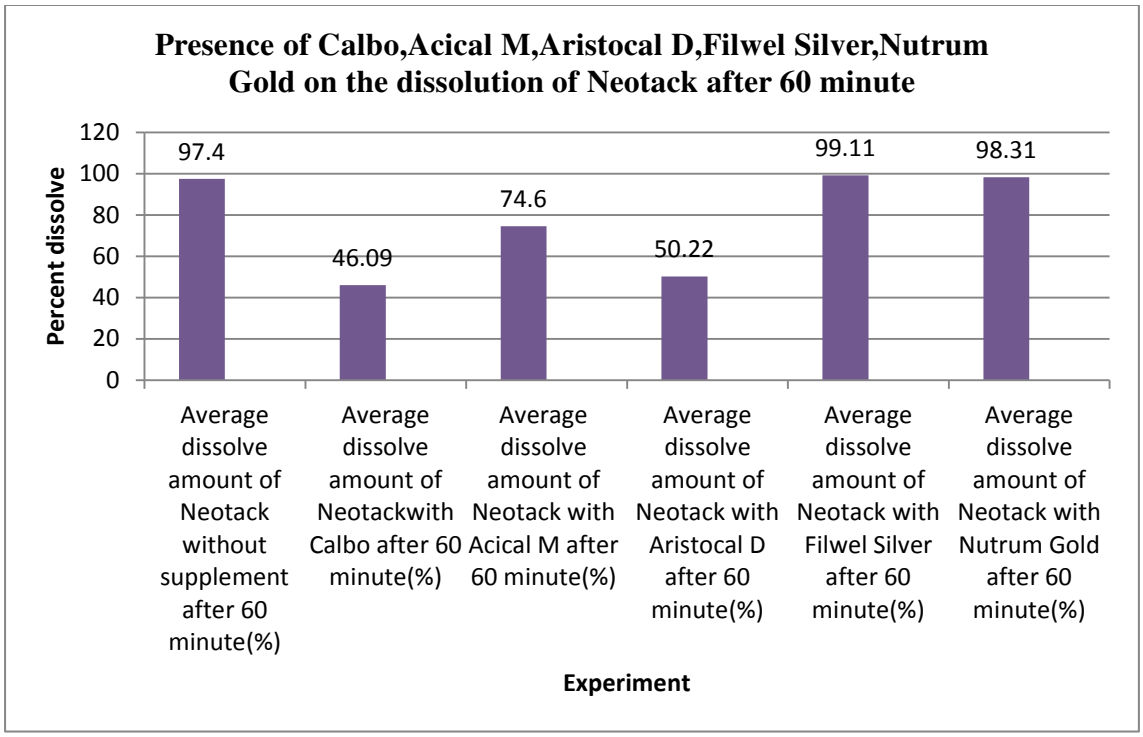

Figure 4.37: Graph represents the presence of Calbo, Aristocal D, Acical M, Nutrum Gold, and Filwel Silver on the dissolution of Neotack after 60 minute.

4.D Result from weight variation test:

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

Tablet No.	Initial weight I (mg)	Averageweight 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 Neotack tablets.

Tablet No.	Initial weight I (mg)	Averageweight A (mg)	% Weight variation (A-I)/I *100
1	0.25		1.2
2	0.25		1.2
3	0.25		1.2
4	0.25		1.2
5	0.25	0.253	1.2
6	0.27		-6.29
7	0.25		1.2
8	0.26		-2.69
9	0.25		1.2
10	0.25		1.2

4.E 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 Neotack Tablets.

Tablet No.	Main scale reading (cm), M	Vernier scale reading (cm), V	Thickness of the tablet (cm), (M+V)
1	0.4	0.09	0.49
2	0.4	0.08	0.48
3	0.4	0.08	0.48
4	0.4	0.08	0.48
5	0.4	0.08	0.48
6	0.4	0.08	0.48
7	0.4	0.08	0.48
8	0.4	0.08	0.48
9	0.4	0.08	0.48
10	0.4	0.08	0.48

4.F 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 NeotackTablets.

Tablet No.	Hardness (Kg)	Average
1	18.5	
2	18.2	18.37
3	18.4	

Chapter 5

DISCUSSION

Discussion

Variation between tablet with respect to dose and weight must be reduced to a minimum. Uniformity of weight is an in process test parameter which ensures consistency of dosage units during compression. (Pharmatreasurers.blogspot.com,2012) Weight variation of sample tablets (Zantac and Neotack) indicated the uniformity of the solid dosage forms.USP provides an accepted percentage for weight variation test and our products were within that range.

The hardness test of samples (Zantac and Neotack) were determined to evaluate its physical parameter. Hardness determination was important because the dissolution of a drug product depends on its hardness. (Pharmatreasurers.blogspot.com,2012)

The thikceness of all tablets (Zantac and Neotack) were determined by vernier calipers and all values were closed. Thickness determination was important because it relates with tablet hardness. (Pharmatreasurers.blogspot.com,2012)

The result of dissolution tests showed that the dissolution of Zantac or Neotack (Ranitidine) was largely decreased in the presence of Calbo (Calcium supplement) and Acical M (Calcium,vitamin D & mineral supplement) 47.84% and 48.47% in case of Zantac and 46.09% and 50.22% in case of Neotack. As the dissolution was affected,Zantac or Neotack will not reach to the Minimum Effective Concentration (MEC)(Merck Manuals Professional Edition, 2016), and it will fail to give the therapeutic effect. So Zantac or Neotack should not be administered with Calbo and Acical M. The dissolution of Zantac or Neotack was moderately decreased in the presence of Aristocal D 72.6% in case of Zantac and 74.6% in case of Neotack. As the dissolution was affected, this indicates the absorption can also be affected (Merck Manuals Professional Edition, 2016). So the dissolution of Zantac or Neotack will be less. So Zantac or Neotack should not be administered with Aristocal D.

The dissolution of Zantac or Neotack with Nutrum Gold and Filwel Silver (Multivitamin and multimineral) were not significantly decreased. So absorption of Zantac or Neotack will not be affected in the presence of Nutrum Gold or Filwel Silver (Multivitamin and multimineral) and therefore the dissolution of Neotack or Zantac will not be hampered. So Zantac or Neotack can be administered with Nutrum Gold.

Chapter Six

CONCLUSION

Conclusion

The study results showed extreme effects on the dissolution of Zantac and Neotack with Calbo and Acical M. Aristocal D moderately decrease the dissolution of Neotack and Zantac. Whereas Filwel Silver and Nutrum Gold has less significant impact on the dissolution profile of Neotack and Zantac. So it can be said that Zantac and Neotack should not be administer with Calbo,Acical M and Aristocal D but can be co-administer with Filwel Silver and Nutrum Gold.

Chapter seven

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