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FAMOTIDINE-EXCIPIENT COMPATIBILITY STUDIES FOR ADVANCED DRUG DELIVERY SYSTEMS DEVELOPMENT

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ABSTRACT

Various scientific and technological advancements have been made in the development of oral drug delivery systems. Orodispersible tablets dissolve rapidly and show higher bioavailability than conventional tablets. Stomach acidity symptoms are treated by many effective drugs; however, they are slow to produce the desirable effect. Therefore, to decrease the patient time in suffering of these symptoms, Orodispersible Drug-Delivery System significantly increased patient acceptance by virtue of rapid disintegration, self-administration without water and finally improved patient compliance. The main objective of the present study was to the preformulation studies were performed to know the physico-chemical and mechanical properties of Famotidine for formulation development of Famotidine ODTs. The safety, efficacy, quality and stability of a formulation are major concepts of any API development process. In API development process, a detailed characterization of the API and other formulation components is usually carried out during the preformulation stage. The drug-excipient compatibility studies were conducted to characterize the drug Famotidine present in Orodispersible Tablets Delivery System

ODTDS. Preformulation, formulation and evaluation of Famotidine to avoid problems associated with conventional delivery system such as limited permeation, low dissolution and bioavailability and also to improve bioavailability and anti-peptic ulcer. In the present study that the compatibility was assessed by, FTIR spectroscopy, and melting point apparatus, precompression parameters and powder flow properties. Results showed that physical mixtures of Famotidine and various excipients as mannitol, avicel PH 101and avicel PH 102 as diluents, and sodium starch glycolate, croscarmellose sodium, and crospovidone as superdisintegrants and sodium lauryl sulfate as wetting agent were evaluated for preformulation studies parameters. It was concluded that the drug Famotidine was found to be compatible with various excipients which were selected for the formulation development of the Famotidine ODTs. Formulation scientist from his experience and knowledge have to significantly in the preformulation study stage and is an important factor in the ADDS (Advanced Drug Delivery Systems) product development process.

KEYWORDS: Famotidine, Compatibility, Excipients, Development, Preformulation, Formulation.

INTRODUCTION

Preformulation Studies[1-150]

Preformulation is essentials of pharmaceutical science that utilizes biopharmaceutical principles in the determination of physicochemical properties of the drug substance. Prior to the development of any dosage form new drug, it is essential that certain fundamental physical and chemical properties of drug powder are determined. This information may dictate many of subsequent event and approaches in formulation development. The safety, efficacy, quality and stability of a formulation are major concepts of any API development process. In API development process, a detailed characterization of the API and other formulation components is usually carried out during the preformulation stage. Formulation scientist from his experience and knowledge have to significantly in the preformulation study stage and is an important factor in the ADDS (Advanced Drug Delivery Systems) product development process.

One of the objectives of this study is to development of drug delivery systems by building scientific pharmaceutical research information depend on formulation scientists to join the knowledge and experience as well as experimental and practical results of this study with regard to information in previous studies, and approved references. It was found to be that the

most important concepts and basics of preformulation studies such as definitions, methods, conclusion, idea, and types of pharmaceutical analysis techniques using in evaluation of preformulation studies parameters, in this study that we focused on developing drug delivery systems and linking the formulation development to establish the basics of pharmaceutical research in studying the drug-excipient compatibility, dug with various excipients, which is important for the safety, effectiveness, quality, formulation, stability, bioavailability, and pharmacokinetics of the drug etc.

Determination of physical chemical properties of API substance with the goal of developing a new drug which is safe stable and efficacious, each API, has intrinsic chemical and physical properties that were considered prior to the development of pharmaceutical formulation, the purpose of preformulation study is to generate useful information for the formulator in the development of stable and bioavailable dosage form, inappropriate preformulation study results in poor stability of active ingredients increase the overall cost of development and increased development time, preformulation studies help to fortify the pharmaceutical scientific foundation of the guidance, provide regulatory relief and conserve resources in the drug development and evaluation process, enhance public safety standards, improve product quality, promote the implementation of new technologies, aids policy development and regulatory decision making and after compiling all data it is transferred to the development pharmacist and for the day work on formulation of dosage form.

Preformulation Study Objectives: To establish the Physico-chemical parameters of a new API entity, determine its kinetics and stability, establish its compatibility with common excipients, it provides insights into how drug products should be processed and stored to ensure their quality, estimate problem may arise during formulation that is stability problem poor *in-vivo* dissolution, poor bioavailability, to interpret BCS classification of drugs and its significance and develop optimal drug delivery system.

Drug-Excipient Compatibility Study: The primary objective of this investigation was to identify a stable storage condition for API in solid state and identification of compatible excipients for its formulation. Incompatibilities are major concerns in formulation development. Selection of the proper excipient during preformulation studies is of prime importance.

Dosage Forms: DF contain API and pharmaceutical excipients, which are intended to generate an ideal formulation and manufacturability of pharmaceutical products, thereby enabling a much safer and more effective administration. Pharmaceutical excipients are ideally inactive and have no impact on the stability or therapeutic effect of the active ingredient. On the other hand, there are studies that have presented that some pharmaceutical excipients are just allegedly described as inactive ingredient. Some pharmaceutical excipients have the capacity to affect API, efficacy by affecting its pharmacokinetics. Excipients can affect the physical and chemical form of pharmaceuticals by several factors such as hydrogen bond interaction, polymorphic conversion, and others. Accordingly, drug-excipient compatibility should be conducted so as to determine any drug-excipient interactions that may obstruct the stability, bioavailability, and manufacturability of pharmaceutical dosage forms.

Importance of Drug-Excipient Compatibility

Studies of active pharmaceutical ingredient (API)-excipient compatibility represent an important study in the preformulation stage of the development of new dosage forms, stability of the dosage form can be maximized, any physical or chemical interaction between API, and excipient can affect bioavailability and stability of drug, it helps to avoid the surprise problem, by performing drug excipient compatibility studies (DECS) we can know the possible reaction before formulating final dosage form, DECS data is essential for IND (investigational new drug) submission, and now, USFDA has made it compulsory to submit DECS data for any new coming formulation before its approval.

The potential physical and chemical interactions between an API, and the excipients can affect the chemical nature, the stability and bioavailability of the former and, consequently, its therapeutic efficacy and safety, solid dosage forms are generally less stable than their API components and despite the importance of API-excipient compatibility testing, there is no universally accepted protocol to assess such interactions.

Pharmaceutical Excipients: Excipients are additive substances used to improve the bulkiness, disintegration, dissolution rate, and bioavailability of a formulation etc. Different dosage forms like powders, granules, capsules, tablets, oral liquids, injectable products, implants, eye products, nasal products, inhalers, topical creams, ointments, gels, transdermal patches and suppositories etc, contains different types of excipients. To make it acceptable and compatible various pharmaceutical excipients are added in pharmaceutical dosage form for

their direct therapeutic action, manufacturing process, to protect, support or enhance stability, for bioavailability or patient compliance. These must be physiologically and chemically stable, must not have any incompatibility with the API, and must meet the standards of regulatory requirements.

Evaluation of Drug-Excipient Compatibility

The compatibility study of API and excipients is important to predict the stability of the API, in the final pharmaceutical product. It's the first time that API was compatible with excipients promoted physical and chemical compatibility studies was achieved by thermal and non-thermal methods. As a part of preformulation study, a compatibility study of API with the other excipients was carried out using physical blends in analytical techniques for the evaluation of drug-excipient interactions. The most commonly used pharmaceutical analytical techniques include, thermal techniques such as Differential Scanning Calorimetry (DSC), Thermogravimetric Analysis (TGA), Isothermal Microcalorimetry (IMC) and Hot stage microscopy (HSM) etc, and non-thermal techniques such as UV-Visible Spectrophotometric (UV), Infrared, Near-Infrared and Raman Spectroscopy (FT-IR), (NIR), Powder *X*-Ray Diffraction (PXRD), Solid-State Nuclear Magnetic Resonance Spectroscopy (ssNMR), Microscopic techniques: Scanning Electron Microscopy (SEM), Chromatographic techniques: Thin Layer Chromatography (TLC), and High-Performance Liquid Chromatography (HPLC) etc.

Preformulation Parameters: According to dosage form of API, mainly solid state, particle size, shape, pKa, pH determination, common ion effect, temperature, partition coefficient, solubility studies, dissolution rate, melting point, powder flow properties, crystallinity, polymorphism, hygroscopicity, stability study and drug-excipient compatibility etc. While other dosage forms according to important of preformulation parameters used in study before start in development of formulation.

Drug-excipient compatibility and formulation stability is not depended on API only but also its affected by excipient. Excipient play important role in dosage form but side by side it also increases compatibility problem so proper selection of excipient is very important in development of formulation. Incompatibility can be result mainly in any of following changes: Changes in organoleptic properties, changes in dissolution performance, decrease in potency, and increase in degradation rate etc.

Drug excipient physicochemical characterization is a systematic approach towards design of therapeutically active and stable dosage forms. The rapid advancements in novel drug delivery systems development have led to an interest by formulation scientists in the role and functionality of the excipients.

In the present study, it was proposed to Famotidine -excipient compatibility studies of the safety, efficacy, quality and stability of a formulation are major concepts of any API development process. In API development process, a detailed characterization of the API and other formulation components is usually carried out during the preformulation stage., with commonly different excipients using for formulation development of Orodispersible tablets ODTs.

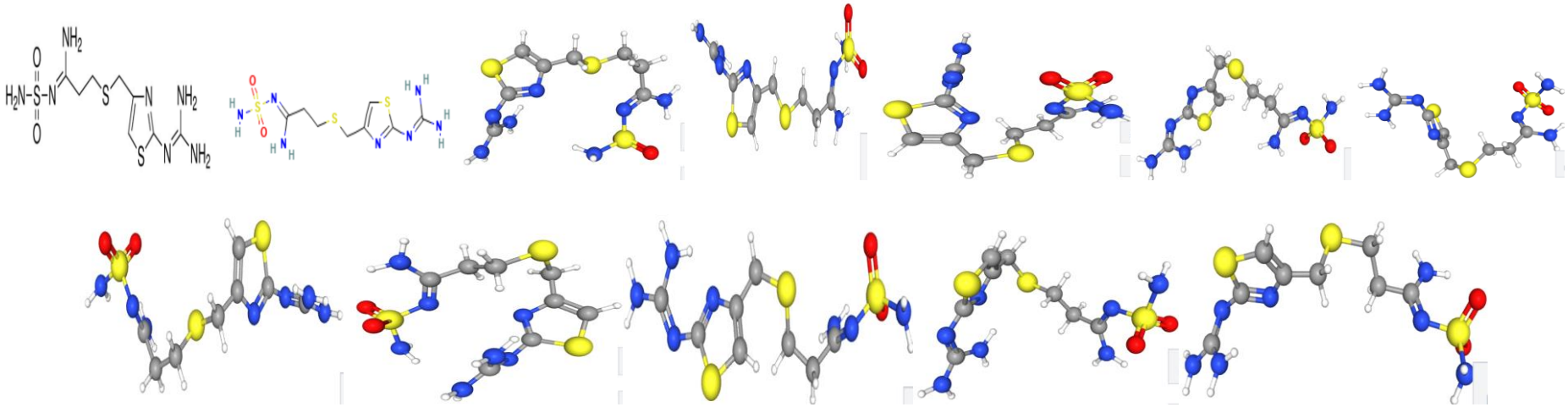
MATERIALS AND METHODS

Famotidine, Talc, Mannitol, Avicel PH 101, Avicel PH 102, Croscarmellose Sodium, Crospovidone, Sodium Starch Glycolate, Aspartame, Sucralose, Magnesium Stearate, Sodium Lauryl Sulfate, Lycatab, Saccharin Sodium, Aerosil, PVP K30, Roseberry Flavor, Methanol, Ethanol, Buffer Solutions, and other materials were obtained as a gift from (Shaphaco Pharmaceutical Industry Company-Yemen).

Evaluation of Drug-Excipient Compatibility Studies Methods[60-324]

Table 1: Famotidine Data.

Characterization of Famotidine



Famotidine Structure and 3D Conformer

Chemical Structure	3-[[2-(diaminomethylideneamino)-1,3-thiazol-4-yl] methylsulfanyl]-N'-sulfamoylpropanimidamide	**Appearance**	Is white to pale yellowish-white, crystalline powder.
Chemical Formula	C8H15N7O2S3	**Drug Solubility**	Is freely soluble in dimethylformamide and glacial acetic acid; slightly soluble in methanol; very slightly soluble in water; practically insoluble in acetone, in alcohol, in chloroform, in ether, and in ethyl acetate.
Molecular Weight	337.5 g/mol.	**BCS**	Class-III Drug
Drug Action and Use	Famotidine is a histamine type 2 receptor antagonist (H2 blocker) which is commonly used for treatment of acid-peptic disease and heartburn. Famotidine is used to prevent and treat heartburn due to acid indigestion and sour stomach caused by eating or drinking certain foods or drinks. Famotidine is in a class of medications called H2 blockers. It works by decreasing		

	the amount of acid made in the stomach.		
Famotidine Pharmacokinetics			
Drug Absorption	Following oral administration, the absorption of famotidine is dose-dependent and incomplete. The oral bioavailability ranges from 40-50%, and the C max is reached in 1-4 hours post-dosing. While the bioavailability can be slightly increased with the intake of food and decreased by antacids, there is no clinical significance.	**Drug Distribution**	Volume of distribution The steady-state volume of distribution ranges from 1.0 to 1.3 L/kg. Famotidine is found in breast milk; however, it is found in breast milk at the lowest concentrations compared to other H2 receptor antagonists. Protein binding The protein binding of famotidine is about 15 to 22%.
Drug Metabolism	Famotidine undergoes minimal first-pass metabolism. About 25-30% of the drug is eliminated through hepatic metabolism. The only metabolite identified in humans is the S-oxide. Famotidine does not interact with the cytochrome P450 drug metabolizing enzyme system.	**Drug Excretion**	Route of elimination About 65-70% of the total administered dose of famotidine undergoes renal elimination, and 30-35% of the dose is cleared by metabolism. Following intravenous administration, about 70% of the drug is eliminated in the urine as an unchanged drug. Clearance Renal clearance is 250-450 mL/min, indicating some tubular excretion. Because the renal clearance rate exceeds the glomerular filtration rate, famotidine is thought to be mainly eliminated via both glomerular filtration and renal tubular secretion
The Elimination Half-Life (T1/2)	The elimination half-life is about 2 to 4 hours. The half-life is expected to increase nonlinearly in patients with decreased renal function.	**Availability**	Tablet 10, 20, 40 mg. - Chewable tablets 10, 20 mg. - Oral suspension 40mg/5mL - Injection solution 10mg/ml , 0.4mg/ml.

Table 2: Pharmaceutical Excipients Data.

Nonproprietary Name	Chemical Name	Functional Category	Concentration%	Solubility	Incompatibilities	Notes
Croscarmellose Sodium (Ac-Di-Sol)	Cellulose, carboxymethyl ether, sodium salt, crosslinked	Tablet and capsule disintegrant.	0.5-5% 10-25%	Insoluble in water	Incompatible with strong acids or with soluble salts of iron and some other metals such as aluminum, mercury, and zinc.	White or grayish-white powder
Sodium Starch Glycolate (Explotab)	Sodium carboxymethyl starch	Tablet and capsule disintegrant.	2–8%	Gives a translucent suspension in water	Incompatible with ascorbic acid.	Very hygroscopic
Microcrystalline Cellulose (Avicel)	Cellulose	Adsorbent, suspending agent, tablet and capsule diluent; tablet disintegrant.	5–20% 20–90%	Practically insoluble in water	Incompatible with strong oxidizing agents.	Crystalline powder
Crospovidone (PVPP)	1-Ethenyl-2-pyrrolidinone homopolymer	Tablet disintegrant.	2–5%	Practically insoluble in water	Compatible with most organic and inorganic pharmaceutical ingredients.	Hygroscopic powder
Mannitol (Emprove)	Mannitol	Diluent, plasticizer, sweetening agent, tablet and capsule diluent, therapeutic agent, tonicity agent.	10–90%	Freely soluble in water	Incompatible with may be salted out by potassium chloride or sodium chloride. Sodium cephapirin. xylitol infusion and may form complexes with some metals	Crystalline powder

					such as aluminum, copper, and iron.	
Magnesium Stearate (magnesium salt)	Octadecanoic acid magnesium salt	Tablet and capsule lubricant.	0.25 - 5.0%	Practically insoluble in water	Incompatible with strong acids, alkalis, and iron salts.	Greasy
Sucralose (SucraPlus)	,6-Dichloro-1,6-dideoxy-b-D-fructofuranosyl-4-chloro-4-deoxya-D-galactopyranoside	Sweetening agent.	0.03–0.24%	Freely soluble in water	---	Crystalline powder
Talc	Altalc, E553b, hydrous magnesium calcium silicate, hydrous magnesium silicate, Luzenac Pharma, magnesium hydrogen metasilicate. $Mg_6(Si_2O_5)_4(OH)_4$.	Anticaking agent, glidant, diluent, lubricant.	1.0–10.0% 5.0–30.0%	Practically insoluble in dilute acids and alkalis, organic solvents, and water.	Incompatible with quaternary ammonium compounds.	is a very fine, white to grayish-white, crystalline powder.
Aerosil	Aerosil; Cab-O-Sil, Cab-OSil M-5P, colloidal silica, fumed silica, fumed silicon dioxide, SAS, silica colloidalis anhydrica	Adsorbent; anticaking agent glidant; viscosity-increasing agent	0.1–1.0% 2.0–10.0% widely used in oral and topical pharmaceutical products and is generally regarded as an essentially nontoxic and nonirritant excipient.	Practically insoluble in organic solvents, water. -hygroscopic but adsorbs large quantities of water without liquefying. When used in aqueous systems at a pH 0–7.5, colloidal silicon dioxide is effective in increasing the viscosity of a system.	Incompatible with diethylstilbestrol preparations.	A submicroscopic fumed silica with a particle size of about 15 nm. It is a light, loose, bluish-white-colored, odorless, tasteless, amorphous powder.
Saccharin	1,2-Benzisothiazolin-3-	Sweetening agent.	0.02–0.5% w/w.	Readily dissolved by	Saccharin can react	White crystals or a

Sodium	one 1,1-dioxide, sodium salt, Crystallose, E954, gendorf 450, sucaryl sodium	Saccharin can be used to mask some unpleasant taste characteristics or to enhance flavor systems. Its sweetening power is approximately 300–600 times that of sucrose.		dilute ammonia solutions, alkali hydroxide solutions, or alkali carbonate solutions. 1 in 290 water.	with large molecules. Saccharin sodium does not undergo Maillard browning.	white crystalline powder.
PVP K30	E1201, Kollidon, Plasdone, polyvidone, polyvinylpyrrolidone, PVP;1vinyl-2-pyrrolidinone polymer.	Disintegrant, tablet binder.	2.0–5.0	Greater than 10% solubility in water, methanol, PG.	Compatible in solution with a wide range of inorganic salts, natural and synthetic resins, and other chemicals.	White to yellowish-white amorphous powder.
Sodium Lauryl Sulfate	Dodecyl alcohol hydrogen sulfate, sodium salt, dodecyl sodium sulfate, dodecyl sulfate sodium salt, Elfan 240. C12H25NaO4S	Anionic surfactant; detergent; emulsifying agent; skin penetrant; tablet and capsule lubricant; wetting agent.	10% 0.5–2.5% 1.0–2.0%	Freely soluble in water, giving an opalescent solution; practically insoluble in chloroform and ether.	Incompatible with salts of polyvalent metal ions, such as aluminum, lead, tin or zinc	White or cream to pale yellow colored crystals, flakes, or powder having a smooth feel, a soapy, bitter taste, and a faint odor of fatty substances

According to Famotidine and excipients data as shown in Tables 1 and 2, it was selected that the different excipients to preformulation study with Famotidine in the present study, the equipments used as shown in Table 3.

Table 3: The Equipment's Used.

No	Equipment's
1	Fourier Transform Infrared Spectrophotometer
2	UV/VIS Spectrophotometer
3	Melting Point Tester
4	Moisture Tester
5	Density Tester
6	pH Meter
7	Ultra-sonic
8	Accelerate Stability Study Chamber
9	Electronic Balance

Determination of The Organoleptic Properties

The organoleptic properties like color, odor and taste of the API was evaluated. Color a small quantity of Famotidine was taken in a butter paper and viewed in well illuminated place. Taste and odor very less quantity of Famotidine was used to assess the taste with the help of tongue as well as smelled to get odor. The organoleptic properties of the API substance were assessed.

Solubility Analysis

Solubility is an important physicochemical factor affecting absorption of drug and its therapeutic effectiveness. Consequences of poor aqueous solubility would lead to failure in formulation development. The poor solubility of drug substances in distilled water and their low dissolution rate in aqueous G.I.T fluid often leads to insufficient bioavailability. The bioavailability of drug is affected by various excipients in formulation. The approximate solubility of a compendial substance is indicated by one of the following descriptive terms. Solubility of Famotidine in distilled water, methanol and ethanol was determined by using Sonicator at room temperature. Approximate solubility of drugs as per B.P was indicated in Table 4.

Table 4: Solubility Specification of Drugs.

Solubility	Approximate Volume of Solvent in ml per gm of Solute
Excellent	Less than 1
Very soluble	1 to 10
Freely soluble	10 to 30
Soluble	30 to 100
Sparingly soluble	30 to 100

Slightly soluble	1000 to 10000
Very slightly soluble	1000 to 10000
Practically insoluble/ Insoluble	More than 10000

UV-Visible Spectrophotometric Method

Determination of λ Max for Famotidine

The standard solution of Famotidine was scanned in the range of 200-400 nm and the λ max was determined.

The absorption spectra of Famotidine in phosphate buffer (PH 6.8), 0.2M HCl and distilled water were studied. A preliminary scanning of Famotidine in phosphate buffer to determine the ʎ max by screening a 100µg/ml solution of Famotidine in phosphate buffer, 0.2M HCl screening 100 µg/ml and distilled water screening 100 µg/ml these between 200- 400 nm.

Preparation of Calibration curve Solutions

Preparation of Phosphate buffer (pH 6.8): 0.896 g of NaOH and 6.804 g of KH2PO4 dissolved in sufficient quantity of water, complete volume to 1000 ml with distilled water and mixed well by sonication.

Calibration curve: 50 mg of Famotidine was weighed accurately and dissolved in 100 ml of phosphate buffer (PH 6.8) in a 100 ml of volumetric flask to obtain a stock solution. 10 ml of this solution was diluted with 50 ml phosphate buffer (pH 6.8) to obtain a diluted solution of 50 mg from this stock solution, aliquots of 2 ml ,4 ml, 10 ml, 15 ml and 20 ml were taken and transferred to 50 ml volumetric flask and volume was made up to 50 ml with phosphate buffer (PH 6.8). The absorbance of these solutions was measured at 272 nm against a blank of phosphate buffer. The calibration curve was plotted between concentration and absorbance.

Calibration Curve of Famotidine

The standard calibration curve graph was obtained by preparing aliquots of standard solution of Famotidine in phosphate buffer (pH 6.8) and the absorbance at 272 nm was measured after suitable dilution using UV/Visible spectrophotometer.

appropriate aliquots were pipette out from standard stock solution into the series of volumetric flask and the volume was made up to the mark with concentration range 2-20µg/ml of Famotidine. Solutions of different concentrations were analyzed 272 nm against

blank solution and absorbance were recorded. The calibration curve was plotted between concentration and absorbance.

Preformulation Studies

Preformulation studies are initiated to define the physical and chemical properties of the agent. The key goals of preformulation studies are to ensure the delivery of drug product with acceptable stability, bioavailability, and manufacturability.

Melting Point Determination of Famotidine

Melting point of the Famotidine was determined by capillary method; one sided closed capillary filled with drug and put into the Melting Point Apparatus. Temperature was noted at which solid drug changed into liquid.

Drug-Excipient Compatibility Studies

A physical mixture including Famotidine and excipient was created in a 1:1 ratio, and it was subjected to analytical techniques such as FTIR spectroscopy. FTIR, of both pure drug and physical mixes were obtained, and the spectra of the both drug and mixture of excipient with drug were compared to look for any incompatibilities.

FTIR Spectroscopy Study

FTIR study KBr-disc method was used to record the FTIR spectra and KBr pellets were made in 1:100 ratio of sample and KBr. FTIR spectra was recorded using FTIR spectrum in a range of 4000-400cm^{-1}. Different functional groups of test compound for distinctive vibrational frequencies are identified using FTIR spectroscopy. FTIR spectra were used for the investigation of interaction in the physical mixture of API and excipient through shifting of peaks to lower or higher wavenumbers and appearance or disappearance of characteristic peaks of functional groups for pure API in physical mixture. FTIR spectroscopic study was performed to check the compatibility between API, and different excipients in amount (5mg:5mg) as ratio (1:1) as shown in Table 5. The FTIR spectra of a API alone and API with excipients were obtained by KBr method and compared with the standard FTIR spectrum of the pure API. Infrared spectrophotometer is not only used for determining the compatibility of excipients with the APIs, but also for API identification.

Preparation of IR Samples

The sample was determined by the disc method. Triturate 5mg of the substance to be examined with 300-400 mg of finely powdered and dried potassium bromide R or potassium chloride R. Each excipient was mix with Famotidine equally then of potassium bromide is added to the mixture. Carefully grind the mixture, spread it uniformly in a suitable die, and submit it to a pressure of about 800 MPa (8 $t \cdot cm^{-2}$). Then the tablets were inserted to the device and the Infrared spectra was recorded at mild-infrared light in wavenumber range of 4000 cm^{-1} to 400 cm^{-1}. After that the spectra were compared with the reference.

Infrared Spectral Study of Samples in Room Condition

Compatibility studies were performed by preparing blend of different excipients with Famotidine in room condition as shown in table 5.

Infrared Spectral Study of Samples after Stored Two Months

Compatibility studies were performed by preparing blend of different excipients with drug and stored at 40°C ±2°C /75±5%RH for two months. The blend was evaluated after one month for changes like caking, liquefaction, discoloration and odor formation and by IR spectra. The drug excipient compatibility studies as shown in Table 5.

Table 5: Samples of Famotidine and Different Excipients for Compatibility Studies.

No	Component(s)	Amount(5mg:5mg)
1	Famotidine	1
2	Famotidine and Avicel PH 101	(1:1)
3	Famotidine and SSG	(1:1)
4	Famotidine and Avicel PH 102	(1:1)
5	Famotidine and SLS	(1:1)
6	Famotidine and Crospovidone	(1:1)
7	Famotidine and Talc	(1:1)
8	Famotidine and Roseberry Flavor	(1:1)
9	Famotidine and Saccharin Sodium	(1:1)
10	Famotidine and Sucralose	(1:1)
11	Famotidine and CCS	(1:1)
12	Famotidine and Mannitol	(1:1)
13	Famotidine and Mg. Stearate	(1:1)
14	Famotidine and PVP K30	(1:1)
15	Famotidine and Aerosil	(1:1)
16	Famotidine and Lycatab	(1:1)

Preparation of Famotidine Formulations

Formulations (F1-F4) each tablet containing 20 mg Famotidine were prepared by wet granulation method using the ingredients given in Table 6. Four formulations were prepared using pure drug Famotidine and three superdisintergrants namely croscarmellose sodium, crospovidone and sodium starch glycolate. The powder blend was mixed with mixture of Lycatab (F1, F3 and F4) or Povidone K30 (F2) and distilled water to obtain a coherent mass. The coherent mass was passed through a 16 mesh to form granules. The wet granules were dried at 600C for 1 hour in a hot air oven. After drying, the granules were passed through 22 mesh and the granules were evaluated for mass-volume relationship. Then the granules were mixed with magnesium stearate. Then the lubricated granules were compressed into tablets weighing 200mg using rotary tablet compression machine of punch size 8mm to produce convex faced tablets with a hardness of 3-4 kg/cm^2. The compressed tablets were evaluated for various tablet properties. Compatibility studies were carried out between Famotidine and commonly used tablet excipients in the performulation stage.

Formulations (F5- F12) each tablet containing 20mg Famotidine were prepared by direct compression method using different ingredients. Various batches of tablet formulations prepared are shown in Table 6. Optimum combination was worked out based on powder blend properties and disintegration time of the tablets.

Table 6: Ingredients Used in The Preparation of Famotidine Formulations ODTs.

Ingredients	Quantity Per Tablet (mg)											
	Formulation Code											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Famotidine	20	20	20	20	20	20	20	20	20	20	20	20
Sodium Starch Glycolate	16	10	16	16	12	12	12	12	12	12	----	12
Croscarmellose Sodium	10	----	10	----	----	----	----	---	----	7.5	7.5	----
Avicel PH 101	105.6	47	86	88	----	----	---	----	----	----	----	----
Avicel PH 102	----	----	----	----	88	----	90.5	59	57	51.5	56	54.5
Mannitol	29	99	45	45	----	88.5	----	30	35	40	40	40
Crospovidone	----	8	----	10	6	6	6	7.5	6	----	7.5	6
Aerosil	2	2	2	2	1	1	1	1	1.5	1	1	1
Talc	2	----	1	1	1.5	1	1	1	1.5	----	1.5	1.5
Povidone K 30	----	4	----	----	----	----	----	----	----	----	----	6
Sodium Saccharin	1.4	----	----	----	----	----	----	----	----	----	----	----
Sucralose	----	2	2	2	5	5	5	1.5	2	3	3	3
Raspberry	2	2	2	2	3	3	3	1.5	1.5	1.5	1.5	1.5
Sodium Lauryl Sulfate	----	4	4	2	2	2	----	----	2	2	2	3
Mg Stearate	2	2	2	2	1.5	1.5	1.5	1.5	1.5	1.5	----	1.5
Lycatab	10	-----	10	10	10	10	10	15	10	10	10	----

Evaluation of Pre-Compression Parameters of Formulations

Bulk Density

Bulk density (ρb) was determined by placing pre sieved drug excipients mixture into a graduated cylinder and measuring the volume (Vb) and weight (M).

ρb = M/Vb.

Tapped Density

The measuring cylinder containing a known quantity of blend was tapped for a fixed number of taps. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the drug excipients mixture was measured. The tapped density (ρt) was calculated using the following formula. ρt = M/Vt.

Angle of Repose

Angle of repose (**θ**) was determined using funnel method. The drug excipients mixture was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of the pile (r) was measured and the angle of repose was calculated. **θ** = tan -1 (h/r). As shown in Table 6.

Carr's Index

Carr's Index or % compressibility is helpful to determine flow properties of powder mixtures, which is calculated as follows:

C = (ρt–ρb)/ρt X 100 Where, ρt - Tapped density, ρb -Untapped bulk density.

Hausner's Ratio

Hausner's ratio is an index of ease of powder flow; it is calculated by the following formula.

Hausner's ratio = ρt\ ρb Where, ρt - Tapped density ρb - Bulk density. As shown in Tables 7 and 8.

Table 7: Powder Flow Properties.

Description of Flow	Angle of Repose (θ)
Excellent	≤25
Very Good	25 – 30
Good	31 – 35
Fair	36 – 40
Passable (but flow aid might be needed)	41 – 45
Poor (agitation or vibration needed)	46 – 55
Very Poor	>56

Table 8: Powder Flow Properties.

Description of Flow	Carr's Index (%)	Hausner Ratio
Excellent	≤10	1.00 – 1.11
Good	11 – 15	1.12 – 1.18
Fair	16 – 20	1.19 – 1.25
Passable	21 – 25	1.26 – 1.34
Poor	26 – 31	1.35 – 1.45
Very Poor	32 – 39	1.46 – 1.59
Very, Very Poor	>40	>1.60

RESULTS AND DISCUSSION

Preformulation Studies

Characterization of Famotidine

The organoleptic properties like color, odor and taste of the API were evaluated. The color of Famotidine was found to be White to pale yellowish white, crystalline powder, no characteristic odor was observed in the study and the taste was found to be bitter. Famotidine showed similar color, taste and odor as per IP specification.

Physical Identification of Famotidine

Famotidine is white to pale yellowish white, crystalline powder.

Solubility Analysis

Solubility profile of Famotidine indicated that the drug is freely soluble in dimethylformamide and glacial acetic acid; slightly soluble in methanol, very slightly soluble in distilled water, practically insoluble in acetone, alcohol, chloroform, ether, and ethyl acetate which confirm with the USP.

Characterization of Famotidine by UV Spectroscopy

Wave length of Famotidine in Phosphate buffer (PH 6.8) by UV Scanning show in Figure 1, at 272 nm, in 0.1M HCl show in Figure 2, at 268 nm and in distilled water show in Figure 3, at 284 nm.

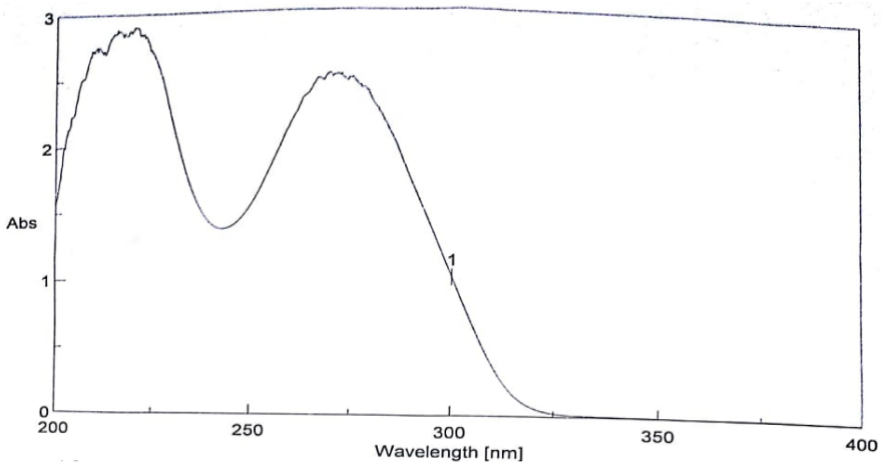


Fig. 1: UV Scanning of Famotidine in Phosphate Buffer (pH 6.8).

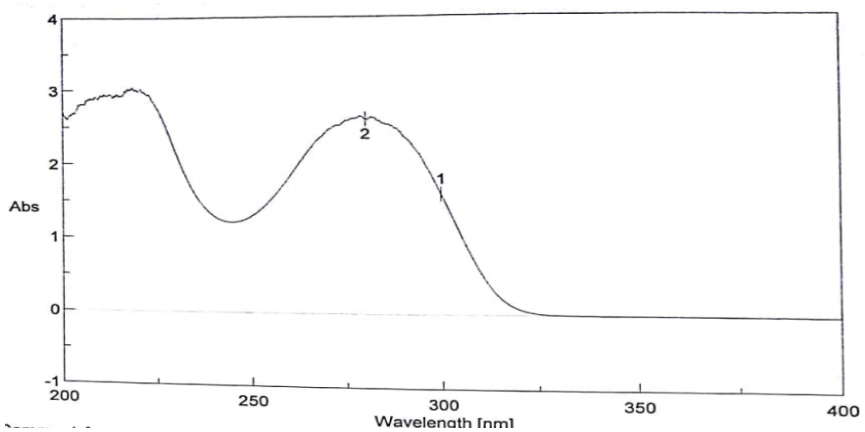


Fig. 2: UV Scanning of Famotidine in 0.1N HCL.

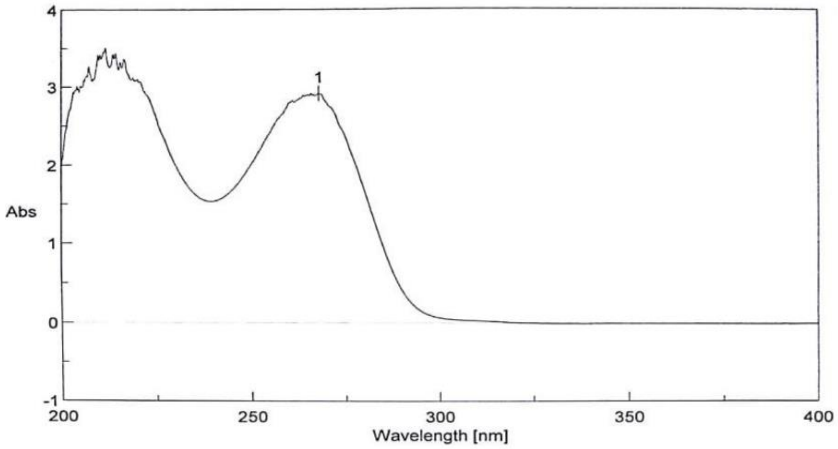


Fig. 3: UV Scanning of Famotidine in Distilled Water.

Calibration Curve of Famotidine

The calibration curve of Famotidine was prepared in phosphate buffer (pH 6.8). The plot of different concentrations of Famotidine versus absorbance was found linear at 272 nm. The

absorbance at different concentrations is shown in Table 9. The data of standard curve was linearly regressed. The slope and correlation coefficient values were found 0.0291 and 0.9987 respectively. The intercept on Y-axis was found 0.0052. The calibration curve is shown in Figure 4.

Table 9: Calibration Curve of Famotidine in Phosphate Buffer (pH 6.8).

No	Concentration µg/ml	Absorbance
1	0	0
2	2	0.0591
3	4	0.1067
4	10	0.2716
5	15	0.4294
6	20	0.5845

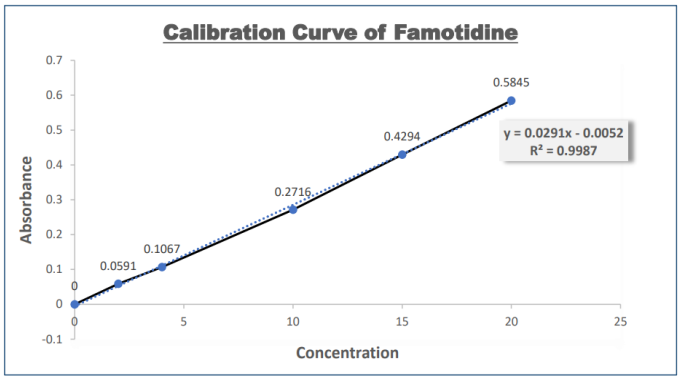


Fig. 4: Standard Calibration Curve of Famotidine in Phosphate Buffer (pH 6.8).

Melting Point Determination of Famotidine

Melting point of pure Famotidine was determined by open capillary method and was identical to 162°C and reference melting point stated in USP (163 – 164°C) The sample started to turned into liquid at 163°C indicating that the sample used was pure as shown in Table 10.

Table 10: Results of Melting Point of Famotidine.

Test	Temp Rang Analyzed (Melting)	Results
Test I Famotidine	(163-164 °C)	163 °C
Test II Famotidine	(163-164 °C)	163 °C

Characterization of Famotidine by FTIR

FTIR spectrum studies indicated that major functional groups present in Famotidine show characteristic peaks in IR spectrum. Figures (5) to (22) show peaks observed at different wave numbers and the functional group associated with these peaks for drug and drug with different excipients show in Tables (11) to (27). The major peaks are identical to functional

group of Famotidine. Hence, it was confirmed that there was compatibility between drug and various excipients, thus conforming that no interaction of drug occurred with the components of the formulation excipients.

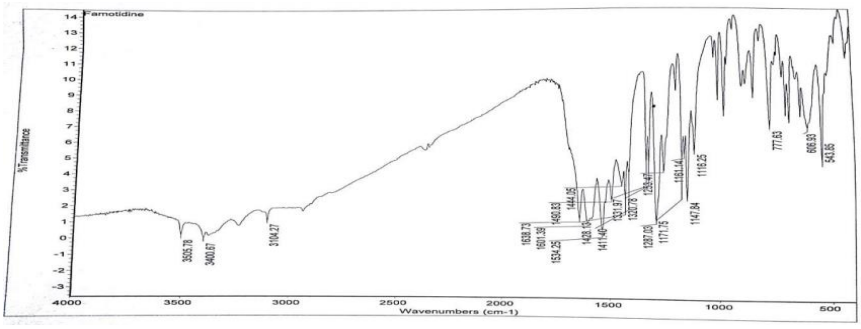


Fig. 5: FTIR Spectrum of Pure Famotidine.

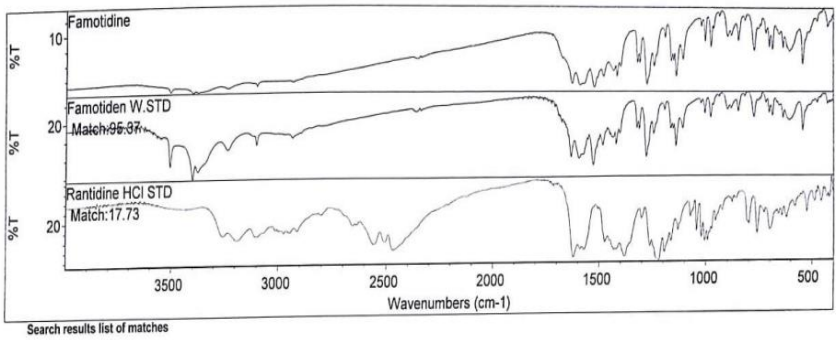


Fig. 6: FTIR Spectrum of Pure Famotidine with STD.

Table 11: Results of IR Spectra Studies.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample ST	3200.67	1638.73	2937.10	777.63

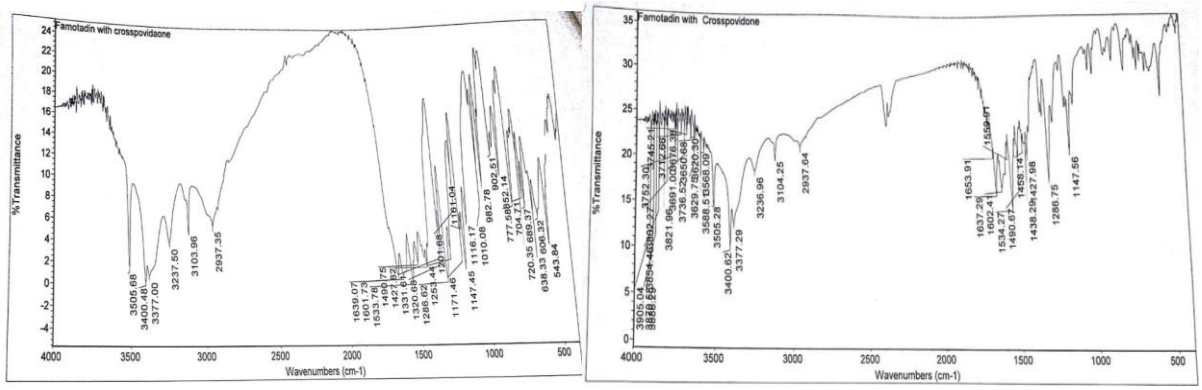


Fig. 7: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Crospovidone.

Table 12: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Crospovidone.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	**3200 – 3300**	**1620 - 1660**	**2900 - 3000**	**1630-1680**
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Crospovidone	3237.50	1639.07	2937.35	777.55
After Stored	3236.96	1637.29	2937.64	777.58

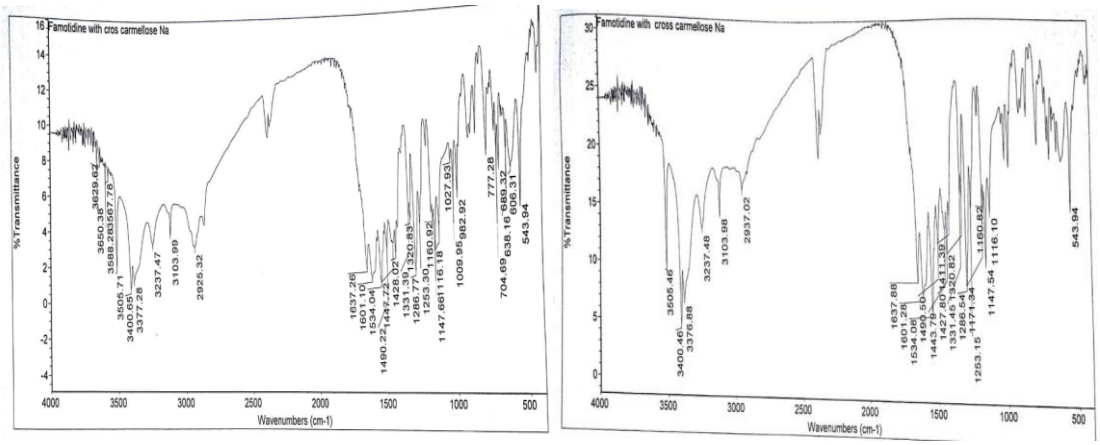


Fig. 8: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and CCS.

Table 13: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and CCS.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	**3200 – 3300**	**1620 - 1660**	**2900 - 3000**	**1630-1680**
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with CCS	3237.47	1637.26	2925.32	777.20
After Stored	3237.48	1637.88	2937.02	777.28

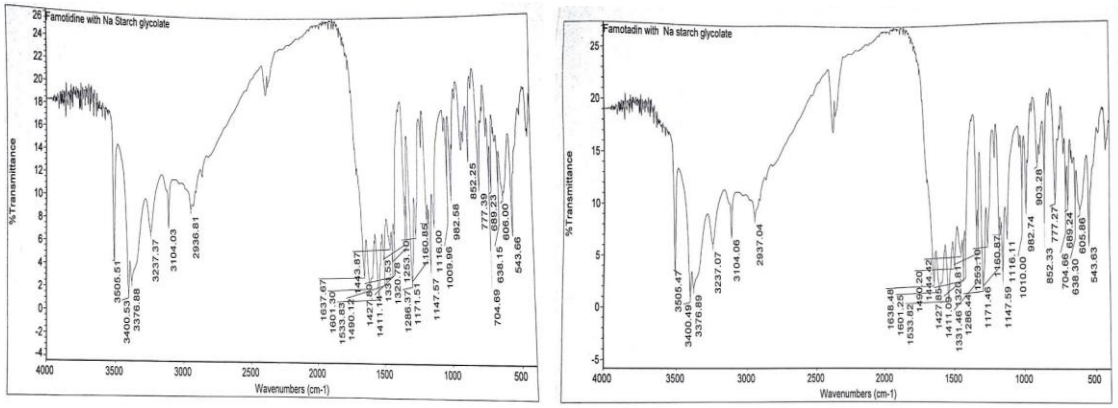


Fig. 9: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and SSG.

Table 14: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and SSG.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with SSG	3237.37	1637.67	2936.81	777.39
After Stored	3237.07	1638.48	2937.04	777.27

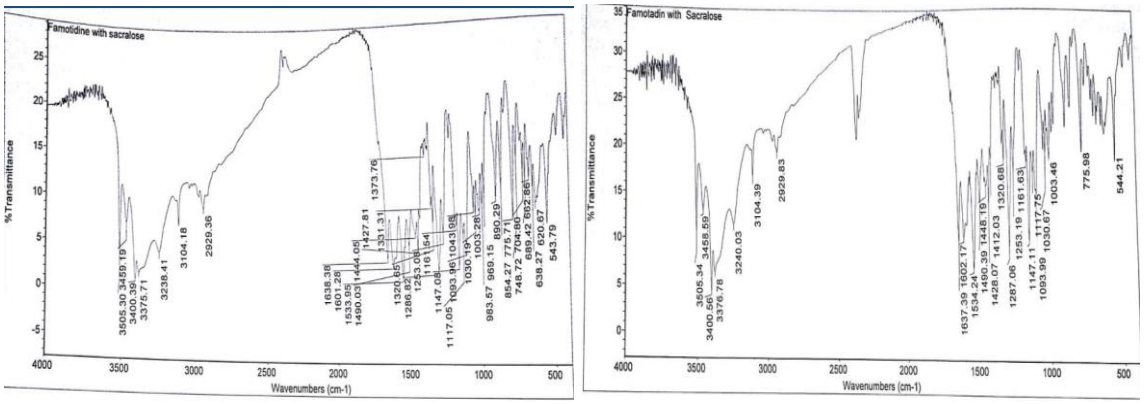


Fig. 10: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Sucralose.

Table 15: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Sucralose.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Sucralose	3238.41	1638.38	2929.36	775.71
After Stored	3240.03	1637.39	2929.83	775.98

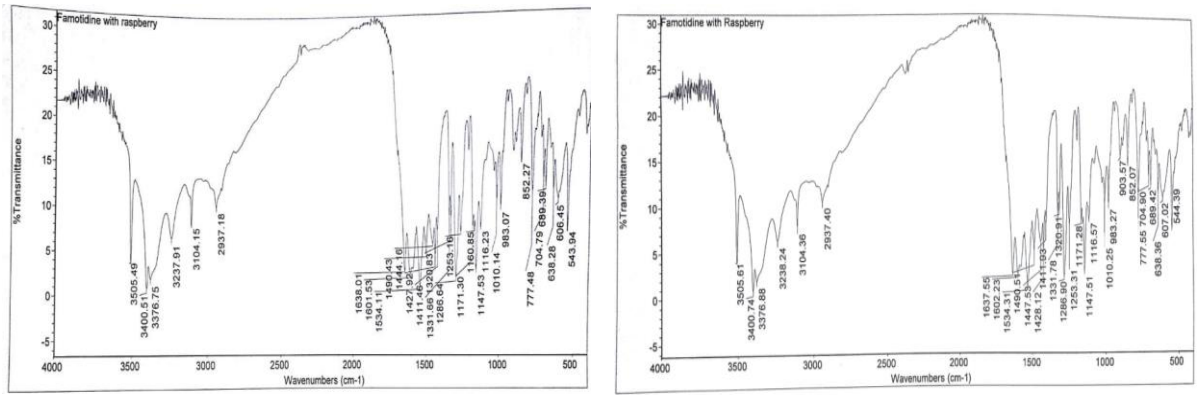


Fig. 11: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Raspberry.

Table 16: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Raspberry.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 – 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Raspberry	3237.91	1638.01	2937.18	777.48
After Stored	3238.24	1637.55	2937.40	777.55

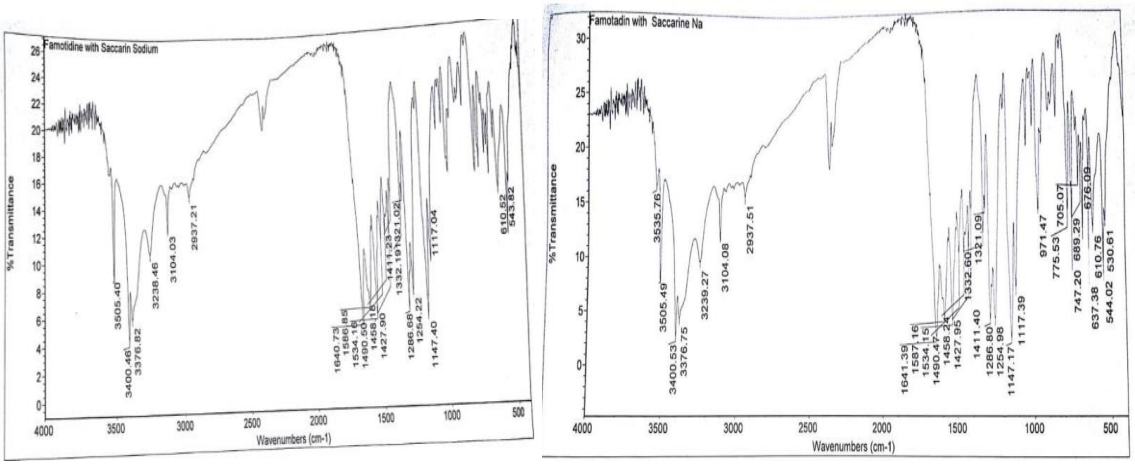


Fig. 12: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Saccharin Sodium.

Table 17: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Saccharin Sodium.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	**3200 – 3300**	**1620 – 1660**	**2900 - 3000**	**1630-1680**
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Saccharin Sodium	3238.46	1640.73	2937.21	747.20
After Stored	3239.27	1641.39	2937.51	775.53

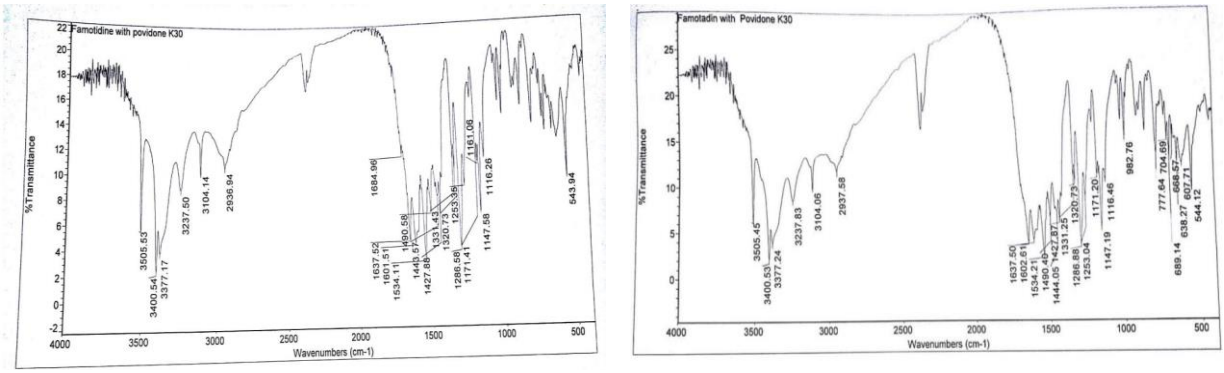


Fig. 13: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and PVP K30.

Table 18: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and PVP K30.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 – 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with PVP K30	3237.50	1637.52	2926.94	777.69
After Stored	3237.83	1637.5	2937.58	777.64

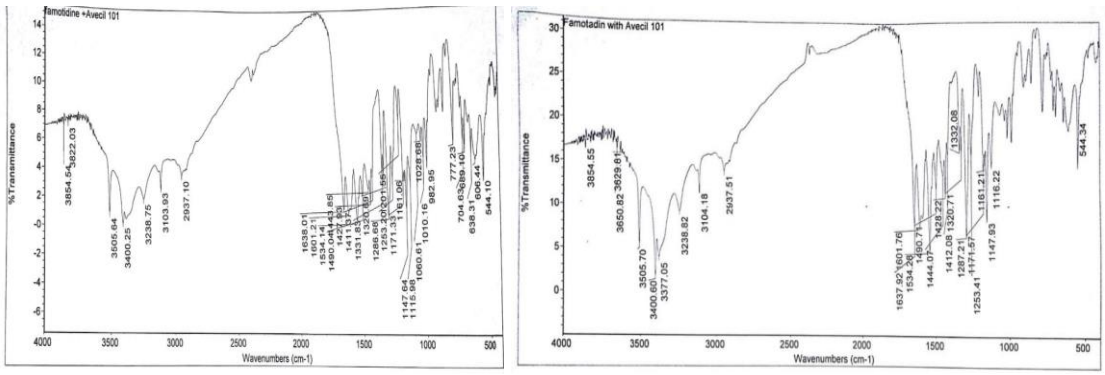


Fig. 14: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Avicel PH 101.

Table 19: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Avicel PH 101.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Avicel PH 101	3238.75	1638.01	2937.10	777.23
After Stored	3238.82	1637.92	2937.51	777.12

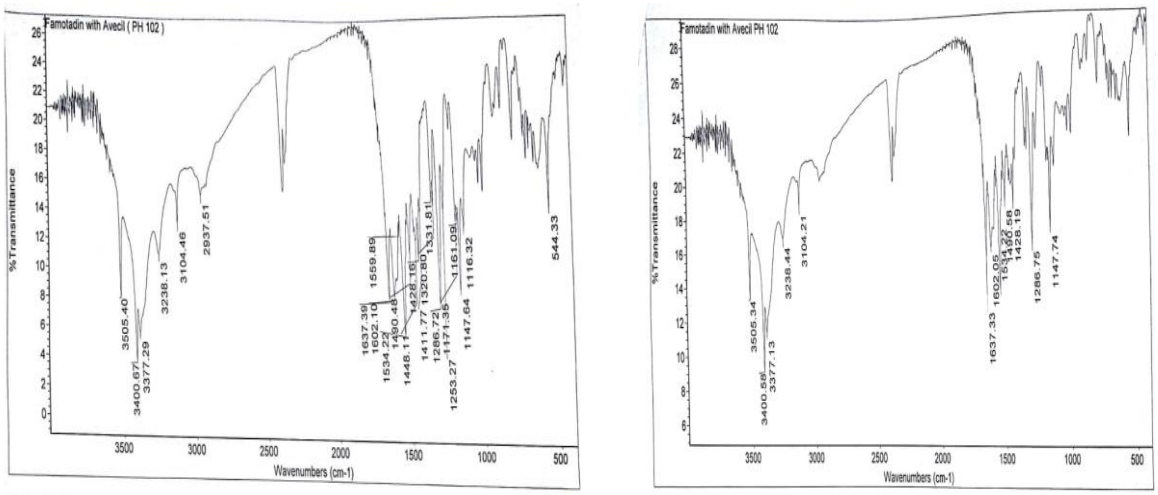


Fig. 15: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Avicel PH 102.

Table 20: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Avicel PH 102.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Avicel PH 102	3238.44	1637.39	2937.51	777.60
After Stored	3238.44	1637.33	2937.51	777.34

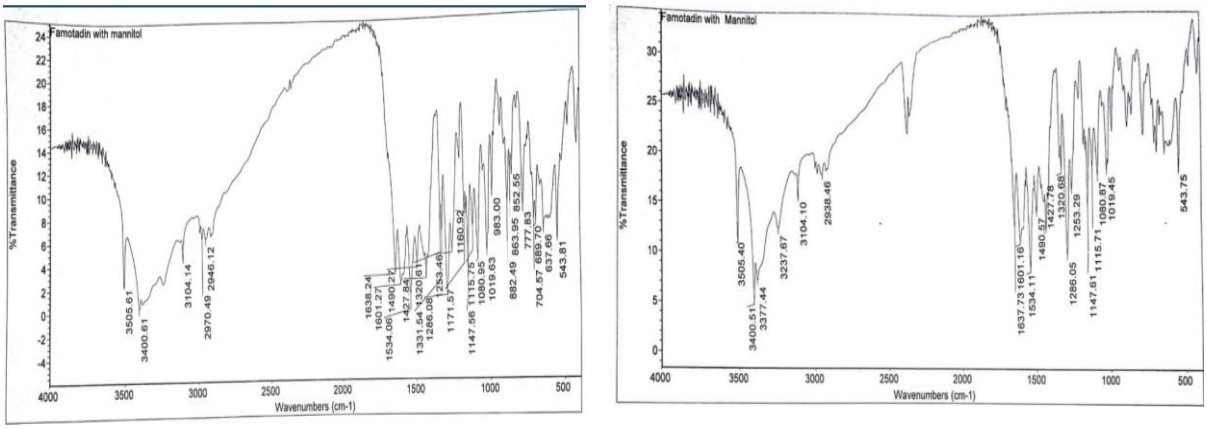


Fig. 16: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Mannitol.

Table 21: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Mannitol.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Mannitol	3202.36	1638.24	2970.49	777.82
After Stored	3237.67	1637.73	2938.46	777.83

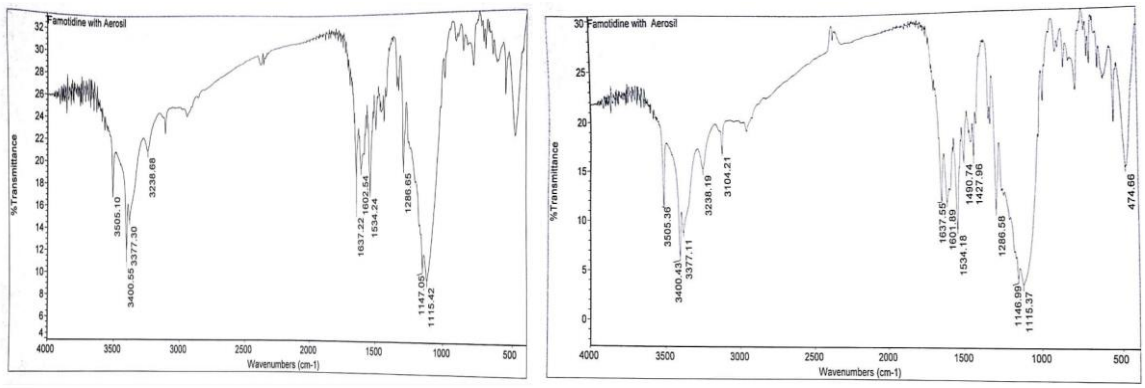


Fig. 17: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Aerosil.

Table 22: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Aerosil.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Aerosil	3238.68	1637.22	2971.18	777.19
After Stored	3238.19	1637.55	2971.19	777.28

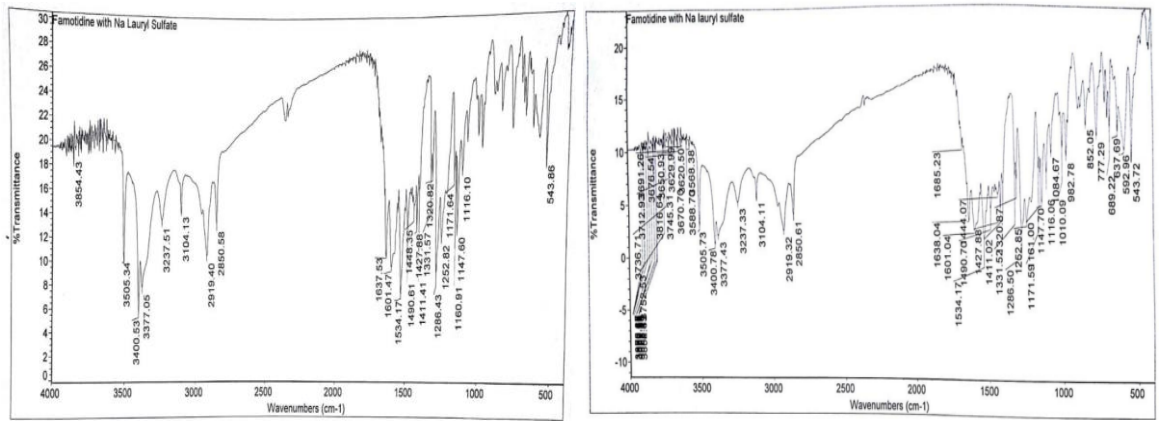


Fig. 18: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and SLS.

Table 23: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and SLS.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with SLS	3237.51	1637.53	2919.40	777.30
After Stored	3237.33	1638.04	2919.32	777.29

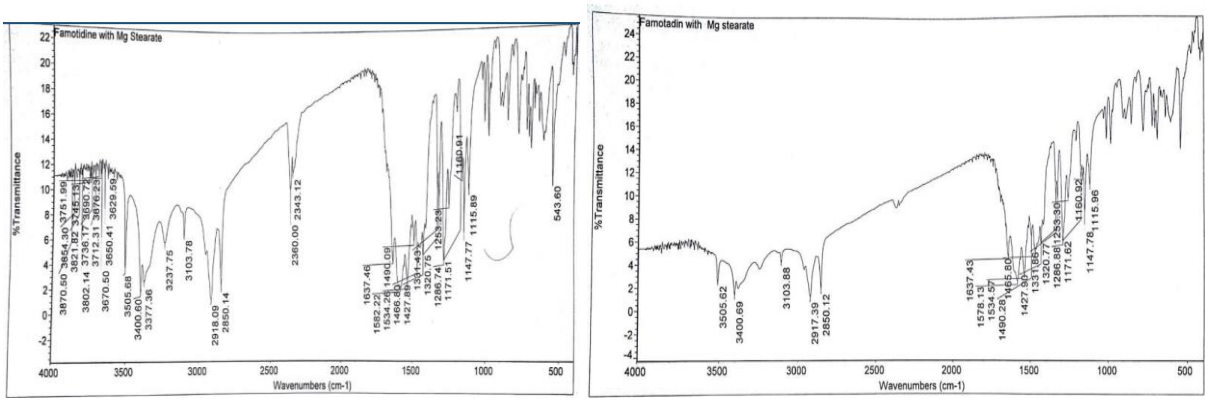


Fig. 19: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Mg. Stearate.

Table 24: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Mg. Stearate.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Mg. Stearate	3237.51	1637.46	2918.09	777.50
After Stored	3241.54	1637.43	2917.39	777.34

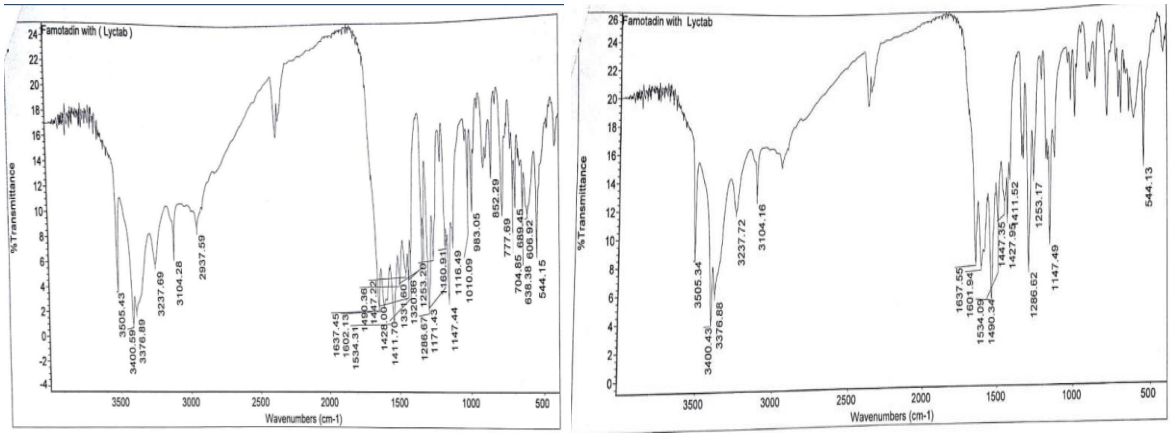


Fig. 20: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Lycatab.

Table 25: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Lycatab.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Lycatab	3237.69	1637.45	2937.59	777.69
After Stored	3237.72	1637.55	2937.50	777.45

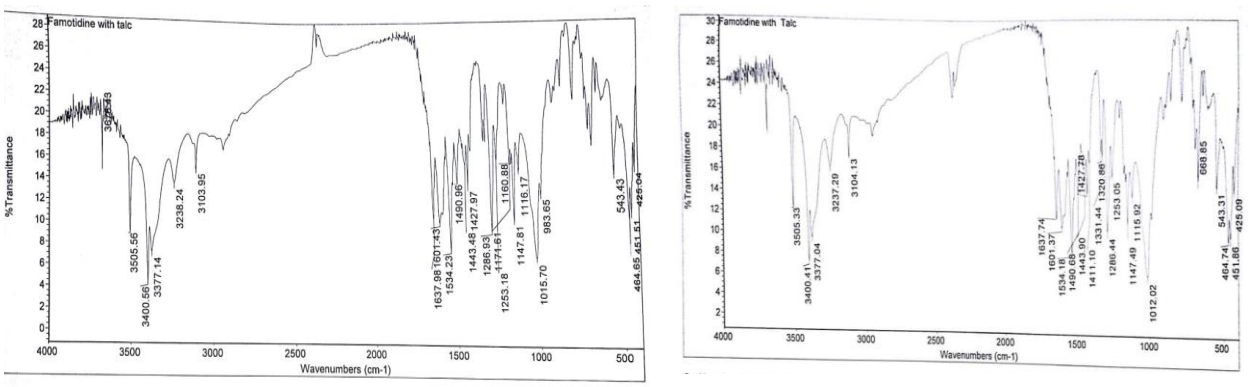


Fig. 21: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Talc.

Table 26: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and Talc.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with Talc	3238.24	1637.98	2937.21	712.55
After Stored	3237.29	1637.74	2937.21	668.85

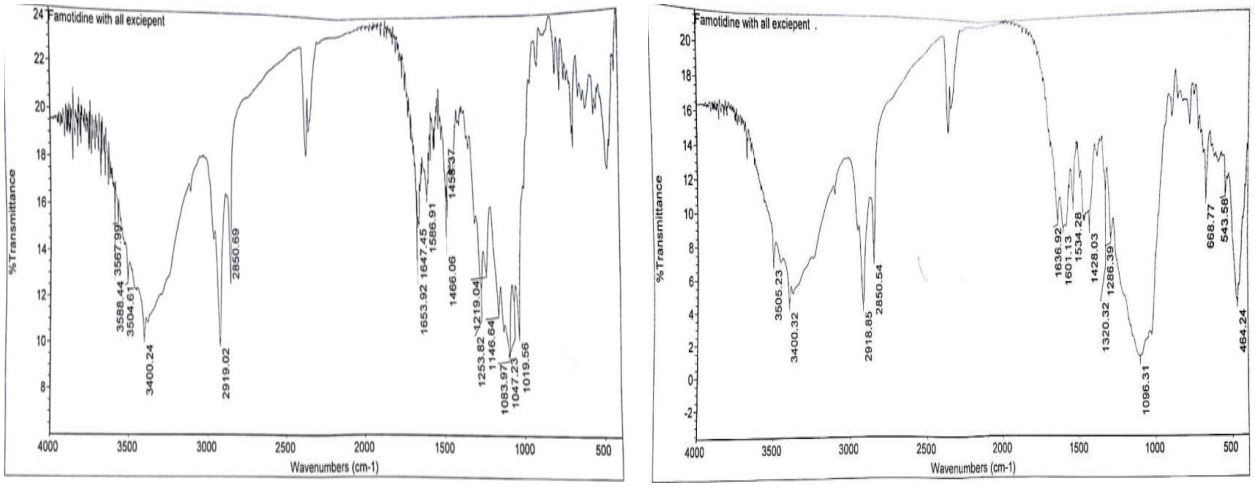


Fig. 22: FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and All Excipients.

Table 27: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Famotidine and All Excipients.

Specific Functional Groups	N-H Amine	C=N Imines	CH-Alkane	CH-Aromatic
The Mid-IR Region (cm^{-1})	3200 – 3300	1620 - 1660	2900 - 3000	1630-1680
Pure Drug STD	3200	1640	2937	777
Famotidine Sample Test	3200.67	1638.73	2937.10	777.63
Famotidine ST with All Excipients	3200.24	1653.92	2919.02	777.94
After Stored	3200.32	1636.92	2918.85	668.77

Micromeritic Properties of Famotidine

The powder of Famotidine was evaluated for the following parameters such as angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The results were shown in Table 28.

Table 28: Micromeritics properties of Famotidine.`

Raw Material (API)	Bulk weight(g)	Tapped weight(g)	Tapped vol	Bulk vol	Bulk Density(g/ml)	Tapped Density(g/ml)	Bulkiness
Famotidine	10 g	10.03 g	24 ml	41 ml	0.243 g/ml	0.416 g/ml	4.115

Table 29: Micromeritics properties of Famotidine.

Raw Material (API)	Voids	Porosity (%)	Compressibility Index (%)	Hausner Ratio	Carr's Index	Evaluation of Angle of Repose
Famotidine	0.414	41.463 %	41.586 %	1.711	0.4158	Very very poor.

The angle of repose of Famotidine was found to be which indicates Very very poor flow property. The bulk density was found to be 0.243 g/ml, the tapped density was found to be

0.416 g/ml, the compressibility index was found in 41.586 % which indicates very poor flowability and the Hausner's ratio was 1.711 as shown in Tables 28 & 29.

Evaluation of Precompression Parameters

The powder blends were evaluated for the following parameters such as angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The results were shown in Tables 30& 31.

Table 30: Preformulation Parameters of Famotidine Powder Flow Properties.

Formulation Code	Bulk weight(g)	Tapped weight(g)	Tapped vol	Bulk vol	Bulk Density(g/ml)	Tapped Density(g/ml)	Bulkiness
F1	17.97	17.9	54	41	0.33	0.44	3.012
E2	18.57	18.58	40	37	0.46	0.50	2.155
F3	23.96	23.96	69	54	0.35	0.44	2.881
F4	23.96	23.61	88	66	0.27	0.36	3.676
F5	17.99	17.89	48	39	0.37	0.45	2.702
F6	17.74	17.75	43	35	0.41	0.50	2.439
F7	17.53	17.55	46	35	0.38	0.50	2.631
F8	17.69	17.89	48	34	0.36	0.52	2.777
F9	17.58	17.5	44	34	0.39	0.51	2.567
F10	17.59	17.6	41	30	0.42	0.58	2.380
F11	17.82	17.73	48	30	0.37	0.54	2.702
F12	17.68	17.7	40	30	0.44	0.58	2.272

Table 31: Preformulation Parameters of Famotidine Powder Flow Properties.

Formulation Code	Voids	Porosity (%)	Compressibility Index (%)	Hausner Ratio	Carr's Index	Angle of Repose(θ)	Evaluation of Angle of Repose
F1	0.240	24	24.2	1.32	0.242	24.08	Excellent
E2	0.075	7.5	7.385	1.08	0.073	25.8	Excellent
F3	0.217	21.7	21.67	1.28	0.2167	27.87	Excellent
F4	0.250	25	25.06	1.33	0.2506	28.28	Excellent
F5	0.187	18.7	17.77	1.21	0.1777	37.07	Fair
F6	0.186	18.6	18	1.21	0.18	37.95	Fair
F7	0.239	23.9	24	1.31	0.24	37.05	Fair
F8	0.291	29.1	30.76	1.44	0.3076	33.18	Good
F9	0.227	22.7	23.52	1.30	0.2352	39.05	Fair
F10	0.268	26.8	27.58	1.38	0.2758	40.62	Fair
F11	0.312	31.2	31.48	1.45	0.3148	37.77	Fair
F12	0.250	25	24.13	1.31	0.2413	31.84	Good

As for preformulation studies results that show in Tables 30 & 31, for micrometrics properties of powder blend. The angle of repose of formulation F1 to F4 that prepared by wet granulation were found to be between (24.08 – 28.28) which indicate excellent flow

properties. The bulk density was found to be between (0.27 to 0.46 g/ml), the tapped density was found to be between (0.36 to 0.50 g/ml), the compressibility index was found in the range of (7.385 to 25.06 %) and the Hausner's ratio lies between (1.08 to 1.33). While the angle of repose of formulation F5 to F12 that prepared by direct compression were found to be between (31.84 – 40.62) which indicate fair and good flow properties. The bulk density was found to be between (0.36 to 0.44 g/ml), the tapped density was found to be between 0.45 to 0.58 g/ml, the compressibility index was found in the range of (17.17 to 31.13 %) and the Hausner's ratio lies between (1.21 to 1.45).

CONCLUSION

The compatibility studies of physical mixtures of Famotidine with different used excipients such as mannitol, avicel PH 101and avicel PH 102 as diluents, and sodium starch glycolate, croscarmellose sodium, and crospovidone as superdisintegrants and sodium lauryl sulfate as wetting agent were investigated by FTIR it was detected that there was no variation or minor deviation in the characteristic peaks in FTIR spectroscopy. The Famotidine formulations prepared were evaluated for precompression parameters and powder flow properties which were found to be within limits. It was concluded that the drug Famotidine was found to be compatible with various excipients which were selected for the formulation development of the Famotidine ODTs. Formulation scientist from his experience and knowledge have to significantly in the preformulation study stage and is an important factor in the ADDS (Advanced Drug Delivery Systems) product development process.

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