ejpmr, 2024, 11(9), 370-404

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

RIVAROXABAN-EXCIPIENT COMPATIBILITY STUDIES FOR ADVANCED DRUG DELIVERY SYSTEMS DEVELOPMENT

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Article Received on 21/07/2024 **Article Revised on 11/08/2024** **Article Accepted on 01/09/2024**

ABSTRACT

The main objective of the present study was to the preformulation studies were performed to know the physico-chemical and mechanical properties of Rivaroxaban for formulation development of ODTs. The drug-excipient compatibility studies were conducted to characterize the drug Rivaroxaban present in Orodispersible tablets (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. Preformulation, formulation and evaluation of Rivaroxaban to avoid problems associated with conventional delivery system such as limited permeation, low dissolution and bioavailability and also to improve bioavailability and oral anticoagulant effect. 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 Rivaroxaban and various excipients as mannitol, microcrystalline cellulose as diluents, and sodium starch glycolate, croscarmellose sodium, and crospovidone as superdisintegrants sodium lauryl sulfate as wetting agents were evaluated for preformulation studies parameters. It was concluded that the drug Rivaroxaban was found to be compatible with various excipients which were selected for the formulation development of the Rivaroxaban 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: Rivaroxaban, Anticoagulant, Compatibility, Excipients, Development, , Preformulation, Drug delivery systems.

INTRODUCTION

Preformulation Studies[1-150]

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.

Preformulation research were evolved in 1950. It is defined as the phase of research and development in which preformulation studies characterize physical and chemical properties of a drug molecule in order to develop safe, effective, bioavailability and stable dosage form. In preformulation studies, physicochemical properties of drug molecules are characterized either alone or in combination with excipients. Preformulation is the first step in the rational formulation of an active pharmaceutical ingredient (API).

Preformulation Study Includes: 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 are 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 drug-excipient compatibility studies of Rivaroxaban, with commonly different excipients using for formulation development of Orodispersible tablets ODTs.

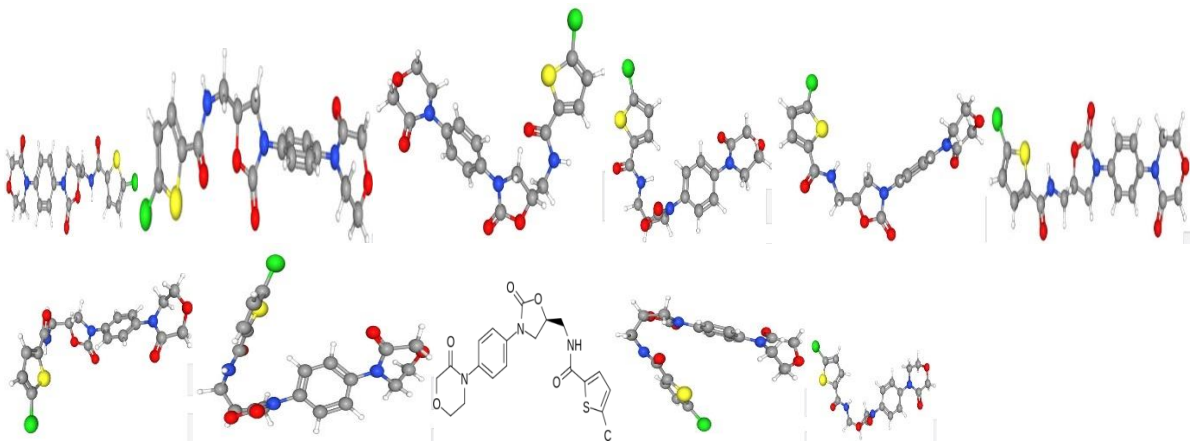
MATERIALS AND METHODS

Rivaroxaban and Acetonitrile were gift from (Modern Pharmaceutical Industry Company-Yemen). Crospovidone, Sodium Starch Glycolate, Croscarmellose Sodium, Avicel 102, Mannitol, PVP K30, Sodium Lauryl Sulfate, Aerosil, Magnesium Stearate, Talc, Aspartame, Saccharin Sodium, Vanilla Flavor, Distilled Water, Sodium Hydroxide, Monobasic Potassium Phosphate and Potassium Bromide were gift from (Shaphaco Pharmaceutical Industry Company-Yemen).

Evaluation of Drug–Excipient Compatibility Studies Methods[55-356]

Table 1: Rivaroxaban Data.

Characterization of Rivaroxaban



Rivaroxaban Structure and 3D Conformer

Chemical Structure	(S)-5-chloro-N-{[2-oxo-3-[4-(3-oxomorpholin-4-yl) phenyl] oxazolidin-5-yl] methyl} thiophene-2-carboxamide	**Appearance**	Non-hygroscopic, white to yellowish powder.
Chemical Formula	C19H18ClN3O5S	**Solubility**	slightly soluble in organic solvents (e.g., acetone, polyethylene glycol 400) and is practically insoluble in

			water and aqueous media.
Molecular Weight	435.88 g·mol−1	**BCS**	Class-II Drug
Action and Use	Inhibits platelet activation and fibrin clot formation via direct, selective and reversible inhibition of factor Xa (FXa) in both the intrinsic and extrinsic coagulation pathways. FXa, as part of the prothrombinase complex consisting also of factor Va, calcium ions, factor II and phospholipid, catalyzes the conversion of prothrombin to thrombin. Thrombin both activates platelets and cata-lyzes the conversion of fibrinogen to fibrin. Rivaroxaban is an anticoagulant which binds directly to factor Xa. Thereafter, it effectively blocks the amplification of the coagulation cascade, preventing the formation of thrombus. Prophylaxis of venous thromboembolism following knee replacement surgery Prophylaxis of venous thromboembolism following hip replacement surgery Treatment of deep-vein thrombosis. Treatment of pulmonary embolism Prophylaxis of recurrent deep-vein thrombosis. Prophylaxis of recurrent pulmonary embolism Prophylaxis of stroke and systemic embolism in patients with non-valvular atrial fibrillation and with at least one of the following risk factors: congestive heart failure, hypertension, previous stroke or transient ischemic attack, age 75 years, or diabetes mellitus. Prophylaxis of atherothrombotic events following an acute coronary syndrome with elevated cardiac biomarkers (in combination with aspirin alone or aspirin and clopidogrel) Prophylaxis of atherothrombotic events in patients with coronary artery disease or symptomatic peripheral artery disease at high risk of ischemic events (in combination with aspirin).	**Duration of Treatment**	Chronic
Pharmacokinetics of Rivaroxaban			
Drug	Rivaroxaban is rapidly absorbed	**Drug Distribution**	Plasma protein binding is about

Absorption	and reaches peak plasma concentration in 2-4 hours. Bioavailability of the 10 mg dose is >80%. However, the 15-20 mg dose have a lower bioavailability if taken in the fasted state and consequently should be taken with food.		92% to 95% The steady state Vd is 50 L.
Drug Metabolism	Approximately two-thirds of the dose is metabolized. It is metabolized by CYP3A4, CYP3A5, CYP2J2 and CYP-independent mechanisms.	**Drug Excretion**	Urine (66% primarily via active tubular secretion [36% as unchanged drug; 30% as inactive metabolites]); feces (28% [7% as unchanged drug; 21 % as inactive metabolites])Systemic clearance is approximately 10 L/h, so Rivaroxaban is considered a drug with low clearance. Renal clearance is ~3-4 L/h.
The Elimination Half-Life (T1/2)	The terminal half-life is 5-9 hours in adults and 11-13 hours in the elderly. Time to peak plasma :2-4 hours.	**Availability**	Tablets: 2.5mg, 10mg, 15mg, 20mg.

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
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
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 PH102)	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
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 such as aluminum, copper, and iron.	Crystalline powder
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
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,	compatible in solution with a wide range of inorganic salts, natural and synthetic	White to yellowish-white amorphous powder.

				PG….	resins, and other chemicals.	
Talc	Altalc, E553b, hydrous magnesium calcium silicate, hydrous magnesium silicate, Luzenac Pharma, magnesium hydrogen metasilicate. Mg6(Si2O5)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.
Aspartame	3-Amino-N-(a carboxyphenethyl) succinamic acid N-methyl ester; 3-Amino-N- (a methoxycarbonylphenethyl) succinamic acid;	Sweetening agent. It enhances flavor systems and can be used to mask some unpleasant taste characteristics; the approximate sweetening power is 180–200 times that of sucrose.	In practice, the small quantity of aspartame consumed provides a minimal nutritive effect.	Slightly soluble in ethanol (95%); sparingly soluble in water. At 208C the solubility is 1% w/v at the isoelectric point (pH 5.2).	incompatible with dibasic calcium phosphate and also with the lubricant magnesium stearate. Reactions between aspartame and sugar alcohols.	occurs as an off white, almost odorless crystalline powder with an intensely sweet taste
Saccharin Sodium	1,2-Benzisothiazolin-3-one 1,1-dioxide, sodium salt, Crystallose, E954, gendorf 450, sucaryl sodium	Sweetening agent. 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.	0.02–0.5% w/w.	Readily dissolved by dilute ammonia solutions, alkali hydroxide solutions, or alkali carbonate solutions. 1 in 290 water.	Saccharin can react with large molecules. Saccharin sodium does not undergo Maillard browning.	white crystals or a 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.
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	10% 0.5–2.5% 1.0–2.0%	Freely soluble in water, giving an opalescent solution; practically insoluble in chloroform and	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

		capsule lubricant; wetting agent.		ether.		taste, and a faint odor of fatty substances
Vanilla Flavor Ethyl Vanillin	Bourbonal; ethylprotal; ethylprotocatechuic aldehyde; 4-hydroxy3-ethoxybenzaldehyde; Rhodiarome; vanillal. C9H10O3	Flavoring agent. also used in perfumery.	0.01% Ethyl vanillin is generally regarded as an essentially nontoxic and nonirritant material.	Freely soluble in Alkaline hydroxide solutions. Soluble in Glycerin, Propylene glycol In Water 1 in 250.	Ethyl vanillin is unstable in contact with iron or steel, forming a red colored, flavorless compound. In aqueous media with neomycin sulfate or succinyl sulfathiazole, tablets of ethyl vanillin produced a yellow color.	White or slightly yellowish crystals with a characteristic intense vanilla odor and flavor.

According to Rivaroxaban and excipients data as shown in Tables 1 and 2, it was selected that the different excipients to preformulation study with Rivaroxaban 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	Electronic Balance
8	Rotary Tablet Compression Machine
9	Accelerate Stability Study Chamber

Drug Identification Test

Determination of The Organoleptic Properties

The organoleptic properties like color, odor and taste of the API were evaluated. Color a small quantity of Rivaroxaban was taken in a butter paper and viewed in well illuminated place. Taste and odor very less quantity of Rivaroxaban 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.

UV Scanning of Rivaroxaban in Phosphate Buffer at PH 6.8

The concentration of Rivaroxaban10µg/ml solution was prepared in phosphate buffer pH 6.8 and was subjected to scanning under UV visible spectrophotometer, between the range 200-400nm.The λmax was found to be at 248 nm.

Preparation of Standard Calibration Curve

Preparation of Phosphate Buffer (pH=6.8): 0.896 g of NaOH and 6.804 g of KH2PO4 dissolved in sufficient quantity of water, the volume was completed to 1000 ml with distilled water and mixed well by sonication. An accurately weighed 1 mg of Rivaroxaban was dissolved in 100ml of phosphate buffer (pH,6.8) to get a concentration of 10 µg/ml. Aliquots of stock solution were pipetted out ranging from volume 1 ml, 2 ml, 3 ml, 4 ml and 5 ml in a 5 ml volumetric flask and the volume was adjusted to 5 ml with phosphate buffer (pH6.8) to produce concentration of 2, 4, 6, 8, and 10 µg/ml respectively. Absorbance of the above solutions was measured at 248 nm by UV visible spectrophotometer against a blank of phosphate buffer solution. The standard calibration curve was obtained by plotting absorbance verses concentration in µg/ml.

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 Rivaroxaban

Melting Point: Melting point of the Rivaroxaban 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 Rivaroxaban 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 Rivaroxaban 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 Rivaroxaban in room condition as shown in Table 5.

Infrared Spectral Study of Samples after Stored One Month

Compatibility studies were performed by preparing blend of different excipients with drug and stored at 40°C ±2°C /75±5%RH for one month. 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 4.

Table 4: Samples of Rivaroxaban and Different Excipients for Compatibility Studies.

No	Component(s)	Amount(5mg:5mg)
1	Rivaroxaban	1
2	Rivaroxaban and Avicel 102	(1:1)
3	Rivaroxaban and SSG	(1:1)
4	Rivaroxaban and SLS	(1:1)
5	Rivaroxaban and Crospovidone	(1:1)
6	Rivaroxaban and Talc	(1:1)
7	Rivaroxaban and Vanilla Flavor	(1:1)
8	Rivaroxaban and Saccharin Sodium	(1:1)
9	Rivaroxaban and Aspartame	(1:1)
10	Rivaroxaban and CCS	(1:1)
11	Rivaroxaban and Mannitol	(1:1)
12	Rivaroxaban and Mg. Stearate	(1:1)
13	Rivaroxaban and PVP K30	(1:1)
14	Rivaroxaban and Aerosil	(1:1)

Mixing and Compression Processes

Mixing was performed Geometrically, in which all excipients were accurately weighed then all of them with the exception of Aerosil, magnesium stearate and Vanilla flavor, were blended with specified quantity of Rivaroxaban for 15minutes, while the other excipients were blended for 5 minutes and added to the former excipients. Then all formulae were passed through sieve no.18 to achieve particle size uniformity. Then each blend was subjected to powder properties examination and that will be shown in the evaluation of precompression parameters section. Finally, each mixture of each formula has been compressed directly into tablets using rotary tablet compression machine of punch size 6.25mm (7mm chamber diameter) to prepare tablets weighing 130 mg. As shown in Table 5.

Table 5: Composition of Rivaroxaban Formulations ODTs.

Ingredients	Quantity Per Tablet (mg)					
	Formula Code					
	F1	F2	F3	F4	F5	F6
Rivaroxaban	2.5	2.5	2.5	2.5	2.5	2.5
Crospovidone	-	10	10	-	5	-
Sodium Starch Glycolate	5	-	5	10	10	7.5
Croscarmellose Sodium	10	5	-	5	-	7.5
Avicel 102	51.5	51.5	51.5	51.5	51.5	51.5
Mannitol	48	48	48	48	48	48
PVP K30	4	4	4	4	4	4
Sodium Lauryl Sulfate	1.5	1.5	1.5	1.5	1.5	1.5

Aerosil	1	1	1	1	1	1
Magnesium Stearate	0.5	0.5	0.5	1	1	1
Talc	1	1	1	0.5	0.5	0.5
Aspartame	2	2	2	2	2	2
Saccharin Sodium	1	1	1	1	1	1
Vanilla Flavor	2	2	2	2	2	2

Pre-Compression Evaluation of The Powder
Micrometric Properties
Angle of Repose (θ)
Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The frictional force in a loose powder or granules can be measured by angle of repose as shown in Table 6.

$\tan \theta = h / r$
$\theta = \tan^{-1} (h/r)$ Where, θ is the angle of repose, h is the height of pile, r is the radius of the base of pile.

Table 6: Relationship Between Angle of Repose and Flow Properties.

Flow Property	Angle of Repose
Excellent	<25
Good	25-30
Passable	40-30
Very Poor	>40

Bulk Density
Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape, and the tendency of the particles to adhere to one another.

$$LBD = \frac{\text{Weight of the powder (m)}}{\text{Volume of the packing (vo)}}$$

Tapped Density
The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (V_t) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (ρ_t) was calculated using the following formula:
$\rho_t = M / V_t$

Compressibility Index
The compressibility index of the granules was determined by Carr's compressibility index as shown in Table 7.
(%) Carr's Index can be calculated by using the following formula:
Carr's Index (%) = TBD -LBD /TBD x100

Hausner Ratio
Hausner ratio is an indirect index of ease of power flow. It is calculated by the following formula:
Hausner ratio = ρ_t / ρ_d

Where ρt is tapped density and ρ_d is bulk density. Lower Hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Table 7: Grading of the Powders for Their Flow Properties According to Carr's Index.

Compressibility Index	Flow Properties
5-15	Excellent
12-16	Good
18-21	Fair to Passable
23-35	Poor
33-38	Very Poor
>40	Very Very Poor

RESULTS AND DISCUSSION
Identification Test
There are many of identification tests used in Rivaroxaban identification. We used Melting point, IR spectrum and calibration curve.

Melting Point
Melting point of pure Rivaroxaban was determined by open capillary method. The capillary tube was closed at one end by fusion and was filled with Rivaroxaban by repeated tapings. The capillary tube was placed in a digital melting point apparatus. The instrument was set to automatically increase the temperature of the heating bath. The rise in temperature was viewed through screen. The temperature at which the drug started melting was recorded. The melting point of Rivaroxaban was identical to reference melting point stated in USP as mentioned in the Table 8.

Table 8: Melting Point of Rivaroxaban.

Material	Specification	Observation
Rivaroxaban	230 °C	230 °C

Calibration Curve of Rivaroxaban

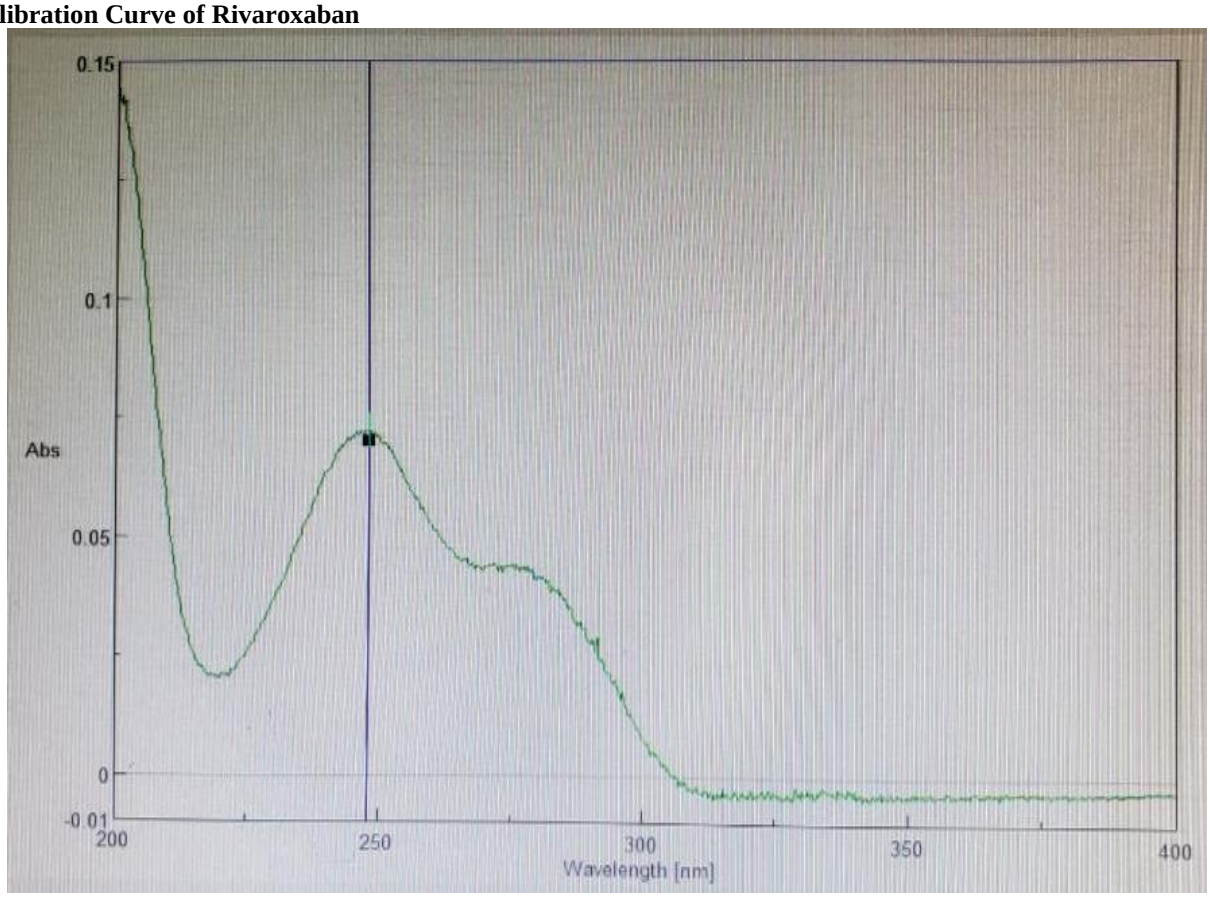


Fig. 1: UV Scanning of Rivaroxaban.

The maximum absorbance of Rivaroxaban in phosphate buffer (pH6.8) was determined by scanning the Rivaroxaban solution from 200-400 nm. The maximum absorbance was found at 248nm. as shown in Figure 1.

Table 9: Calibration Curve of Rivaroxaban in Phosphate Buffer at pH 6.8.

No. Samples	Concentration mcg/ml	Absorbance
1	0	0
2	2	0.0579
3	4	0.1249
4	6	0.1901
5	8	0.2602
6	10	0.3294

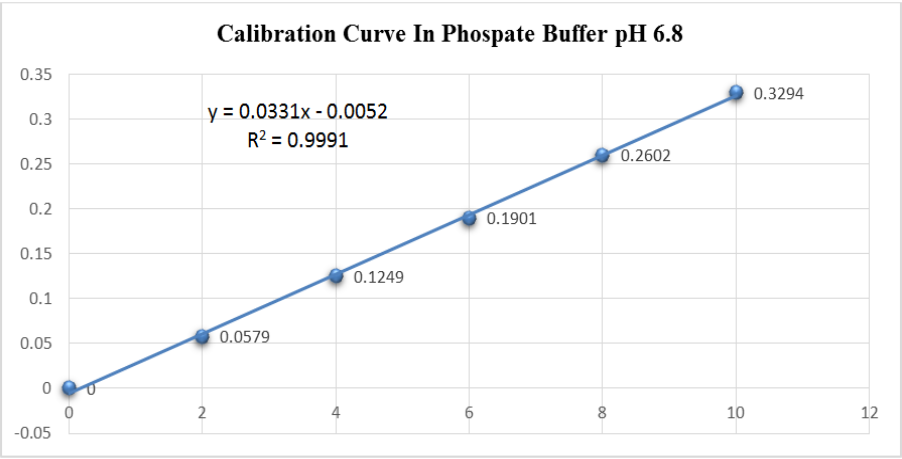


Fig. 2: Calibration Curve of Rivaroxaban in Phosphate Buffer pH (6.8).

The calibration curve of Rivaroxaban was prepared in phosphate buffer (pH 6.8). The plot of different concentrations of Rivaroxaban versus absorbance was found linear at 248 nm in calibrations. The absorbance at different concentrations is shown in Table 9. The regression equation for Rivaroxaban was obtained by plotting absorbance (A) versus concentration of Rivaroxaban (C). The data of standard curve was linearly regressed. The linear regression equation was Y = 0.0331C - 0.0052. The regression coefficient (R2 = 0.9991) was very much significant. The calibration curve was shown in Figure *2*.

Preformulation Tests of Powder

Organoleptic Properties

The organoleptic properties of Rivaroxaban were shown in Table 10.

Table 10: Organoleptic Properties of Rivaroxaban.

Tests	Specification	Observation
Color	Non-hygroscopic, White to Yellowish Powder	Non-hygroscopic, White to Yellow Powder
Odor	Odorless	Odorless
Taste	Bitter	Bitter

The organoleptic properties like color, odor and taste of the API were evaluated. The color of Rivaroxaban was found to be a white to yellow powder, no characteristic odor was observed in the study and the taste was found to be bitter. Rivaroxaban showed similar color, taste and odor as per IP specification as shown in Table 10.

Characterization of Rivaroxaban by FTIR

FT-IR spectral studies indicated that the drug is compatible with all the excipients. The FT-IR spectrum of physical mixture showed all the characteristic peaks of Rivaroxaban, thus conforming that no interaction of drug occurred with the components of the formulation excipients as shown in Figures (3-18) and Tables (11-25).

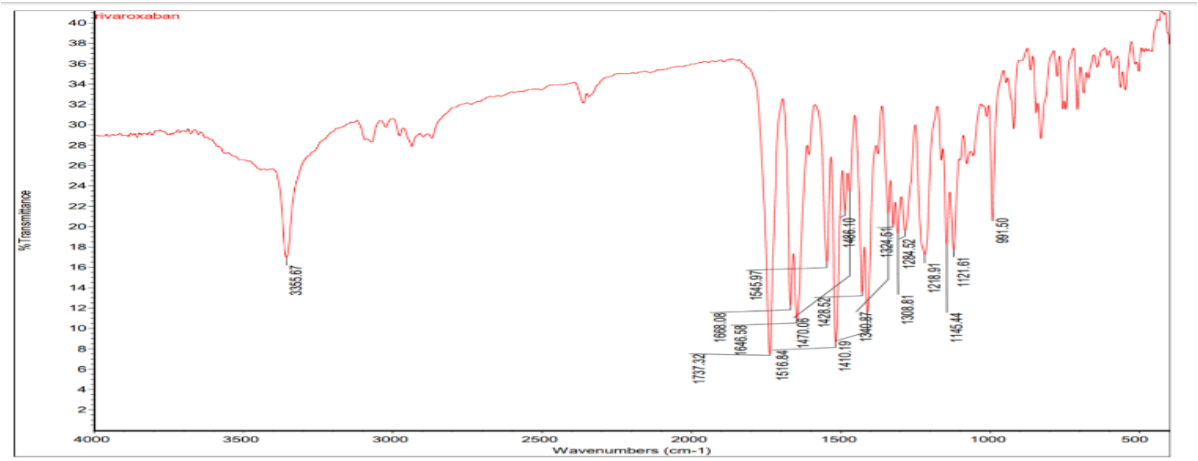


Fig. 3: FTIR Spectrum of Pure Rivaroxaban.

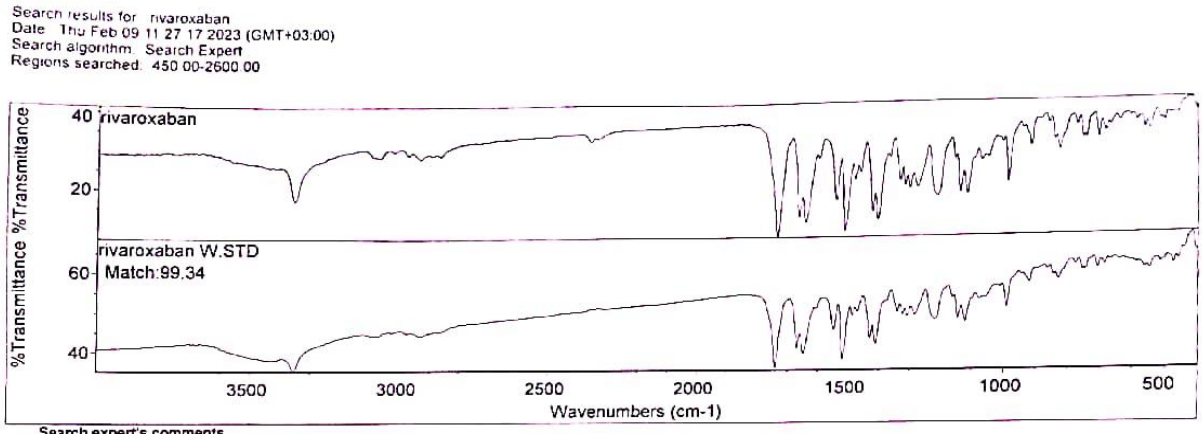


Fig. 4: FTIR Spectrum of Pure Rivaroxaban with STD.

Table 11: Results of IR Spectra Studies.

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample ST	1737.32	1668.08	1545.97	1218.91	1121.61	991.50

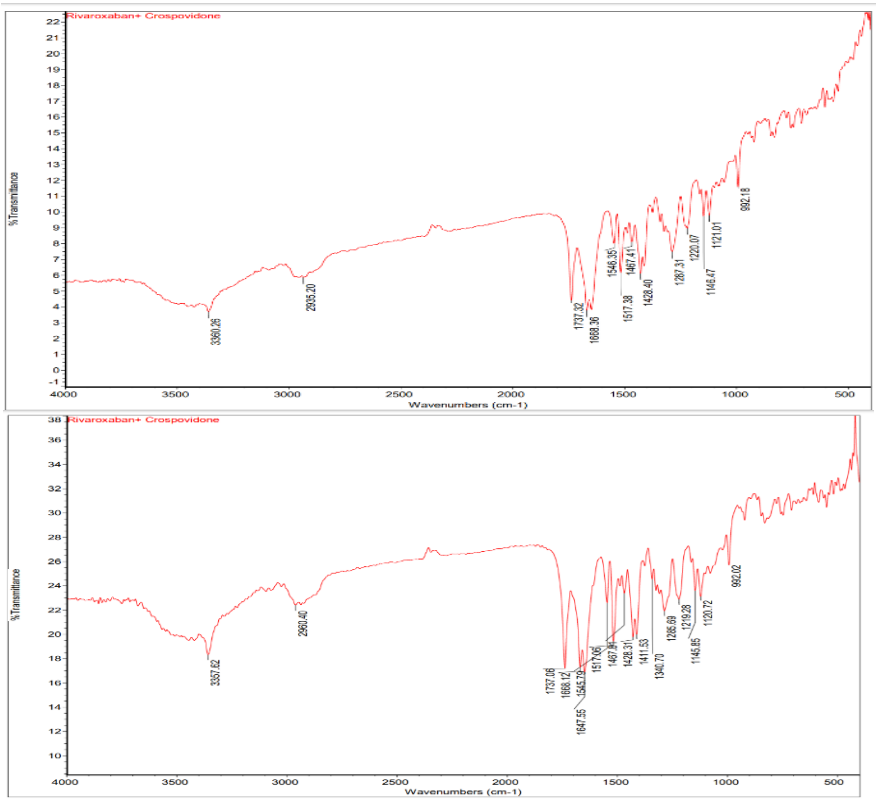
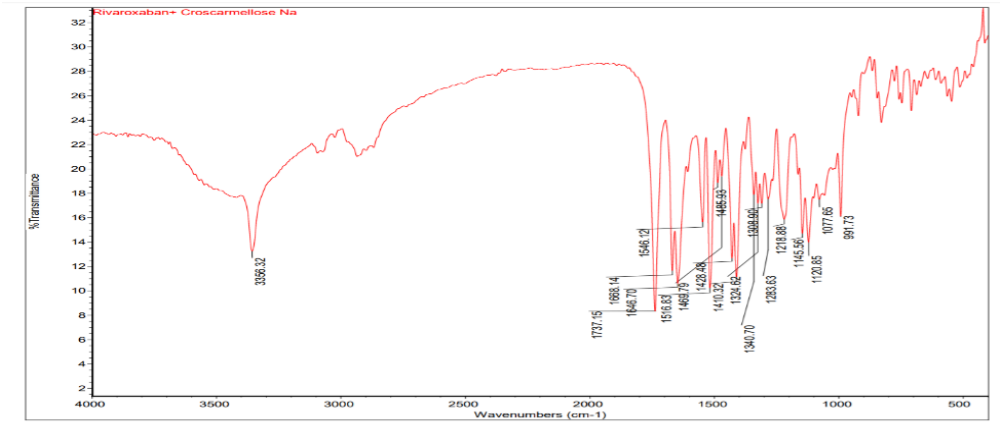


Fig. 5: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Crospovidone.

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

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with Crospovidone	1737.32	1668.36	1546.35	1220.07	1121.01	992.18
After Stored	1737.06	1668.12	1545.79	1219.28	1120.72	992.02



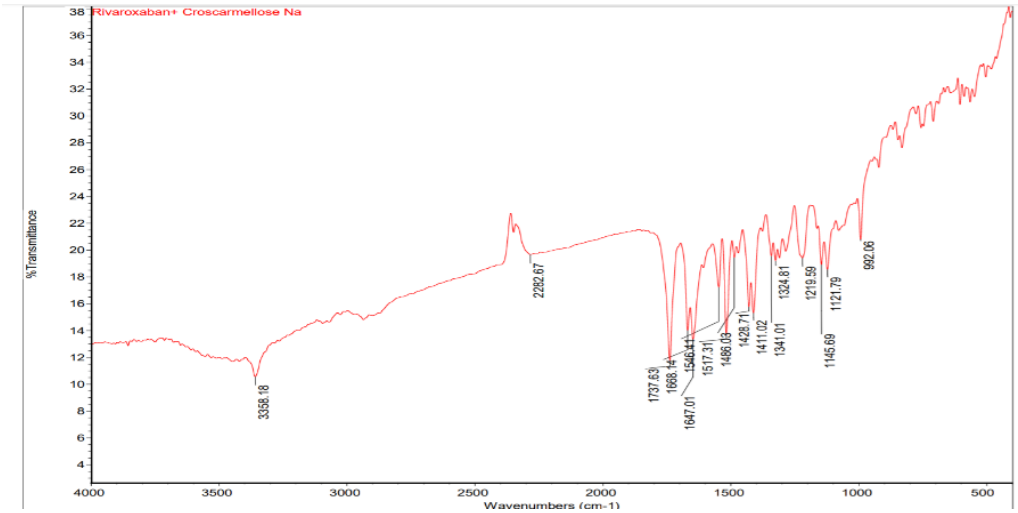


Fig. 6: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and CCS.

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

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with CCS	1737.63	1668.14	1546.41	1219.59	1121.79	992.06
After Stored	1737.15	1668.09	1546.12	1218.86	1120.85	991.73

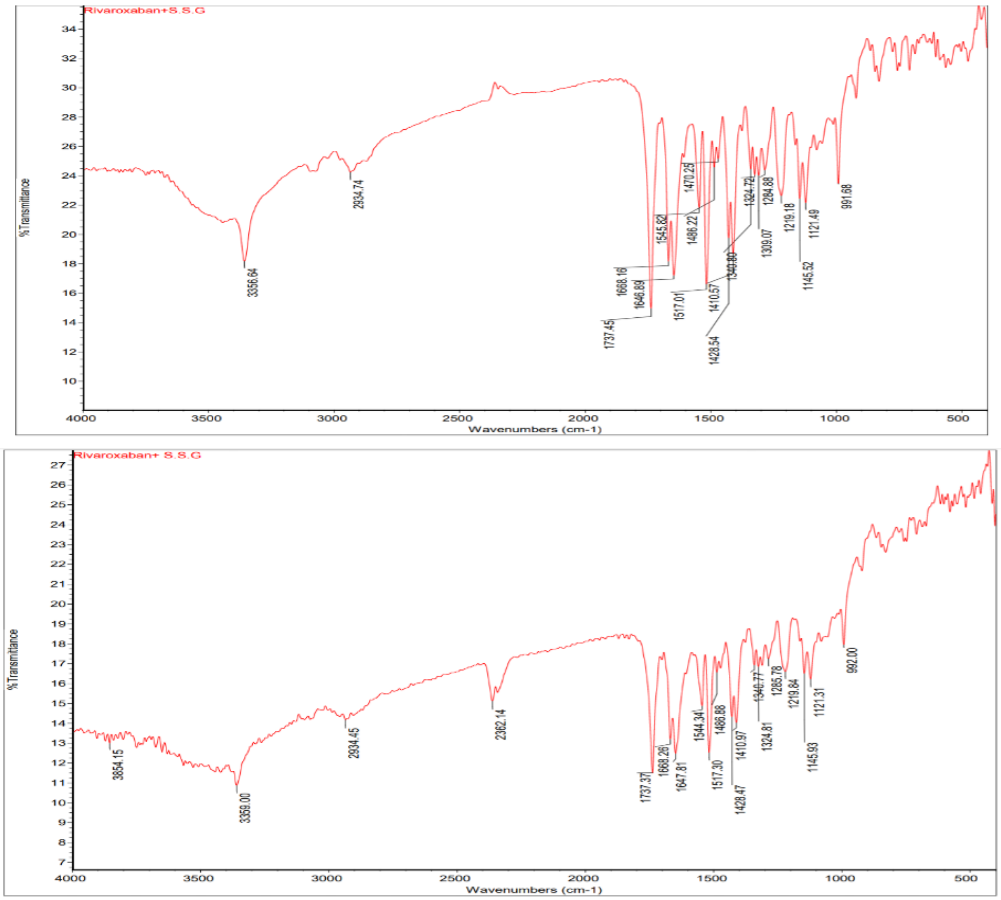


Fig. 7: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and SSG.

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

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with SSG	1737.45	1668.16	1545.82	1219.18	1121.49	991.68
After Stored	1737.37	1668.26	1544.34	1219.84	1121.31	992.00

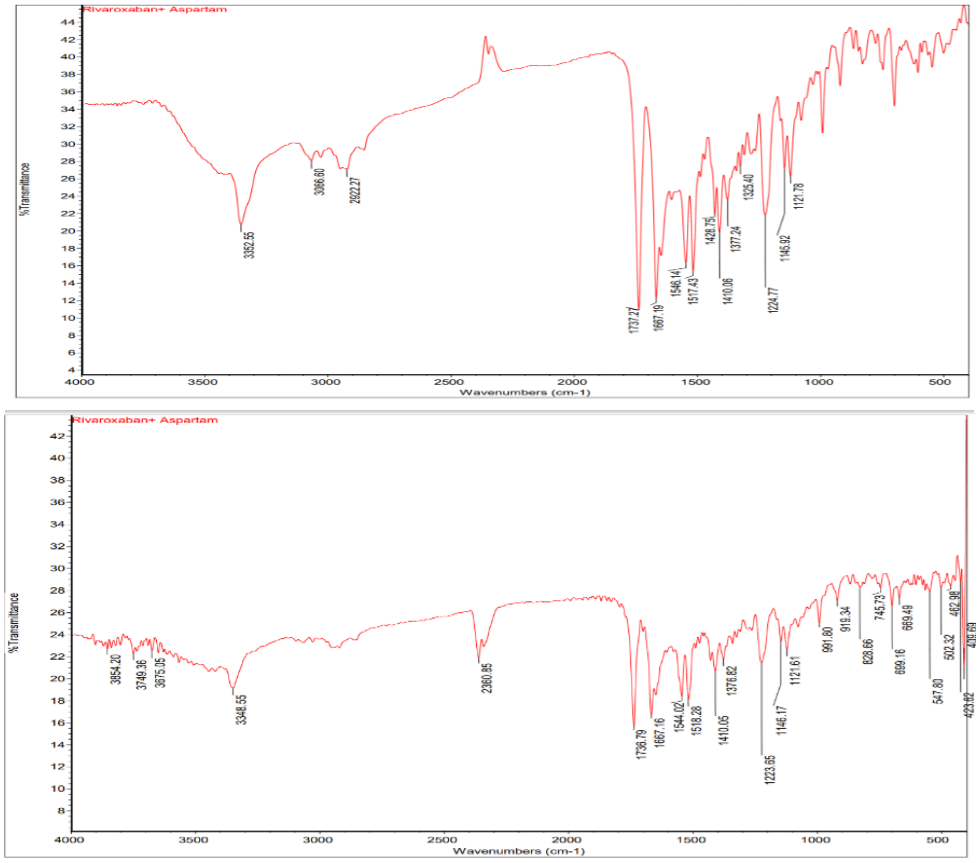


Fig. 8: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Aspartame.

Table 15: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Aspartame.

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with Aspartame	1737.27	-1667.19	1546.14	1224.77	1121.78	----
After Stored	1736.79	1667.16	1544.02	1223.65	1121.61	991.80

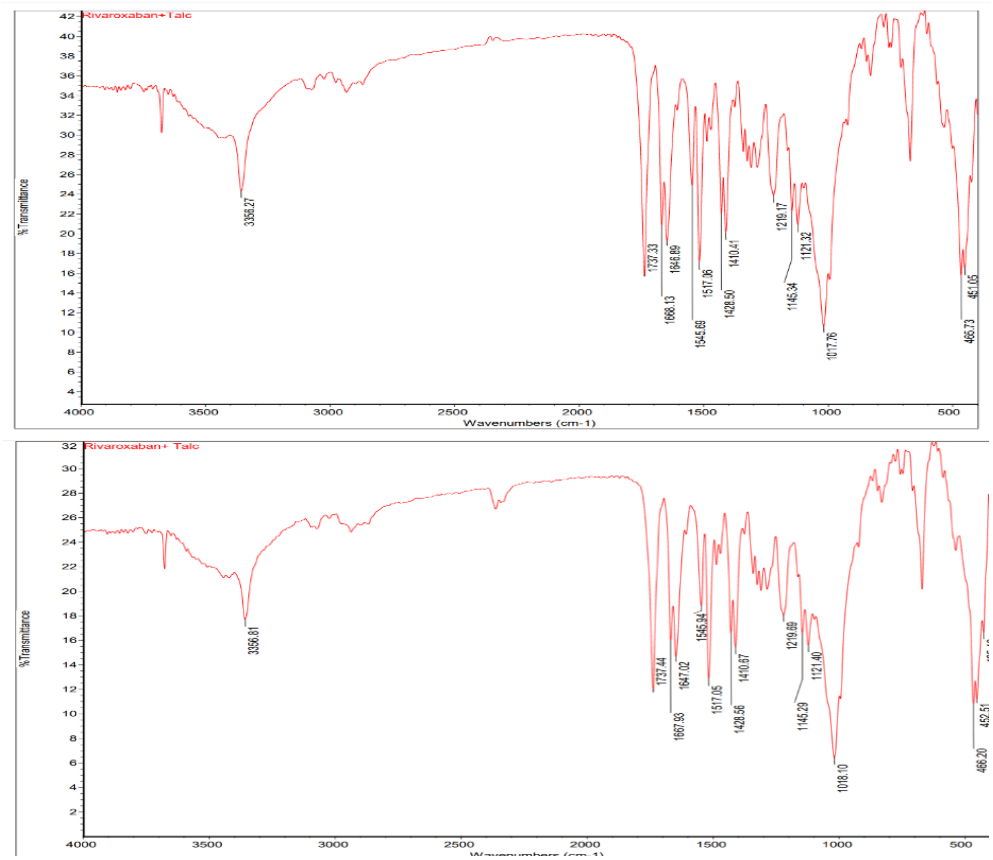
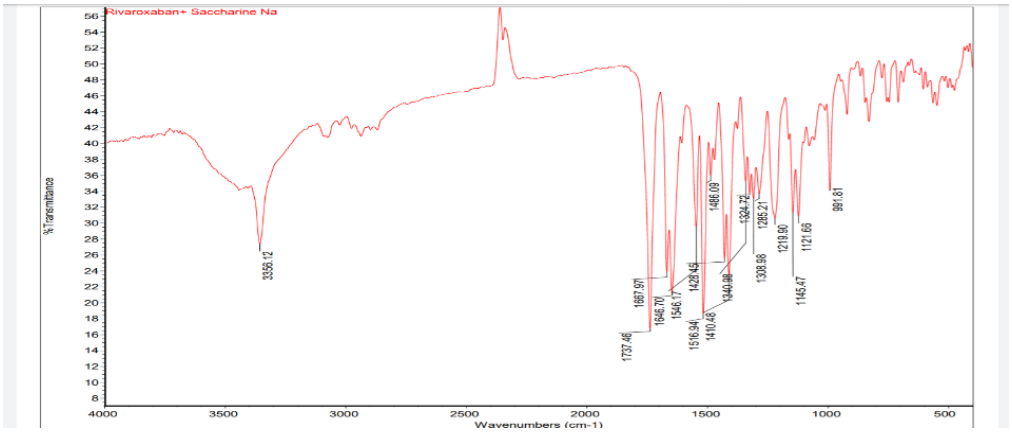


Fig. 9: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Talc.

Table 16: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Talc.

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with Talc	1737.33	1668,13	1545.69	1219.17	1121.32	1017.76
After Stored	1737.44	1667.93	1545.94	1219.69	1121.40	1018.10



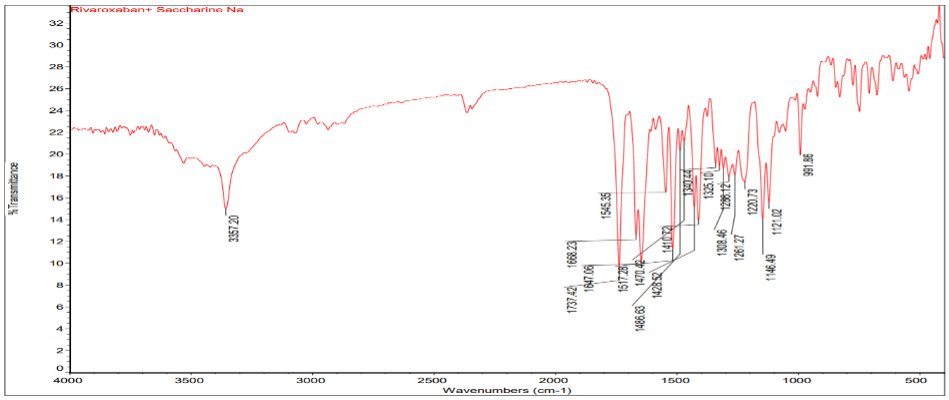


Fig. 10: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Saccharin Sodium.

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

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with Saccharin Sodium	1737.46	1667.97	1546.17	1219.90	1121.66	991.81
After Stored	1737.42	1668.23	1545.35	1220.73	1121.02	991.86

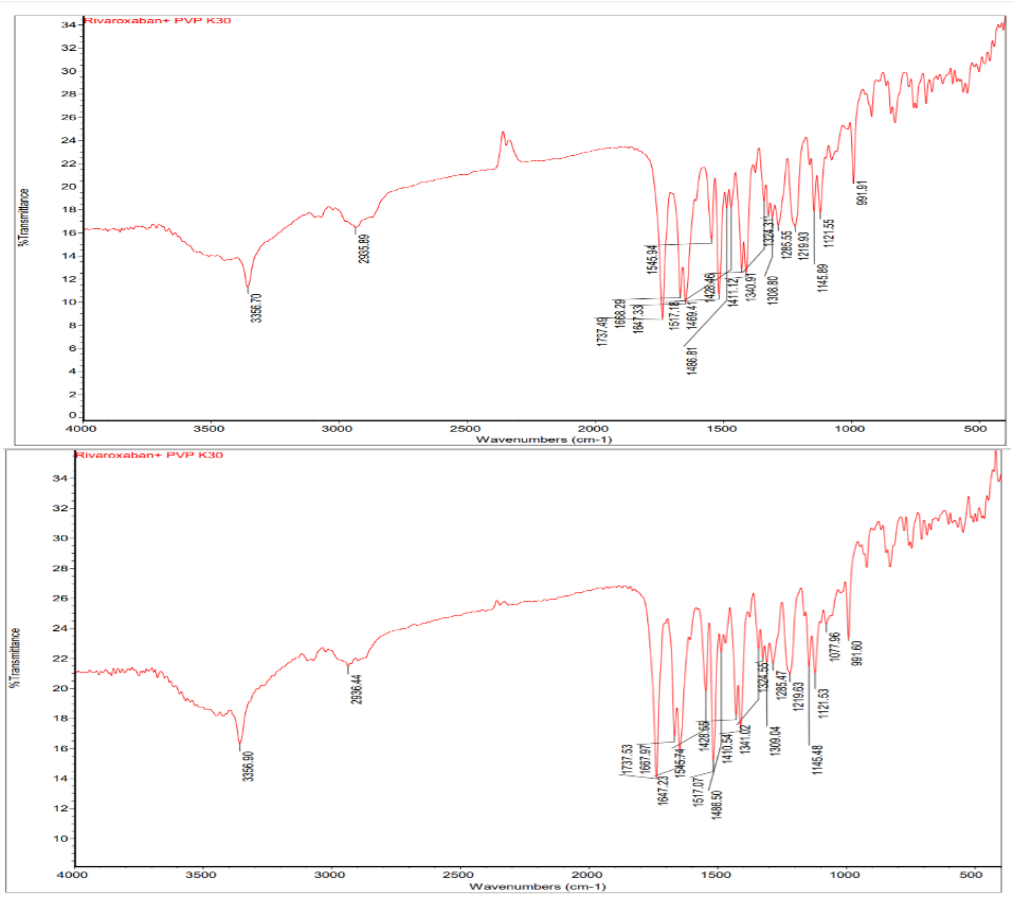


Fig. 11: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and PVP K30.

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

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with PVP K30	1737.49	1668.29	1545.94	1219.93	1121.55	991.91
After Stored	1737.53	1667.97	1545.74	1210.63	1121.53	991.60

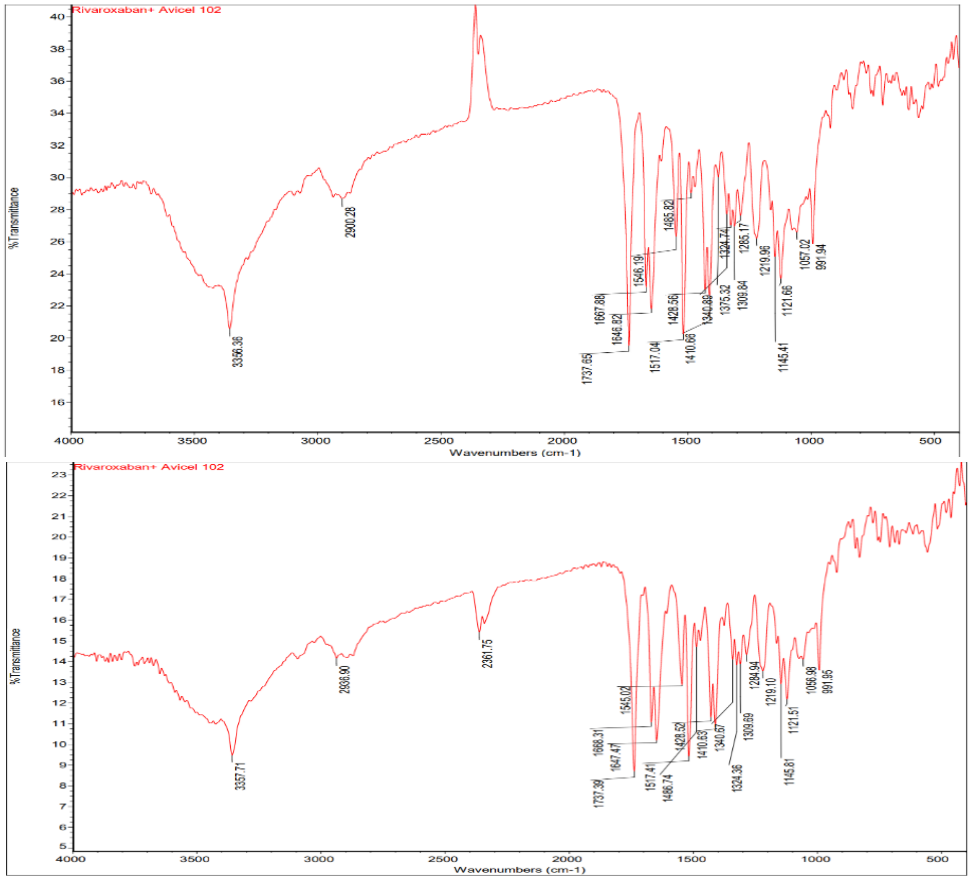


Fig. 12: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Avicel 102.

Table 19: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Avicel 102.

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with Avicel 102	1737.65	1667.88	1546.19	1219.69	1121.66	991.94
After Stored	1737.39	1668.31	1545.02	1219.10	1121.51	991.95

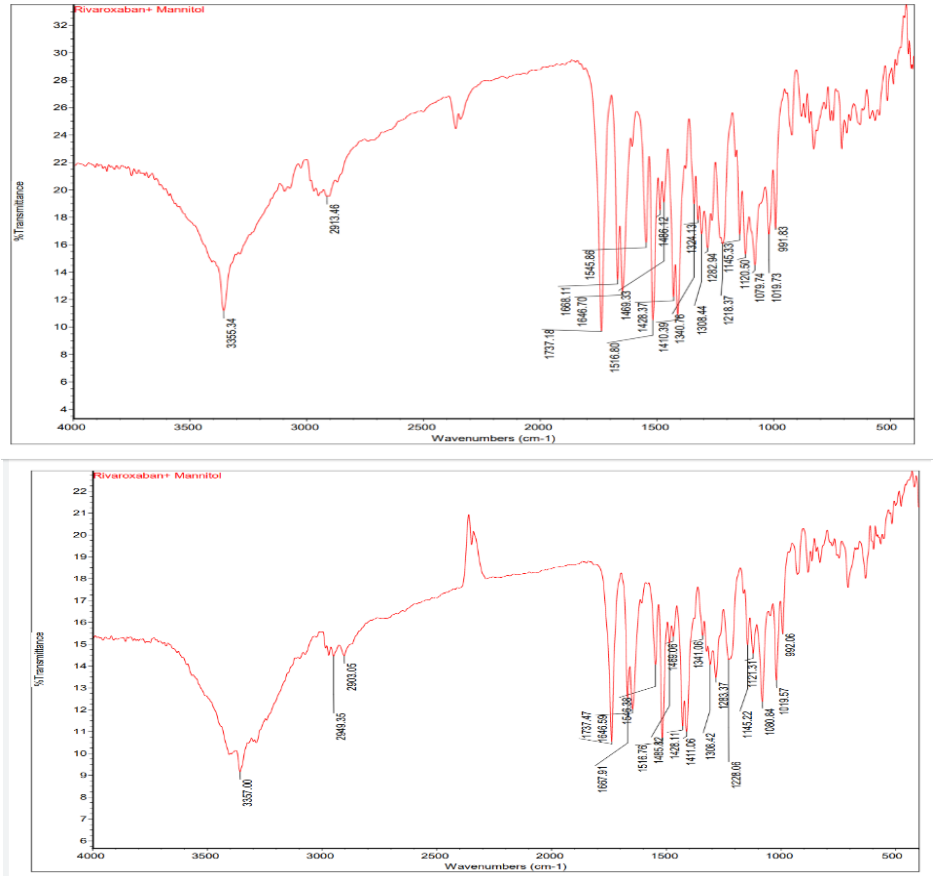
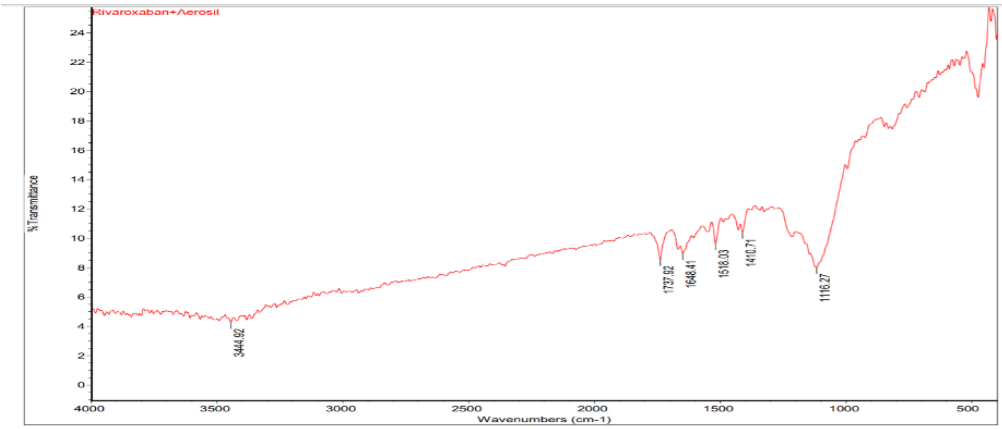


Fig. 13: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Mannitol.

Table 20: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Mannitol.

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with Mannitol	1737.47	1667.91	1546.38	1218.06	1121.31	992.06
After Stored	1737.18	1668.11	1545.86	1218.37	1120.50	991.83



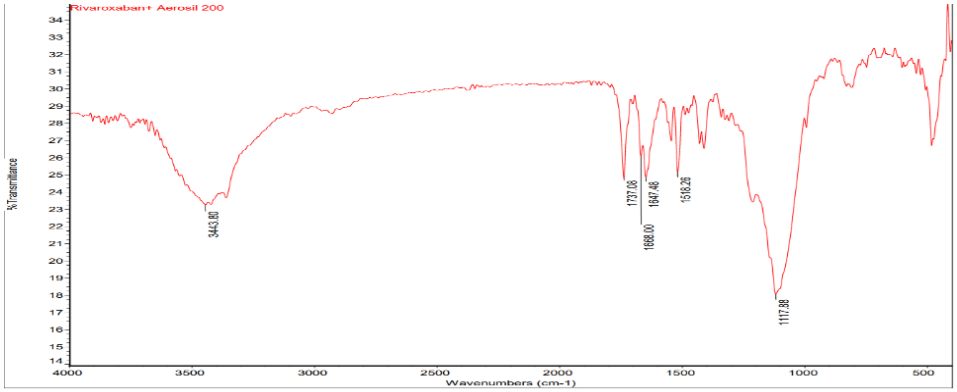


Fig. 14: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Aerosil.

Table 21: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Aerosil.

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with Aerosil	1737.92	1648.41	1518.03	—	1116.27	—
After Stored	1737.08	1668.00	1518.26	—	1117.88	—

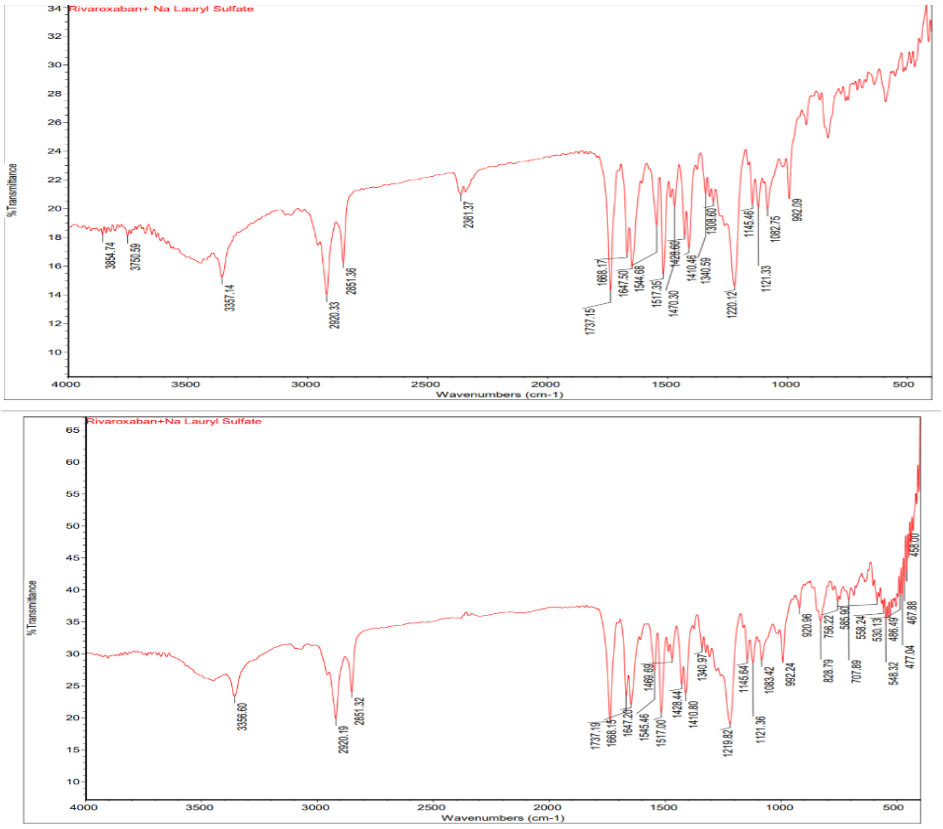


Fig. 15: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and SLS.

Table 22: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and SLS.

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50

Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with SLS	1737.19	1668.15	1545.46	1219.82	1121.36	992.24
After Stored	1737.15	1668.17	1544.68	1220.12	1121.33	992.09

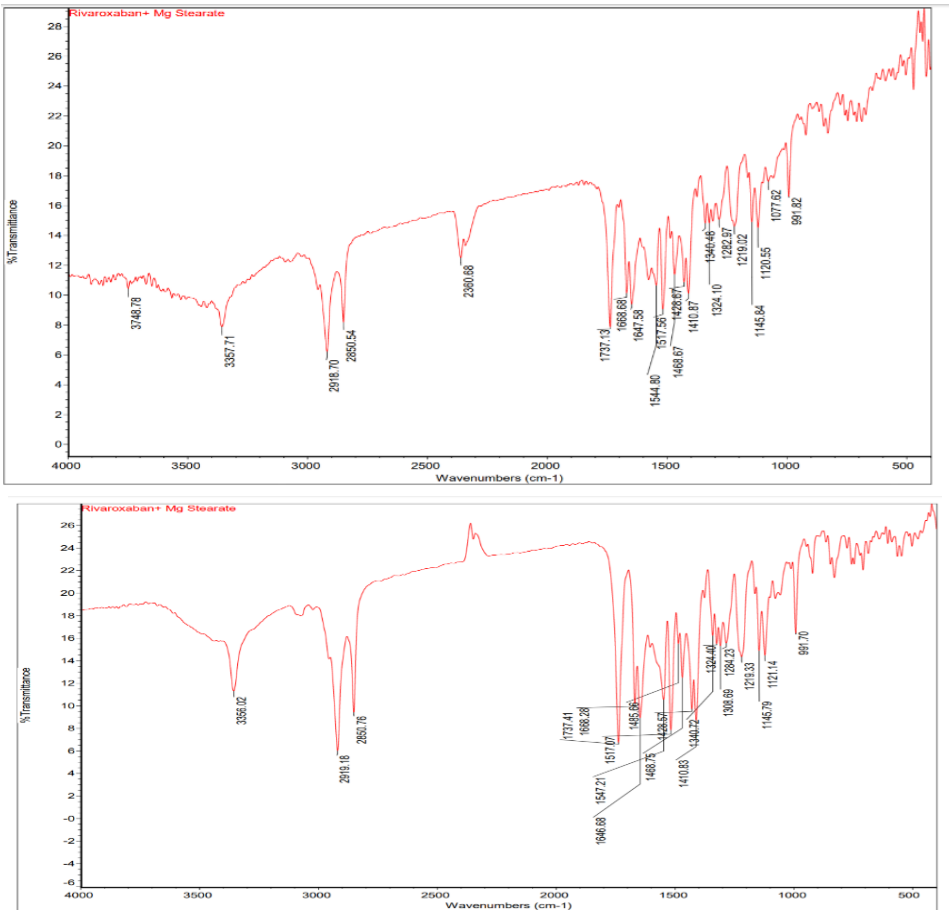
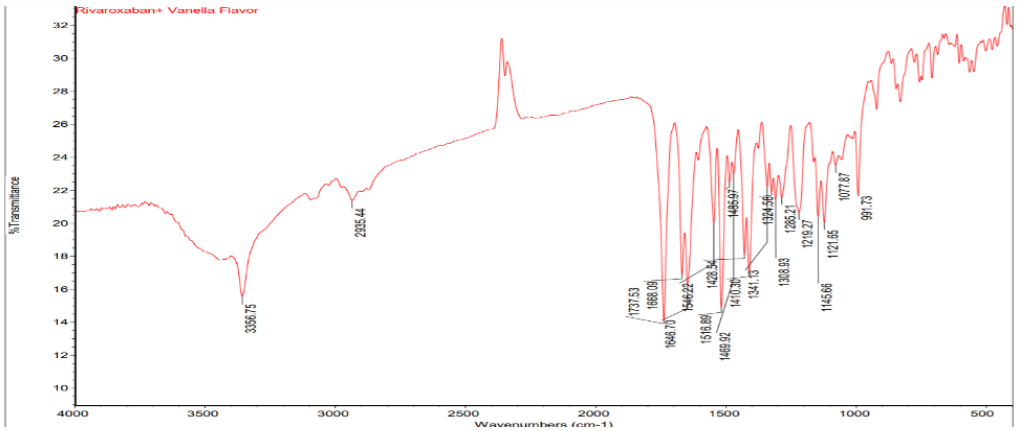


Fig. 16: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Mg. Stearate.

Table 23: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Mg. Stearate.

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with Mg. Stearate	1737.41	1668.28	1547.21	1219.33	1121.14	991.70
After Stored	1737.13	1668.68	1544.80	1219.02	1120.55	991.82



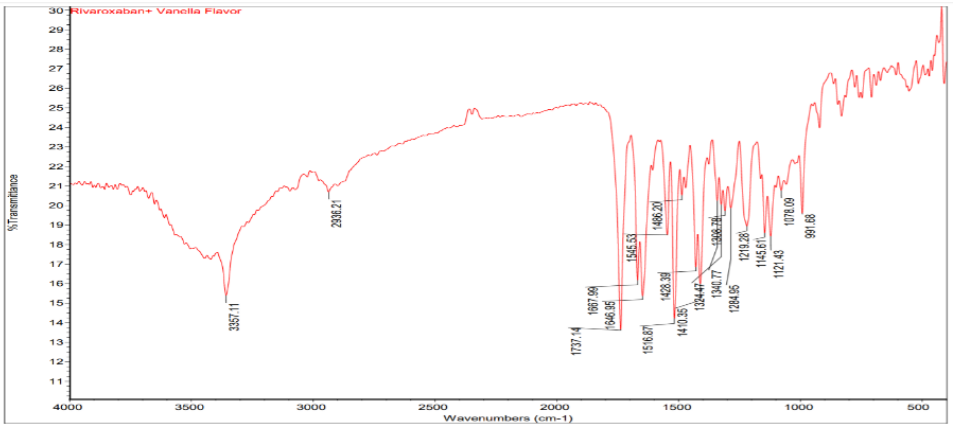


Fig. 17: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Vanilla Flavor.

Table 24: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and Vanilla Flavor.

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50
Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with Vanilla Flavor	1737.53	1668.09	1546.22	1219.27	1121.65	991.73
After Stored	1737.14	1667.99	1545.53	1219.28	1121.43	991.68

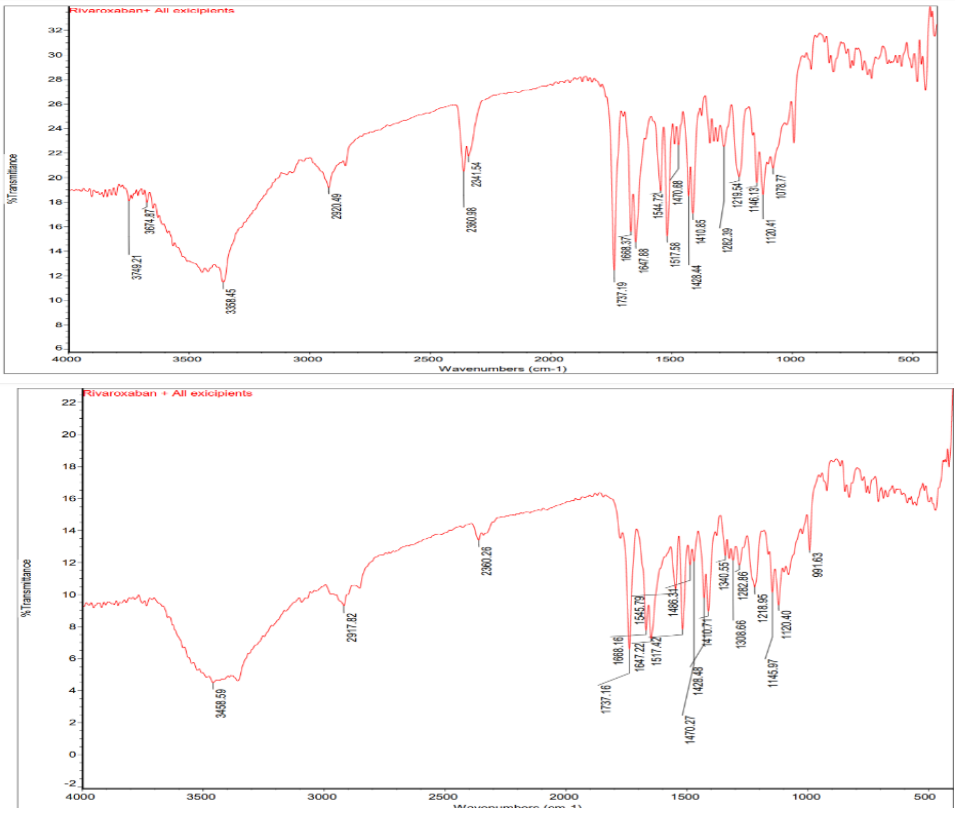


Fig. 18: FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and All Excipients.

Table 25: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Rivaroxaban and All Excipients.

Specific Functional Groups	Carbonyl C=O Stretching	Amide C=O Stretching	Aromatic C=C Stretching	C-N Stretching	S=O Stretching	C-H Bending
The Mid-IR Region (cm^{-1})	**Around 1730**	**1640-1680**	**1500-1600**	**1200-1350**	**1000-1150**	**800-1500**
Pure Drug STD	1737.44	1668.09	1545.83	1218.98	1121.72	991.50

Rivaroxaban Sample Test	1737.32	1668.08	1545.97	1218.91	1121.61	991.50
Rivaroxaban ST with All Excipients	1737.16	1668.16	1545.79	1218.95	1120.40	991.63
After Stored	1737.19	1668.37	1544.72	1219.54	1120.41	1078.77

Micrometric Properties of Rivaroxaban

The powder of Rivaroxaban was evaluated for the following parameters such as angle of repose, bulk density, tapped density, compressibility index and Hausner ratio. The results are given in Table 26.

Table 26: Micrometric Properties of Rivaroxaban.

Raw Material	Bulk Vol	Tapp Vol	Bulk D (g/ml)	Tapp D(g/ml)	Bulkiness
Rivaroxaban	12ml	5ml	0.231	0.5546	4.33
Raw Material	**Voids**	**Porosity (%)**	**Compressibility Index (%)**	**Hausner Ratio**	**Angle of Repose(θ)**
Rivaroxaban	0.583	58.33%	58.34%	2.3982	44.33

The Angle of repose of Rivaroxaban was found to be 44.33%, which indicated Passable –may hang up flow property. The bulk density was found to be 0.231 (g/ml), the tapped density was found to be 0.5546(g/ml). The compressibility index was found to be 58.34% which indicates very, very poor flowability. The hausner ratio was found to be 2.3982.

Evaluation of Precompression Parameter

Micromeritic Properties

Table 27: Evaluation of Precompression Parameters of Rivaroxaban Powder Blend.

Formulation Code	Angle of Repose (ɵ)	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Compressibility Index (%)	Hausner Ratio	Evaluation of Angle of Repose
F1	36.027	0.418	0.570	26.66	1.36	Fair
F2	35.93	0.370	0.481	23.07	1.3	Good
F3	33.514	0.370	0.510	27.45	1.37	Good
F4	36.86	0.408	0.572	28.67	1.40	Fair
F5	37.303	0.411	0.548	29.91	1.33	Fair
F6	36.21	0.424	0.530	20.0	1.25	Fair

The angle of repose of formulation 2 and 3 found to be between 33.514 to 35.93 that means its good. The angle of repose of other formulation were found to be between from 36.027 to 37.303, which indicates fair flow properties. The bulk density was found to be between 0.370 to 0.424 g/cm^3. The tapped density was found to be between 0.481 to 0.570 g/cm^3, the compressibility index was found in the range of 20.0 to 29.91% and the hausner ratio lies between 1.25 to 1.40, the results in terms of micromeritics properties revealed that the flow property of formulations F2, F3 were good and other formulations were fair as shown in Table 27.

CONCLUSION

The compatibility studies of physical mixtures of Rivaroxaban with different used excipients such as mannitol, microcrystalline cellulose 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 Rivaroxaban formulations prepared were evaluated for precompression parameters and powder flow properties which were found to be within limits. It was concluded that the drug Rivaroxaban was found to be compatible with various excipients which were selected for the formulation development of the Rivaroxaban 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.

ACKNOWLEDGEMENT

The authors are thankful to Modern Pharmaceutical Industry Company -Yemen and Shaphaco Pharmaceutical Industry Company-Yemen for their support and facilities.

REFERENCES

1. Sastry SV, Nyshadham JR, Fix JA. Recent Technological Advances in Oral Drug Delivery - A Review. Pharm Sci Technol Today., 2000; 3(4): 138-145.
2. Sravani M. Formulation and Evaluation of Mouth Dissolving Tablets of Nebivolol HCl for Treatment of Hypertension. Int J Pharma Chem Res., 2017; 3: 200-212.
3. Gandhi L, Akhtar MS. Comparative Study on Effect of Natural and Synthetic Superdisintegrants in the Formulation of Orodispersible Tablets. J Drug Deliv Ther., 2019; 9(2): 507-513.
4. Santosh Kumar R, Kumari A. Fast Dissolving Tablets: Waterless Patient Compliance Dosage Forms. J Drug Deliv Ther., 2019; 9(1): 303-317.
5. LexiChem. Available from:

https://pubchem.ncbi.nlm.nih.gov/compound/9875401.
6. Mueck W, Stampfuss J, Kubitza D, Becka M. Clinical Pharmacokinetic and Pharmacodynamic Profile of Rivaroxaban. Clin Pharmacokinet., 2014; 53: 1–16.
7. Roy A. Orodispersible Tablets: A Review. Asian J Pharm Clin Res., 2016; 9(1): 19-26.
8. Raymond CR, Paul JS, Marian EQ. Handbook of Pharmaceutical Excipients, 6th Edition. Pharmaceutical Press and American Pharmacists Association., 2009; S48-S760.
9. Vishali T, Damodharan N. Orodispersible Tablets: A Review. Res J Pharm Tech., 2020; 13(5): 2522-2529.
10. Nagar P, Singh K, Chauhan I, Verma M, Yasir M, Khan A, Sharma R, Gupta N. Orally disintegrating Tablets: Formulation, Preparation Techniques and Evaluation. J Appl Pharm Sci., 2011; 35-45.
11. Sivagurunathan D. Formulation and *In-Vitro* Evaluation of Rivaroxaban Immediate Release Tablets: An Approach to Improving Oral Bioavailability Using Solid Dispersion Technique. The Tamil Nadu Dr. M.G.R. Medical University., 2020; 600032.
12. Sandhyarani G, Sarangapani M. Formulation and Evaluation of Orodispersible Tablets of Domperidone. IOSR J Pharm., 2016; 6(9): 39-47.
13. Upadhyay P, et al. A Review on Formulation and Evaluation Approaches for Fast Release Tablet. Mathews J Pharma Sci., 2023; 7(1): 15.
14. Ramu S, Kumar YA, Rao DS, Ramakrishna G. Formulation and Evaluation of Valsartan Oral Dispersible Tablets by Direct Compression Method. Am J Adv Drug Deliv., 2014; 1: 2321-547X.
15. Pankaj M. A Discriminatory Drug Dissolution Method for Estimation of Rivaroxaban from Rivaroxaban Tablets. Scholars Res Library Der Pharmacia Lett., 2019; 11(2): 97-103.
16. Gupta H, Bhandari D, Sharma A. Recent Trends in Oral Drug Delivery: A Review. Recent Pat Drug Deliv Formul., 2009; 3: 162-173.
17. Kakar S, Singh R, Kumar S. Orodispersible Tablets: an Overview. MOJ Proteomics Bioinform., 2018; 7(3): 180-182.
18. Hirani JJ, Rathod DA, Vadalia KR. Orally Disintegrating Tablets: A Review. Trop J Pharm Res., 2009; 8(2): 161-172.
19. Gupta DK, Maurya A, Varshney MM. Orodispersible Tablet: An Overview of Formulation and Technology. World J Pharm Pharm Sci., 2020; 9(2): 1408.
20. Pandy P, Dahiya M. Oral disintegrating Tablets: A Review. Int J Pharma Res., 2016; 5(1): 51.
21. Bhowmik D, Chiranjib B, Krishnath P, Chaandira RM. Fast Dissolving Tablet: an Overview. J Chem Pharm Res., 2009; 1(1): 165.
22. Arora P, Sethi VA. Orodispersible Tablet: a Comprehensive Review. Int J Res Drug Dev Pharm Life Sci., 2013; 2(2): 271-272.
23. Jassem NA. Orodispersible Tablets: a Review on Recent Trends in Drug Delivery. IJDDT., 2022; 12: 433.
24. Nehal SM, Garima G, Pramod KS. Fast Dissolving Tablets: Preparation, Characterization and Evaluation: an Overview. Int J Pharm Sci Rev Res., 2015; 31(2): 243-250.
25. Deshmukh H, Chandrashekhara S, Nagesh C, Murade A, Usgaunkar S. Superdisintegrants: a Recent Investigation and Current Approach. Asian J Pharm Tech., 2012; 2: 19-25.
26. Abha, Kaur LP. Superdisintegrations: an Arising Exemplar in Orodispersible Tablets. Int J Drug Res Technol., 2015; 5(1): 1-12.
27. Patil NC, Raja K. Formulation and Evaluation of Orodispersible Tablets of Metoclopramide Hydrochloride. Tamilnadu Dr.M.G.R. Medical University., 2012; 638-652.
28. Drug Information Handbook: a Comprehensive Resource for All Clinicians and Healthcare Professionals. 21st ed. American Pharmacist Association and Lexi-Comp., 2012; S1620.
29. BNF. BMJ Group and Royal Pharmaceutical Society. September 2022-March 2023; S140-S141.
30. Preston CL. Stockley's Drug Interaction Pocket Companion. 2nd ed. Pharmaceutical Press., 2015; S119-S576.
31. Borse LB, Bendale AR, Borse SL, Naphade VD, Jadhav AG. Formulation and Evaluation of Mouth Dissolving Tablet Rivaroxaban and its Validation. Biosci Biotechnol Res Asia., 2022; 19(4): 943-954.
32. Stuart BH. Infrared Spectroscopy: Fundamentals and Applications. 1st ed. Wiley., 2004; S168.
33. Bharate SS, Bharate SB, Bajaj AN. Interactions and Incompatibilities of Pharmaceutical Excipients with Active Pharmaceutical Ingredients: A Comprehensive Review. J Excip Food Chem., 2010; 1: 3-26.
34. Moyano MA, Broussalis AM, Segall A. Thermal Analysis of Lipoic Acid and Evaluation of the Compatibility with Excipients. J Therm Anal Cal., 2010; 99: 631-637.
35. Ceresole R, Han Y, Rosasco MA, Orelli LR, Segall AI. Drug-Excipient Compatibility Studies in Binary Mixtures of Avobenzone. J Cosmet Sci., 2013; 64: 317-328.
36. Chadha R, Bhandari S. Drug–Excipient Compatibility Screening—Role of Thermoanalytical and Spectroscopic Techniques. J Pharm Biomed Anal., 2014; 87: 82-97.
37. McDaid FM, Barker SA, Fitzpatrick S, Petts C, Craig DQM. Further Investigations into The Use of High Sensitivity Differential Scanning Calorimetry as A Means of Predicting Drug–Excipient Interactions. Int J Pharm., 2003; 252: 235-240.
38. O'Neill MA, Gaisford S. Application and Use of Isothermal Calorimetry in Pharmaceutical Development. Int J Pharm., 2011; 417: 83-93.
39. Ferraz Pinto M, Afonso de Moura E, Santos de Souza F, Oliveira Macêdo R. Thermal Compatibility

Studies of Nitroimidazoles and Excipients. J Therm Anal Cal., 2010; 102: 323-329.
40. Oliveira Santos AF, Basilio Jr ID, Souza FS,Medeiros AFD, Ferraz Pinto M, de Santana DP. Application of Thermal Analysis of Binary Mixtures with Metformin. J Therm. Anal Cal., 2008; 93: 361-364.
41. Chou YP, Huang JY, Tseng JM, Cheng Y, Shu CM. Reaction Hazard Analysis for The Thermal Decomposition of Cumene Hydroperoxide in The Presence of Sodium Hydroxide. J Therm Anal Cal., 2008; 93: 275-280.
42. Sashima ES, Janowska G, Zaborski M, Vnuchkin AV. Compatibility of Fibroin/Chitosan and Fibroin/Cellulose Blends by Thermal Analysis. J Therm Anal Cal., 2007; 89: 887-891.
43. Medeiros AFD, Santos AFO, de Souza FS, Júnior IDB, Valdilânio J, Procópio JVV, de Santana DP, Macêdo RO. Thermal Studies of Preformulates of Metronidazole Obtained by Spray Drying Technique. J Therm Anal Cal., 2007; 89: 775-781.
44. Silva MAS, Kelmann RG, Foppa T, Cruz AP, Bertol CD Sartori T, Granada A, Carmignan F, Murakami FS. Thermoanalytical Study of Fluoxetine Hydrochloride. J Therm Anal Cal., 2007; 87: 463-467.
45. Lira AM, Araújo AAS, Basílio IDJ, Santos BLL, Santana DP, Macêdo RO. Compatibility Studies of Lapachol with Pharmaceutical Excipients for The Development of Topical Formulations. Thermochim Acta., 2007; 457: 1- 6.
46. Mura P, Furlanetto S, Cirri M, Maestrelli F, Marras AM, Pinzauti S. Optimization of Glibenclamide Tablet Composition Through the Combined Use of Differential Scanning Calorimetry and D-Optimal Mixture Experimental Design. J Pharm Biomed Anal., 2005; 37: 65-71.
47. Araújo AAS, Storpirtis S, Mercuri LP, Carvalho FMS, dos Santos Filho M, Matos JR. Thermal Analysis of The Antirretroviral zidovudine (AZT) and Evaluation of The Compatibility with Excipients Used in Solid Dosage Forms. Int J Pharm., 2003; 260: 303-314.
48. Matos APS, Costa JS, Boniatti J, Seiceira RC, Pitaluga Jr A, Oliveira DL, Visçosa AL, Holandino C. Compatibility Study Between Diazepam and Tablet Excipients. J Therm Anal Cal., 2017; 127: 1675-1682.
49. Liltorp K, Larsen TG, Willumsen B, Holm R. Solid State Compatibility Studies with Tablet Excipients Using Non Thermal Methods. J Pharm Biomed Anal., 2011; 55: 424-428.
50. Verma RK, Garg S. Selection of Excipients for Extended-Release Formulations of Glipizide Through Drug–Excipient Compatibility Testing. J Pharm Biomed Anal., 2005; 38: 633-644.
51. Verma RK, Garg S. Compatibility Studies between Isosorbide Mononitrate and Selected Excipients Used in The Development of Extended-Release Formulations. J Pharm Biomed Anal., 2004; 35: 449-458.
52. Silva LAD, Teixeira FV, Serpa RC, Esteves NL, dos Santos RR, Lima EM, da Cunha-Filho MSS, de Souza Araújo AA, Taveira SF, Marreto RN. Evaluation of Carvedilol Compatibility with Lipid Excipients for The Development of Lipid-Based Drug Delivery Systems. J Therm Anal Cal., 2016; 123: 2337-2344.
53. Veiga A, Oliveira PR, Bernardi LS, Mendes C, Silva MAS, Sangoi MS, Janissek PR, Murakami FS. Solid-State Compatibility Studies of A Drug Without Melting Point. J Therm Anal Cal., 2018; 131: 3201-3209.
54. Rus LM, Tomuta I, Iuga C, Maier C, Kacso I, Borodi G, Bratu I, Bojita M. Compatibility Studies of Indapamide/Pharmaceutical Excipients Used in Tablet Preformulation. Farmacia., 2012; 60: 92-101.
55. Tomassetti M, Catalani A, Rossi V, Vecchio S. Thermal Analysis Study of The Interactions between Acetaminophen and Excipients in Solid Dosage Forms and in Some Binary Mixtures. J Pharm Biomed Anal., 2005; 35: 949-955.
56. Ding T, Chen L, Zhai LH, Fu Y, Wang-Sun B. Compatibility Study of Rivaroxaban and Its Pharmaceutical Excipients. J Therm Anal Cal., 2017; 130: 1569-1573.
57. Pires SA, Mussel WN, Yoshida MI. Solid-State Characterization and Pharmaceutical Compatibility between Citalopram and Excipients Using Thermal and Non-Thermal Techniques. J Therm Anal Cal., 2017; 127: 535- 542.
58. Joshi BV, Patil VB, Pokharkar VB. Compatibility Studies between Carbamazepine and Tablet Excipients Using Thermal and Non-Thermal Methods. Drug Devel Ind Pharm., 2002; 28: 687–694.
59. Stulzer HK, Rodrigues PO, Cardoso TM, Matos JSR, Silva MAS. Compatibility Studies between Captopril and Pharmaceutical Excipients Used in Tablets Formulations. J Therm Anal Cal., 2008; 9: 323-328.
60. USP-NF Rivaroxaban Tablets. Available from: https://online.uspnf.com.
61. DrugBank. Rivaroxaban \ (https://go.drugbank.com/drugs/DB06228).
62. Reddy RA, Ramesh B. Kishan V. Drug-Excipient Interaction During Formulation Development In -Vitro and In -Vivo Evaluation of Gastroretentive Drug Delivery System for Nizatidine. Int J Pharm Sci Nanotech., 2013; 6: 2281-2293.
63. Prathyusha CH, Murthy TEGK. Compatibility Studies of Donepezil with Different Excipients by Using HPLC and FTIR. J Adv Pharm Tech Res., 2013; 3: 273-278.
64. Jangde R, Singh D. Compatibility Studies of Quercetin with Pharmaceutical Excipients used in The Development of Novel Formulation. Research J Pharm and Tech., 2014; 7: 1101-1105.

65. Tiwari SP, Vidyasagar G. Identification, Characterization, and Drug Excipient Compatibility of Diltiazem Hydrochloride by Physico-Chemical Techniques UK. J Pharm Bio Sci., 2014; 2: 49-53.
66. Gupta A, Kar HK. Solid State Compatibility Studies of Miconazole Using Thermal and Spectroscopic Methods. Adv Anal Chem., 2015; 5: 51-55.
67. Khan MI, Madni A, Ahmad S, Khan A, Rehman M, Mahmood MA. ATRFTIR Based Pre and Post Formulation Compatibility Studies for The Design of Niosomal Drug Delivery System Containing Nonionic Amphiphiles and Chondroprotective Drug. J Chem Soc Pak., 2015; 37: 527-534.
68. da Silva EP, Pereira MAV, de Barros Lima IP, Barros Lima NGP, Barboza EG, Aragã CFS, Gomes APB. Compatibility Study between Atorvastatin and Excipients Using DSC and FTIR. J Therm Anal Cal., 2016; 123: 933- 939.
69. Amir IM, Amir ME, Osama AA, Suzan A, Alaa IM. Investigation of Drug–Polymer Compatibility Using Chemometric-Assisted UV Spectrophotometry. Pharmaceutics., 2017; 9: 1-13.
70. Canbay HS, Doğantürk M. Application of Differential Scanning Calorimetry and Fourier Transform Infrared Spectroscopy to The Study of Metoprolol-Excipient and Lisinopril-Excipient Compatibility. Eurasian., J Anal Chem., 2018; 13: 1-7.
71. Monajjemzadeh F, Hassanzadeh D, Valizadeh H, Siahi-Shadbad MR, Mojarrad JS, Robertson TH, Roberts MS. Compatibility Studies of Acyclovir and Lactose in Physical Mixtures and Commercial Tablets. Eur J Pharm Biopharm., 2009; 73: 404-413.
72. Mura P, Manderioli A, Bramanti G, Furlanetto S, Pinzauti S. Utilization of Differential Scanning Calorimetry as A Screening Technique to Determine The Compatibility of ketoprofen with Excipients. Int J Pharm., 1995; 119: 71-79.
73. Malan CEP, de Villiers MM, Lötter AP. Application of Differential Scanning Calorimetry and High-Performance Liquid Chromatography to Determine the Effects of Mixture Composition and Preparation During The Evaluation of Niclosamide-Excipient Compatibility. J Pharm Biomed Anal., 1997; 15: 549-557.
74. Daniel JSP, Veronez IP, Lopez Rodriguez L, Trevisan MG, García JS. Risperidone – Solid-State Characterization and Pharmaceutical Compatibility Using Thermal and Non-Thermal Techniques. Thermochim Acta., 2013; 568: 148-155.
75. Lima NGPB, Lima IP, Barros DMC, Oliveira TS, Raffin FN, de Lima e Moura TFA, Medeiros ACD, Gomes APB, Aragão CFS. Compatibility Studies of Trioxsalen with Excipients by DSC, DTA, and FTIR. J Therm Anal Cal., 2014; 115: 2311-2318.
76. Rosasco MA, Bonafede SL, Faudone SN, Segall AI. Compatibility Study Between Tobramycin and Pharmaceutical Excipients Using Differential Scanning Calorimetry, FT-IR, DRX and HPLC. J Therm Anal Cal., 2018; 134: 1929-1941.
77. Rojek B, Wesolowski M. Fourier Transform Infrared Spectroscopy Supported by Multivariate Statistics in Compatibility Study of Atenolol with Excipients. Vib Spectrosc., 2016; 86: 190–197.
78. Prasanna Kumar et al. An Overview on Preformulation Studies. Indo Am J Pharm Sci., 2015; 2(10).
79. Allen L, Ansel H. Pharmaceutical Dosage Forms and Drug Delivery Systems by Ansel (10th Edition). Lippincott Williams & Wilkins, Philadelphia., 2014.
80. Beringer P, Gupta PK, Felton L. Stability of Pharmaceutical Products. Remington: The Science and Practice of Pharmacy., 2005; 01: 1029-30.
81. Kumar BP, Sahu RK, Ramamurthy KV, Rao S, Ramu B. A Review on Mechanism, Importance and Methods of Compatibility Testing in the Formulation of Dosage Forms. Journal of Chemical and Pharmaceutical Sciences., 2011; 4(4): 141-151.
82. Nishath F, Tirunagari M, Husna KQ, Nandagopa A, Rao JV. Drug-Excipient Interaction and its Importance in Dosage Form Development. J Applied Pharma Sci., 2011; 1(06): 66-71.
83. Crowely P, Martini LG. Drug Excipient Interactions. Pharmaceutical Technology., 2001; 3: 0582.
84. Chadha R, Arora P, Bhandari S, Bala M. Thermomicroscopy and its Pharmaceuticals Applications. Current Microscopy Contributions to Advances in Science and Technology., 2012; 1017-23.
85. Harding L, Qi S, Hill G, Reading M, Craig DQM. The Development of Microthermal Analysis and Photo Thermal micro-Spectroscopy as Novel Approaches to Drug–Excipient Compatibility Studies. Int J Pharm., 2008; 354: 149-57.
86. Stephenson GA, Forbes RA, Reutzel-Edens SM. Characterization of the Solid State: Quantitative Issue. Advanced Drug Delivery Reviews., 2001; 48: 67-90.
87. Tishmack PA, Bugay DE, Byrn SR. Solid-State Nuclear Magnetic Resonance Spectroscopy-Pharmaceutical Applications. J Pharm Sci., 2003; 92: 441-474.
88. Karin LA, Trine GL, Birgitte W, Holma R. Solid State Compatibility Studies with Tablet Excipients Using Non Thermal Methods. J Pharm and Biomedical Analysis., 2011; 55: 424-28.
89. Deokate U, Gorde AM. Forced Degradation and Stability Testing: Strategies and Analytical Perspectives. Int J Pharm Sci Rev and Res., 2014; 42: 242-250.
90. Lena Ohannesian, Antony J. Streeter. Handbook of Pharmaceutical Analysis, Marcel Dekker, Inc., 2002.
91. Banker G, Rhodes CT. Modern Pharmaceutics, Marcel Dekker, Inc., 2000.
92. Harry G Britain. Spectroscopic Methods for the Characterization of Drug Substances, Marcel Dekker, Inc., 2008.
93. Lewis IR, Edwards HGM. Handbook of Raman Spectroscopy, New York: Marcel Dekker., 2001.

94. Blachere JR, Harry G. Brittain. X-Ray Diffraction Methods for the Characterization of Solid Pharmaceutical Materials, Marcel Dekker, Inc., 2008.
95. US Pharmacopoeia 30, National Formulary 25, USP Convention, Rockville., 2007.
96. Pires SA, Mussel WN, Yoshida MI. Solid-State Characterization and Pharmaceutical Compatibility between Citalopram and Excipients Using Thermal and Non-thermal Techniques. J Therm Anal Cal., 2017; 127: 535- 542.
97. Dave, VS, et al. Investigation of the Physical-Mechanical Properties of Eudragit(R) RS PO/RL PO and their Mixtures with Common Pharmaceutical Excipients. Drug Dev Ind. Pharm., 2013; 39(7): 1113-1125.
98. Cantor SL, et al. Development and Optimization of Taste-Masked Orally Disintegrating Tablets (ODTs) of Clindamycin Hydrochloride. Drug Dev Ind Pharm., 2014; 7: 1-9.
99. Tita B, et al., Compatibility Study between Ketoprofen and Pharmaceutical Excipients Used in Solid Dosage Forms. J Pharm Biomed Anal., 2011; 56(2): 221-227.
100. Tita D, et al., Compatibility Study of the Acetylsalicylic Acid with Different Solid Dosage Forms Excipients. J Therm Anal Calorim., 2013; 112(1): 407-419.
101. USFDA, Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach., 2004.
102. USFDA, Guidance for Industry - ICH Q8 (R2) Pharmaceutical Development, C. CDER, Editor. USFDA: Silver Spring, MD., 2009; 1-20.
103. Wu Y, et al. Reactive Impurities in Excipients: Profiling, Identification and Mitigation of Drug-Excipient Incompatibility. AAPS PharmSciTech., 2011; 12(4): 1248-1263.
104. Narang A, et al. Impact of Excipient Interactions on Solid Dosage Form Stability. Pharm Res., 2012; 29(10): 2660-2683.
105. Rowe RC, Sheskey PJ, Quinn ME. Handbook of Pharmaceutical Excipients. Sixth Edition. London. APhA/Pharmaceutical Press., 2009.
106. Sims J, et al. A New Approach to Accelerated Drug-Excipient Compatibility Testing. Pharm Dev Technol., 2003; 8(2): 119.
107. Skotnicki M, et al. Bisoprolol and Bisoprolol-Valsartan Compatibility Studied by Differential Scanning Calorimetry, Nuclear Magnetic Resonance and X-Ray Powder Diffractometry. Pharm Res., 2014.
108. Liltorp K, et al. Solid-State Compatibility Studies with Tablet Excipients Using Non-Thermal Methods. J Pharm Biomed Anal., 2011; 55(3): 424-428.
109. Épshtein NA. Compatibility of Medicinal and Excipient Substances in the Development of Medicinal Formulations. Pharm Chem J., 2018; 52(7): 648–57.
110. ICH Topic Q8 (R2). Pharmaceutical development., 2009; 8.
111. Thomas VH, Naath M. Design and Utilization of the Drug-Excipient Chemical Compatibility Automated System. Int J Pharm., 2008; 359(1– 2): 150–7.
112. Michael E Aulton, Pharmaceutics- The Sciences of Dosage Form Design, 4rth International Edition, Churchill Livingstone, USA., 2013; 367-389.
113. Leon Lachman, Lieberman's. The Theory and Practice of Industrial Pharmacy. Indian 4rth Edition, CBS Publisher, Reprint., 2020; 217-251.
114. Mark Gibson. Pharmaceutical Preformulation and Formulation. HIS Health Group, CRC, United state of America., 2004; 20- 45.
115. WHO. Annex (3). Pharmaceutical Development of Multisource (Generic) Finished Pharmaceutical Products.
116. Rewar S, Singh CJ, Bansal BK, Pareek R, Sharma AK. Oral Dispersible Tablet: an Overview, Development, Technologies and Evaluation. Int J Res Dev Pharma Life Sci., 2014; 3(4, Suppl 6): 1223-35.
117. Sunil Kumar BG, Felix JV, Vishwanath BA. Formulation and Evaluation of Dispersible Tablet of Cefixime Trihydrate. Int J Pharma Drug Analysis., 2014; 2(1): 858-68.
118. Walke PS, Pawar AY, Sonawane DD, Bhamber RS. Liquisolid. A Novel Technique to Enhance Solubility and Dissolution Rate of BSC Class II Pharmaceutical. J Pharm Res., 2011; 4(11): 4011-4.
119. Brough C, Williams RO. Amorphous Solid Dispersions and Nanocrystal Technologies for Poorly Water-Soluble Drug Delivery. Int J Pharm., 2013; 453: 157–66.
120. Samal HB, Debata. Solubility and Dissolution Improvement of Aceclofenac Using β-Cyclodextrin. Int J Drug Dev Res., 2012; 4: 326-33.
121. Zingone G, Rubessa F. Preformulation Study of the Inclusion Complex Warfarin-β-Cyclodextrin. Int J Pharm., 2005; 291: 3-10.
122. Hrishav DP, Nath B. Formulation and Evaluation of Oral Fast Disintegrating Tablet of Ibuprofen Using Two Super Disintegrants. Int J Curr Pharm Res., 2017; 9: 92-5.
123. Guo Y, Luo J, Tan S, Otieno BO, Zhang Z. The Applications of Vitamin E TPGS in Drug Delivery. Eur J Pharm Sci., 2013; 49(2): 175-86.
124. Lipinski CA, Lombardo. Experimental and Computational Approaches to Estimate Solubility and Permeability in Drug Discovery and Development Settings. Adv Drug Deliv Rev., 2011; 46: 3-26.
125. Alburyhi MM. Doctor Thesis, Faculty of Pharmacy, Cairo University., 2009.
126. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Pandanus Odoratissimus Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Breast Cancer. World Journal of Pharmaceutical Research., 2024; 13(8): 1092-1112.

127. Alburyhi MM, Noman MA, Saif AA, Salim YA, Hamidaddin MA, Yahya TA, Al-Ghorafi MA, Abdullah JH. Lisinopril-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(16): 59-111.
128. Alburyhi MM, Noman MA, Saif AA, Hamidaddin MA, Yahya TA, Al-Ghorafi MA. Rosuvastatin-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(13): 1549-1582.
129. Alburyhi MM, Noman MA, Saif AA, Al-Ghorafi MA, Yahya TA, Yassin SH, Al Khawlani MA. Diclofenac-Excipient Compatibility Studies for Advanced Drug delivery Systems Development. World Journal of Pharmaceutical Research., 2024; 13(14): 1297-1333.
130. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Vera Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(4): 1408-1423.
131. Hamidaddin MA, Alburyhi MM, Noman MA, Saif AA. Formulation and Evaluation of Rosuvastatin Fast Dissolving Tablets. World Journal of Pharmacy and Pharmaceutical Sciences., 2023; 12(9): 2293-2303.
132. Saif AA, Alburyhi MM, Noman MA, Almaktari AM. Formulation and Evaluation of Trimetazidine Hydrochloride and Clopidogrel Bisulphate Multi-Unit Solid Dosage Forms. Journal of Chemical Pharm Research., 2014; 6(2): 421-426.
133. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Curcuma Longa Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(6): 37-43.
134. Alburyhi MM, Saif AA, Noman MA, Al Ghoury AA. Formulation and Evaluation of Antimalarial Drugs Suppositories. World Journal of Pharmaceutical Research., 2023; 12(20): 89-108.
135. Alburyhi MM, Saif AA, Noman MA, Salim YA, Hamidaddin MA. Formulation and Evaluation of Lisinopril Orally Disintegrating Tablets. World Journal of Pharmacy and Pharmaceutical Sciences., 2023; 12(9): 357-369.
136. Alburyhi MM, Saif AA, Noman MA. Stability Study of Six Brands of Amoxicillin Trihydrate and Clavulanic Acid Oral Suspension Present in Yemen Markets. Journal of Chemical Pharm Research., 2013; 5(5): 293-296.
137. Saif AA, Alburyhi MM, Noman MA. Formulation and Evaluation of Ketoprofen Fast Dissolving Tablets. International Journal of Sciences., 2018; 7(09): 27- 39.
138. Alburyhi MM, Saif AA, Saif RM. Preformulation Study of Ceftriaxone and Ciprofloxacin for Lipid Based Drug Delivery Systems. EJUA-BA., 2022; 3(4): 339-350.
139. Bary AA, El-Gazayerly ON, Alburyhi MM. Formulation of Immediate Release Lamotrigine Tablets and Bioequivalence Study. Journal of Chemical Pharm Research., 2013; 5(10): 266–271.
140. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Tribulus Terrestris Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. World Journal of Pharmaceutical Research., 2024; 13(7): 1264-1282.
141. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Antitumor Activity of Artemisia Arborescence Extract Capsules as Dietary Supplement Herbal Product Against Breast Cancer. World Journal of Pharmaceutical Research., 2024; 13(3): 95-114.
142. Alburyhi MM, Hamidaddin MA, Saif AA, Noman MA. Formulation and Evaluation of Rivaroxaban Orodispersible Tablets. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(2): 2066-2092.
143. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Vera Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. World Journal of Pharmaceutical Research., 2024; 13(8): 1052-1072.
144. Alburyhi MM, Noman MA, Saif AA, Al-Ghorafi MA, Al Khawlani MA, Yahya TA. Formulation and Evaluation of Anti-acne Spironolactone Emulgel Novel Trend in Topical Drug Delivery System. World Journal of Pharmaceutical Research., 2023; 12 (22): 96-119.
145. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Aloe Rubroviolaceae Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Hepatoprotective. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(4): 53-61.
146. Alburyhi MM, Saif AA, Noman MA, Hamidaddin MA. Formulation and Evaluation of Clopidogrel Orodispersible Tablets. World Journal of Pharmaceutical Research., 2024; 13(6): 42-64.
147. Alburyhi MM, Saif AA, Noman MA, Yahya TA. Formulation, Development and Evaluation of Famotidine Orodispersible Tablets. European Journal of Pharmaceutical and Medical Research., 2023; 10(10): 56-62.
148. Noman MA, Alburyhi MM, El-Shaibany A, Alwesabi NA. Preformulation and Characterization Studies of Pandanus Odoratissimus L Extract Active Ingredient in Treatment of Nocturnal Enuresis. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(2): 1603-1620.
149. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Antibacterial Orodispersible Tablets of Artemisia Arborescence Extract Herbal Product.

European Journal of Pharmaceutical and Medical Research., 2024; 11(2): 409-417.
150. Alburyhi MM, Saif AA, Noman MA, Yassin SH. Formulation and Evaluation of Simvastatin Orodispersible Tablets. World Journal of Pharmaceutical Research., 2023; 12(16): 1033-1047.
151. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Oral Pharmaceutical Solution of Pandanus Odoratissimus L Extract Herbal Product in Treatment of Nocturnal Enuresis. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(1): 1840-1851.
152. Al-Ghorafi MA, Alburyhi MM. Evaluation and Formulation of Antifungal Activity of Dragon Blood Extract and Inorganic Salts on Dermatophytosis and Candidiasis. European Journal of Pharmaceutical and Medical Research., 2024; 11(1): 09-17.
153. Alburyhi MM, Saif AA, Noman MA, Saif RM. Recent Innovations of Delivery Systems for Antimicrobial Susceptibility Study of Ciprofloxacin Biodegradable Formulations for Post-Operative Infection Prophylaxis. European Journal of Pharmaceutical and Medical Research., 2023; 10(9): 32-36.
154. Saif AA, Alburyhi MM, Noman MA. Evaluation of Vitamin and Mineral Tablets and Capsules in Yemen Market. Journal of Chemical Pharm Research., 2013; 5(9):15-26.
155. Alburyhi MM, Saif AA, Noman MA, Al khawlani MA. Formulation and Evaluation of Bisoprolol Fast Dissolving Tablets. World Journal of Pharmaceutical Research., 2023; 12(16): 01-10.
156. Alburyhi MM, Saif AA, Noman MA, Al-Ghorafi MA. Comparative Study of Certain Commercially Available Brands of Paracetamol Tablets in Sana'a City, Yemen. European Journal of Pharmaceutical and Medical Research., 2018; 5(12): 36-42.
157. Patel PA, Ahir K, Patel VB et al. Drug-Excipient Compatibility Studies: First Step for Dosage form Development. Pharm Innov., 2015; 4: 14-20.
158. Panakanti R, Narang AS. Impact of Excipient Interactions on Drug Bioavailability from Solid Dosage Forms. Pharm Res Dordr., 2012; 29: 2639-2659.
159. Da Silveiraa LM, Fiorota AB, Xaviera TP, et al. Drug-Excipient Compatibility Assessment of Solid Formulations Containing Meloxicam. Eur J Pharm Sci., 2018; 112: 146-151.
160. Cortese F, Gesualdo M, Cortese A, et al. Rosuvastatin: Beyond the Cholesterol-Lowering Effect. Pharm Res-Dordr., 2016; 107: 1-18.
161. McTaggart F. Comparative Pharmacology of Rosuvastatin. Atherosclerosis Supp., 2003; 4: 9-14.
162. Mishra A, Sinha VR, Sharma S, et al. Molecular and Qualitative Characterization of Compatibility Between Valacyclovir Hydrochloride and Excipients as Raw Materials for Development of Solid Oral Dosage Formulation. Am J Biopharmacy Pharm Sci., 2023.
163. Berthomieu C, Hienerwadel R. Fourier Transform Infrared (FTIR) Spectroscopy. Photosynth Res., 2009; 101: 157-170.
164. Krishna BJ, Satyanarayana J, Rao NR. Rivaroxaban: Compatibility with Pharmaceutical Excipients using DSC and FTIR Spectrophotometry. J Pharm Res Int., 2022; 43-50.
165. Bele AA, Khale A. An Overview on Thin Layer Chromatography. Int J Pharm Pharm Sci., 2011; 6: 256-267.
166. Iqubal MK, Singh PK, Shuaib M, et al. Recent Advances in Direct Compression Technique for Pharmaceutical Tablet Formulation. Int J Pharm Res Develop., 2014; 6: 49-57.
167. Chavan H, Chhabra G, Gujarathi N, et al. Comparative Study of in-Process and Finished Products Quality Control Test for Tablet and Capsules According to Pharmacopoeias. Asian J Pharm Res Develop., 2018; 6: 60-68.
168. Bozal-Palabiyik B, Uslu B, Ozkan Y, et al. In-Vitro Drug Dissolution Studies in Medicinal Compounds. Curr Med Chem., 2018; 25: 4020-4036.
169. Jain P, Goel A, Sharma S, Parmar M. Solubility Enhancement Techniques with Special Emphasis on Hydrotrophy. International Journal of Pharmaceutical Research., 2009; 1(1): 34-45.
170. Patil S K, Wagh K S, Parik V B, Akarte A M, Baviskar D T. Strategies for Solubility Enhancement of Poorly Soluble Drugs, Int J Pharm Sci Rev Res., 2011; 8(2): 74-80.
171. Tyagi S, Patel C, Dadrwal P, MangukiaD,Sojitra I, NimbiwalBk, Sigh V, Subrahmanyamkv. Anovel Concept for Solubilization and Bioavailability of Poorly Soluble Drugs: Hydrotropy. Int J Pharmes and Bio Sci., 2013; 2(1): 372-381.
172. Aulton's Pharmaceutics: Pharmaceutics-the Science of Dosage Forms Design. Churchill Livingstone Elsevier.3rd Edition., 2007; 322-538.
173. Jagtap S, Magdum C, Jadge D, Rajesh Jagtap R. Solubility Enhancement Technique: A Review Published by Journal of Pharmaceutical Sciences & Research., 2018; 10(9): 2205-2211.
174. Chavda HV, Patel CN, Anand IS. A Review Article on Biopharmaceutics Classification System: Published by Systematic Reviews in Pharmacy, January-June., 2010; 1(1).
175. Shukla AK, et al. Review Article on Biopharmaceutical Classification System: Tool Based Prediction for Drug Dosage Formulation, Advance Pharmaceutical Journal., 2017; 2(6): 204-209.
176. Verma S, Rawat A, Kaul M, Saini S. Solid Dispersion: A Strategy for Solubility Enhancement. Int J Pharm Technol., 2011; 3: 1062-99.
177. Vidya N. Remington the Science & Practice of Pharmacy 21st Edition Volume 1st Lippincott Williams & Wilkins. International Journal of Pharmaceutical Sciences and Research., 2016; 7(12): 4882-4892.

178. Lindenberg M, Kopp S, Dressman J. Classification of orally administered drugs on the WHO model list of essential medicines according to biopharmaceutical classification system. European Journal of Pharmaceutics & Biopharmaceutics., 2004; 58(2): 265-278.
179. Jatwani S, Rana AC, Singh G, Aggarwal G. An Overview on Solubility Enhancement Techniques for Poorly Soluble Drugs and Solid Dispersion as an Eminent Strategic Approach. International Journal of Pharmaceutical Sciences and Research., 2012; 3(4): 942-956.
180. Thorat YS, Gonjari ID, Hosmani AH. Solubility Enhancement Techniques: A Review on Conventional and Novel Approaches. International Journal of Pharmaceutical Sciences and Research., 2011; 2(10): 2501-2513.
181. Pokharkar V, Khanna A, Venkatpurwar V, Dhar S, Mandpe L. Ternary Complexation of Carvedilol, β-Cyclodextrin and Citric acid for Mouth-Dissolving Tablet Formulation. Acta pharmaceutica., 2009; 59(2): 121-132.
182. Wells J. Pharmaceutical Preformulation, the Physiochemical Properties of Drug Substances in: M. E. Aulton (Ed), Pharmaceutics-the Science of Dosage Forms Design. 2nd Ed. Churchill LivingStone, CN, London., 2002; 113-138.
183. www.drugbank.com.
184. Patel VP, Soniwala MM. Pulsatile Drug Delivery System for Treatment of Various Inflammatory Disorders: A Review. International Journal of Drug Development and Research., 2012; 4(3).
185. Sandeep P, Venkateswara Reddy B, Navaneetha K. Formulation and Evaluation of Rosuvastatin Pulsatile Drug Delivery System by Using Press Coating Technique. Int J Res Pharm Sci., 2014; 5(1): 46-52.
186. Garg BK, Gnanarajan G, Kothiyal P. Formulation and Evaluation of Pulsatile Drug Delivery System of Rosuvastatin Calcium Using Different Swelling Polymers. The Pharma Innovation., 2012; 1(7).
187. Rane AB, Gattani SG, Kadam VD, Tekade AR. Formulation and Evaluation of Press Coated Tablets for Pulsatile Drug Delivery Using Hydrophilic and Hydrophobic Polymers. Chemical and Pharmaceutical Bulletin., 2009; 57(11): 1213-1217.
188. Jayasree B, Sridhar Babu G, Srikanth L. Formulation and Evaluation of Press Coated Pulsatile Delivery of Flurbiprofen Tablets. International Journal of Innovative Research in Technology., 2021; 8(3).
189. Giri S, Mohapatra S. Formulation and InVitro Characterization of Time Release Tablets of Propranolol Hydrochloride. Indian Journal of Pharmaceutical Sciences., 2020; 82(2): 216-221.
190. Kumar PJ, Muzib YI, Misra G. Formulation and Evaluation of Pulsatile Drug Delivery of Lovastatin. Research Journal of Pharmacy and Technology., 2018; 11(7): 2797-2803.
191. Reddy NV, Kishore K, Kumar GV. Formulation and Evaluation of Enalapril Floating Pulsatile Tablets. EPRA International Journal of Research & Development (IJRD)., 2021; 6(11): 1-11.
192. Golla C. Design and Evaluation of Press Coated Pulsatile Delivery of Doxofylline Tablets. Acta Scientific Pharmaceutical Sciences., 2018; 2(11): 58- 62.
193. Borgaonkar PA, Bushetti SS, Najmuddin M. Formulation and Evaluation of Pulsatile Drug Delivery System of Metoprolol Tartrate Using Core in Cup Tablet. American Journal of Medicine and Medical Sciences., 2012; 2(6): 114-122.
194. Adhikari C, Kulkarni GS, Swamy S. Formulation and Evaluation of Pulsatile Drug Delivery System of Salbutamol Sulfate for the Chronotherapy of Asthma. Asian J Pharm Clin Res., 2018; 11(9): 305-311.
195. Gupta MK, Saraf S. Formulation and Evaluation of Pulsatile Drug Delivery System of Ramipril for Controlling Morning Spate of BP. Journal of Pharmaceutical Research., 2018; 17(1): 2-12.
196. Rambabu S, Vallabhbhai P. Formulation and Optimization of Press-Coated Pulsatile Tablet of Felodipine by Chronopharmaceutical Approach in Treatment of Hypertension. International Journal of Pharmacy and Pharmaceutical Research., 2015; 4(2): 2349-7203.
197. Kumar B, Shah M, Kumar R. Comparison of Atorvastatin and Rosuvastatin in Reduction of Inflammatory Biomarkers in Patients with Acute Coronary Syndrome. Cureus., 2019; 11: e4898.
198. Shekhawat P, Pokharker V. Understanding Peroral Absorption: Regulatory Aspects and Contemporary Approaches to Tackling Solubility and Permeability Hurdles. Acta Pharma Sin B., 2017; 7: 260-280.
199. Rohini P, Pavani A, Raja Reddy R. Formulation and Evaluation of Orally Disintegrating Tablets of Rosuvastatin. Int J Pharm Sci Rev Res., 2014; 24: 209-214.
200. Karaźniewicz-Łada M, Bąba K, Dolatowski F. The Polymorphism of Statins and its Effect on Their Physicochemical Properties. Polim Med., 2018; 48: 77–82.
201. Tannebaum EJ. Oral Solid Dosage Facilities. in: Good Design Practices for GMP Pharmaceutical Facilities, 2nd Ed.; New York, NY, USA., 2005.
202. Lee B.J. Pharmaceutical Preformulation: Physicochemical Properties of Excipients and Powders and Tablet Characterization. in: Pharmaceutical Manufacturing Handbook: Production and Processes, John Wiley & Sons Inc: New Jersey, USA., 2008.
203. Narang AS, Mantri RV, Ragahavan KS. Excipient Compatibility and Functionality. in: Developing Solid Oral Dosage Forms: Pharmaceutical Theory and Practice, 2nd Ed.; Elsevier Inc: London., 2017.
204. Sachin TV, Deodhar MN, Prakya V. Advances in Analytical Techniques Used in Predicting Drug-

Excipient Interactions. Int J Pharm Tech., 2014; 6: 6388-6417.
205. Rameshbai M, Manikkath J, Sivkumar K. Long Circulating PEGylated-Chitosan Nanoparticles of Rosuvastatin Calcium: Development and InVitro and In Vivo Evaluations. Int J Biol Macromol., 2018; 107: 2190-2200.
206. Davies P. Oral Solid Dosage Form. in: Pharmacetuical Preformulation and Formulation, 2nd Ed., Gibson M, Ed. Informa HealthCare: New York, NY, USA., 2009.
207. Creekmore JR, Wiggins NA. Pharmaceutical Composition Comprising an HMG COA Reductase Inhibitor. European Patent Office. Patent No. EP1223918., 2002.
208. Singh J, Walia M, Harikumar S. Formulation and Evaluation of Fast Dissolving Tablets of Rosuvastatin: Research Article. Journal of Drug Delivery & Therapeutics. JDDT., 2014; 4: 173-81.
209. Kiss D, Zelko R, Novak C. Application of DSC and NIRS to Study the Compatibility of Metronidazole with Different Pharmaceutical Excipients. J Therm Anal Calorim., 2006; 84: 447-451.
210. Chamarthi, RP, Kishore GV, Krishna Mohan. Structural Identification, and Estimation of Rosuvastatin Calcium Related Impurities in Rosuvastatin Calcium Tablet Dosage Form. Anal Chem Research., 2017; 12: 17-27.
211. Schwartz JB. Scale Up of the Compaction and Tableting process. in Pharmaceutical Process Scale Up; Marcel Dekker Inc.: New York, NY, USA., 2002.
212. Zhou C, Gao W, Lu G. Preparation, Characterization, and InVitro Release of Microparticles Based on Dextran-Rosuvastatin Conjugate. Carbohydrate Polymers., 2013; 96: 156–162.
213. Chaves L, Rolim L, Gonc¸alves M, Couto A. Study of Stability and Drug-Excipient Compatibility of DiethylCarbamazine Citrate. Journal of Thermal Analysis and Calorimetry., 2013; 111: 2179–2186.
214. Hariharan M, Gupta VK. A Novel Compression Coated Tablet Dosage Form. Pharm Tech., 2001; 14–19.
215. Akbari BV, Valaki BP, Maradiya VH Akbari AK, Vidyasagar G. Development and Evaluation of Oral Dispersible Tablets of Rosuvastatin Calcium-HP-β-CD Inclusion Complex by Using Different Superdisintegrants. Int J Pharm Technol., 2011; 3(1): 1842-1859.
216. Leon La Sreenivas SA, Dangagi PM, Gadad AP, Godbole AM, Hiremath SP, Bhagawati ST. Orodispersible tablets: Newfangled Drug Delivery System-A Review. Indian J Pharm Educ., 2005; 39(4): 177-181.
217. ICH Guidelines Q1A (R2), Guidelines for Industry, Stability Testing of New Drug Substance and Product. Availale online: http://www.ICH.org.
218. Cao QR, Kim TB, Lee JB. Photoimages and the Release Characteristics of Lipophilic Matrix Tablets Containing Highly Water-Soluble Potassium Citrate with High Drug Loadings. Int J Pharm., 2007; 339: 19–24.
219. Corti G, Cirri M, Maestrelli F, Mennini N. Sustained-Release Matrix Tablets of Metformin Hydrochloride in Combination with Triacetyl-B-Cyclodextrin. European Journal of Pharmaceutics and Biopharmaceutics., 2008; 68: 303–309.
220. Furlanetto S, Cirri, M, Maestrelli F, Corti G, Mura P. Study of Formulation Variables Influencing the Drug Release Rate from Matrix Tablets by Experimental Design Pharm Tech., 2006; 62: 77–84.
221. Masaki A, Sayaka K, Yuichi O, Yukiharu N. Development and Evaluation of a Novel Dry-Coated Tablet Technology for Pellets as a Substitute for the Conventional Encapsulation Technology. International Journal of Pharmaceutics., 2004; 336(1): 99–107.
222. Holte K, Onsøyen E, Myrvold R, Karlsen J. Sustained Release of Water-Soluble Drug from Directly Compressed Alginate Tablets, E. J of Pharmaceutical Sciences., 2003; 20: 403–407.
223. Jeong HS, Park K. Development of Sustained Release Fast-Disintegrating Tablets Using Various Polymer Coated Ion-Exchange Resin Complexes. Int J Phar., 2008; 353: 195–204.
224. Indian Pharmacopoeia, The Indian Pharmacopoeia Commission, Ghaziabad, 6th Ed., 2010; 2: 806, 1337, 2071.
225. Martindale. The Extra Pharmacopoeia, The Complete Drug Reference, edited by Sean C Sweetman, Pharmaceutical press, 34th Ed., 2005; 862,915,966,968,996-997.
226. Herbert A Lieberman, Leon Lachman, Joseph B, Schwartz. Pharmaceutical dosage forms tablets. Marcel Dekker, New York, USA, 2 nd Edition., 2009.
227. Leon Lachman, Lieberman H A.The Theory and Practice of Industrial Pharmacy, Lea and Febiger, Philadelphia, USA, 3 rd Edition., 2003.
228. Markl D, Zeitler JA. A Review of Disintegration Mechanisms and Measurement Techniques, Pharmaceutical research., 2017; 34(5): 890.
229. Seo KS, Bajracharya R, Lee SH, Han HK. Pharmaceutical Application of Tablet Film Coating, Pharmaceutics., 2020; 12(9): 853-862.
230. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Pandanus Odoratissimus Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Hepatoprotective. European Journal of Pharmaceutical and Medical Research., 2024; 11(4): 06-13.
231. Noman MA, Alburyhi MM, Alqubati MA. Preformulation and Characterization Studies of Clopidogrel Active Ingredient for Orodispersible Tablets Development. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(3): 996-1015.

232. Noman MA, Alburyhi MM, El-Shaibany A, Alwesabi NA. Formulation and Evaluation of Pandanus Odoratissimus L Extract for Treatment of Nocturnal Enuresis as Orodispersible Tablets Delivery System. World Journal of Pharmaceutical Research., 2024; 13(5): 56-71.
233. Alburyhi MM, Saif AA, Noman MA. Formulation and Evaluation of Ticagrelor Orodispersible Tablets. World Journal of Pharmaceutical Research., 2024; 13(5): 26-55.
234. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Tribulus Terrestris Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Kidney Stones. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(5): 1425-1443.
235. Alburyhi MM, Noman MA, Saif AA, Salim YA, Abdullah JH. Formulation and Evaluation of Domperidone Orodispersible Tablets. World Journal of Pharmacy and Pharmaceutical Sciences., 2024; 13(3): 49-68.
236. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Dictyota Dichotoma Extract Medicinal Seaweed Capsules Delivery System as an Advanced Phytotherapy Approach for Cancer. European Journal of Biomedical and Pharmaceutical Sciences., 2024; 11(4): 63-70.
237. Aboghanem A, Alburyhi MM, Noman MA. Effect of Different Excipients on Formulation of Immediate Release Artemether/Lumefantrine Tablets. Journal of Chemical Pharm Research., 2013; 5(11): 617-625.
238. Alburyhi MM, Saif AA, Noman MA, Saeed SA, Al-Ghorafi MA. Formulation and Evaluation of Diclofenac Orodispersible Tablets. European Journal of Pharmaceutical and Medical Research., 2023; 10(9): 01-06.
239. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Celery Extract Capsules Delivery System as an Advanced Phytotherapy Approach for Gout. World Journal of Pharmaceutical Research., 2024; 13(11): 2383-2404.
240. Raweh SM, Noman MA, Alburyhi MM, Saif AA. Formulation and Evaluation of Anti-acne Gel of Azadirachta Indica Extract Herbal Product. European Journal of Pharmaceutical and Medical Research, 2024; 11(2): 427-433.
241. Othman AM, Alburyhi MM, Al-Hadad GH. Formulation and Evaluation of Captopril Mouth Dissolving Tablets. European Journal of Pharmaceutical and Medical Research, 2024; 11(1): 18-28.
242. Alburyhi MM, El-Shaibany A. Formulation, Development and Evaluation of Acalypha Fruticosa Extract Tablets Delivery System as an Advanced Phytotherapy Approach for Controlling Diabetes. World Journal of Pharmaceutical Research., 2024; 13(8): 1073-1091.
243. Al-Ghorafi MA, Alburyhi MM. Formulation and Evaluation of Novel Antiaging Cream Containing Dragon's Blood Extract. European Journal of Pharmaceutical and Medical Research., 2024; 11(1): 239-244.
244. Patel D, Patel U, Shukla M, Bhimani B, Patel G. Formulation and Evaluation of Immediate Release Tablet of Simvastatin. Research Journal of Pharmacy and Technology., 2020; 13(1): 421-224.
245. Patel MA, Pingale PL. High Functionality Coprocessed Excipients: A Review. World J Pharm Sci., 2014; 3(3): 795-806.
246. World Health Organization. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials, Good Manufacturing Practices and Inspection., 2007.
247. Sreenivas S A, Gadad AP, Patil MB. Formulation and Evaluation of Ondansetron Hydrochloride Directly Compressed Mouth Disintegrating Tablets. Indian Drug., 2006; 43: 35-37.
248. Mishra B, Panigrahi D. Mouth Dissolving Tablets an Overview of Preparation Techniques, Evaluation and Patented Technologies', Indian Journal of Pharmaceutical Sciences., 2005.
249. Jin Y, Li Tong, Ping Ai, Miao Li, Xinpu Hou. Self-Assembled Drug Delivery Systems Properties and In Vitro –In Vivo Behavior of Acyclovir Self-Assembled Nanoparticles (san). Int J Pharm., 2006; 309(1–2): 199–207.
250. Goyal P, et al. Liposomal Drug Delivery Systems: Clinical Applications. Acta Pharm., 2005; 55: 1–25.
251. Sheetal B, Raval K, Sandip B. Formulation and Evaluation of Fast Dissolving Tablets of Amlodipine and Rosuvastatin. Int J Pharm Bio Sci., 2015; 2(1): 1-12.
252. Neelamma G, Chaitanya MV, Satyavathi B. Design and Evaluation of Solubility Enhancement of Poorly Soluble Drug Rosuvastatin Using Liquid Solid Compacts. Int J Pharmacol Res., 2015; 5(5): 231-8.
253. Ahai Luvai, Wycliffe Mbagaya, Alistair S. Hall, and Julian H. Barth., Rosuvastatin: A Review of the Pharmacology and Clinical Effectiveness in Cardiovascular Disease, Clin Med Insights Cardiol., 2012; 6: 17–33.
254. Venkatesh N, Spandana K, Samba Moorthy U, Suresh K. Formulation and Evaluation of Fast Dispersible Tablet of Rosuvastatin Using Cyclodextrin Complexation Method. Int J Med Pharm Res., 2014; 2: 785-93.
255. Tabbouche OS. Validation of a UV-Spectrophotometeric Method for the Assay Paracetamol in Solutions. Int J Pharm., 2013; 3(1): 24-7.
256. Biradar S S, Bhagavati S T, Kuppasad I J. Fast Dissolving Drug Delivery Systems: A Brief Overview. Int J Pharmacol., 2006; 4(2).
257. Bahlul Z Awen, Varun Dasari, Babu Rao Chandu, Mukkanti Khagga. New UV-Spectrophotometeric Method for the Estimation of Valganciclovir in Bulk and its Formulation. Int J Pharm Studies Res., 2011; 2(1): 1-4.

258. Maswadeh H, Abdulhalim A, Demetzos C. Improvement of Encapsulation Efficiency of Diclofenac Sodium into Uncoated and Chitosan-Coated Liposomes. Indian J Pharm Sci., 2004; 66: 607–612.
259. Kannan K, Karar PK, Manavalan R. Formulation and Evaluation of Sustained Release Microspheres of Diclofenac Sodium by Solvent Evaporation Technique. J Pharm Sci & Res., 2009; 1(1): 3639.
260. Lakshmana Prabu S, Shirwaikar AA, Shirwaikar A, Kumar A. Formulation and Evaluation of Sustained Release Microspheres of Rosin Containing Aceclofenac. Ars Pharm., 2009; 50(2): 51-62.
261. Kumar MU, Babu MK. Design and Evaluation of Fast Dissolving Tablets Containing Diclofenac Sodium Using Fenugreek Gum as a Natural Superdisintegrant. Asian Pacific Journal of Tropical Biomedicine., 2014; 4: S329-S334.
262. Allen LV, Ansel HC, Popovich NG. Pharmaceutical Dosage Forms and Drug Delivery Systems. Evaluation., 2011: 56: 44.
263. Aulton ME, Summers M. Tablets and compaction. Aulton's Pharmaceutics: The Design and Manufacture of Medicines., 2013; 5: 520-530.
264. Chang RK, Guo X, Burnside BA, Couch RA. Fast-Dissolving Tablets. Pharmaceutical Technology., 2000; 24(6): 52-52.
265. Naz A. Pharmacokinetics Study of Aceclofenac in Pakistani Population and Effects of Sucralfate Co Administration on Bioavailability of Aceclofenac. The Journal of Applied Research., 2011; 11(1): 55-63.
266. Seyda A. A Non-Steroidal Anti-Inflammatory Drug, Aceclofenac. FABAD Journal of Pharmaceutical Science., 2010; 35: 105-118.
267. Chandel N. Co-Crystalization of Aceclofenac and Paracetamol and Their Characterization. International Journal of Pharmacy & Life Science., 2011; 2(8): 1020- 1028.
268. Jayanthi B, Madhusudhan S. Preformulation Characterization, Designing and Formulation of Aceclofenac Loaded Microparticles. International Journal of Drug Development & Research., 2012; 4(3): 186-196.
269. Segun A, Aderibigbe Olajire A. Sensitive Spectrophotometric Determination of Aceclofenac Following Azo Dye Formation with 4-Carboxyl-2,6-Dinitrobenzene Diazonium Ion, Acta Poloniae Pharmaceutical- Drug Research., 2012; 69(2): 203-211.
270. Sharma S. Spectrophotometric Method Development for Estimation of Aceclofenac in Phosphate Buffer Dissolution Media. International Journal of Pharmaceutical Quality Assurance., 2010; 2(1): 5-8.
271. Bansal SY. Effect of Aceclofenac on Pharmacokinetic of Phenytoin. Pakistan Journal of Pharmaceutical Science., 2012; 25(2): 295-299.
272. Amit Modi, Abhishek Pandey, Vandana Singh, Bonde CG, Dheeraj Jain, Sandeep Shinde. Formulation and Evaluation of Fast Dissolving Tablets of Diclofenac Sodium Using Different Superdisintegrants by Direct Compression Method. International Journal of Pharmaceutical & Biological Archives 2012.
273. Renati Damodar, Babji Movva1, Mallikarjun Chaitanya Pasumarthy, Nishanth Kona. Formulation and Evaluation of Fast Dissolving Tablets of Diclofenac Sodium by Novel Hole Technology. Molecular Pharmaceutics & Organic Process Research., 2014.
274. Sona PS, Muthulingam C. Formulation and Evaluation of Taste Masked Orally Disintegrating Tablets of Diclofenac Sodium. International Journal of Pharm Tech Research., 2011.
275. Jagadeesh Induruand, Padmaja Bookya. Excipient Screening and Development of Formulation Design Space for Diclofenac Sodium Fast Dissolving Tablets. International Journal Pharmaceutical, Pharmaceutical sciences., 2011.
276. Prabhakar Shirse. Formulation and Evaluation of Bilayer Tablets of Diclofenac Sodium with Ranitidine HCL for Sustained and Immediate Release. J Appl Pharm Sci., 2012; 2: 136-4.
277. United States Pharmacopoeia. 30th edition NF 25, The Official Compendia of Standards., 2007.
278. Rajlakshmi G, Vamsi C, Balchandar R, Damodharan N. Formulation and Evaluation of Effervescent Tablets of Diclofenac Potassium. Int J Pharm Biomed Res., 2011; 2(4): 237- 243.
279. Alburyhi MM, Saif AA, Noman MA, Yahya TA, Al-Ghorafi MA. Formulation and Evaluation of Drotaverine Orally Disintegrating Tablets. World Journal of Pharmaceutical Research., 2023; 12(18): 66-79.
280. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Effervescent Granules of Artemisia Arborescence Herbal Product for Foodborne Illness. World Journal of Pharmacy and Pharmaceutical Sciences., 2023; 12(12): 1429-1444.
281. Alburyhi MM, Saif AA, Noman MA, Saif RM. Recent Innovations of Delivery Systems for Antimicrobial Susceptibility Study of Ceftriaxone Biodegradable Formulations for Post-Operative Infection Prophylaxis. European Journal of Pharmaceutical and Medical Research., 2023; 10(8): 95-99.
282. Alburyhi MM, El-Shaibany A. Formulation and Evaluation of Anti-peptic Ulcer Capsules of Curcuma Longa Herbal Product. World Journal of Pharmaceutical Research., 2023; 12(22): 76-96.
283. Bolhuis GK, Armstrong NA. Excipients for Direct Compaction - an Update. Pharma Dev and Tech., 2006; 11(1): 111-124.
284. Bravo SA, Lamas MC, Salomon CJ. Swellable Matrices for The Controlled-Release of Diclofenac Sodium: Formulation and In-Vitro Studies Pharm Dev and Tech., 2004; 9(1): 75-83.
285. Shivakumar H, Desai BG, Deshmukh G. Design and Optimization of Diclofenac Sodium Controlled

Release Solid Dispersions by Response Surface Methodology. Ind J Pharma Sci., 2008; 70(1): 22-30.
286. Ravichandiran V. Modern Pharmaceutics. Rev J Pharm Res., 2011; 4(8): 2590–2.
287. Ganesh GNK, Shanmukhasrinivas M, Sureshkumar R, Jawahar N, Senthil V, Nagasamyvenkatesh D, et al. Preparation and Evaluation of Sustained Release Matrix Tablet of Diclofenac Sodium Using Natural Polymer. J Pharm Sci Res., 2010; 2(6): 360–8.
288. Alford N, Martin PJ. Martin's Physical Pharmacy and Pharmaceutical Sciences. and Others, Editor., 2006.
289. Treatise DM. Biopharmaceutics and Pharmacokinetics -A Treatise. and Others, Editor., 2009.
290. Sankar S V, Chandrasekharan AK, Durga S, Prasanth KG, Nilani P. Formulation and Stability Evaluation of Diclofenac Sodium Ophthalmic Gels. Ind J Pharm Sci., 2005; 67(4): 473-476.
291. Swamy NGN, Mazhar P, Zaheer A. Formulation and Evaluation of Diclofenac Sodium Gels Using Sodium Carboxymethyl Hydroxypropyl Guar and Hydroxypropyl Methylcellulose. Indian J Pharm Educ Res., 2010; 44(4): 310-314.
292. Patil PB, Datir SK, Saudagar RB. Journal of Drug Delivery and Therapeutics., 2019; 9(3-S): 989-994.
293. Priya P, Munshi DS, Mohale R, Akkalwar AV Chandewar. Formulation and Evaluation of Diclofenac Gel. Research J Pharm and Tech., 2011; 4(9): 1394- 1399.
294. Remington, The Science and Practice of Pharmacy. Lippincott Williams & Wilkins, 20th Edition., 2002.
295. Khokhar P, Shukla V. Formulation and Evaluation of Fast Dissolving Tablets of Diclofenac Sodium Using PVP. International Journal of Pharma Research and Review., 2014; 7: 12-9.
296. Sangale Shamrao S, Khatal Vaibhav, Mahale NB, Chaudhari SR. Formulation Development and Evaluation of Orodispersible Tablet of Diclofenac Sodium by Sublimation Technique. World Journal of Pharmaceutical Research., 2016; 5(2): 1300-1306.
297. Malviya R, Srivastava P, Bansal M, Sharma PK. Formulation and Optimization of Sustained Release Tablets of Diclofenac Sodium Using Guar Gum as Release Modifier. Int J Pharm Sci Res., 2010; 1: 82-88.
298. Joshi Y, Chaudhary RK, Teotia UV. Formulation and Evaluation of Diclofenac Sodium Sustained Release Matrix Tablets Using Aegle Marmelos Gum. Int J Curr Trends Pharm Res., 2013; 1(3): 174-80.
299. Savaşer A, Özkan Y, Işımer A. Preparation and In-Vitro Evaluation of Sustained Release Tablet Formulations of Diclofenac Sodium. Il Farmaco., 2005; 1,60(2): 171-7.
300. Ganesh GNK, Sureshkumar R, Jawahar N, Senthil V, Venkatesh DN, Srinivas MS. Preparation and Evaluation of Sustained Release Matrix Tablet of Diclofenac Sodium Using Natural Polymer. Journal of Pharmaceutical Sciences and Research., 2010; 2(6): 360.
301. Savale SK. Formulation and Evaluation of Diclofenac Sustained Released Tablet. Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry., 2015; 3(4).
302. Pawan P, Nitin N. Formulation, Evaluation and Comparison of Sustained Release Matrix Tablet of Diclofenac Sodium Using Natural Polymer. Int J Res Pharm Biomed Sci., 2013; 4(1): 367-79.
303. Asija Rajesh et al. Formulation and Evaluation of Diclofenac Sodium Sustained Released Tablets Using Melt Granulation Technique. International Research Journal in Pharmacy and Science., 2012; 3(5): 217.
304. Martindale: The Complete Drug Reference, 37Th Edn. The Pharmaceutical Press, London., 2011.
305. Patel KN, Patel HR, Patel VA. Formulation and Characterization of Drug in Adhesive Transdermal Patches of Diclofenac Acid. Int J Pharm Sci., 2012; 4(1): 296-299.
306. Wagh MP. Formulation and Evaluation of Fast Dispersible Tablets of Aceclofenac Using Different Superdisintegrant. Int J Pharm Pharm Sci., 2010; 2(1): 154–7.
307. Debjit B, et al. Fast Dissolving Tablet: An Overview. Journal of Chemical and Pharmaceutical Research., 2009; 1(1): 163-177.
308. Mizumoto T, et al. Formulation Design of a Novel Fast Disintegrating Tablet. Int J Pharm., 2008; 306: 3- 9.
309. Nikku D Y, Prashanth P, Sagar R T. Comparative Study on Effect of Natural and Artificial Superdisintegrants in The Fast-Dissolving Aspirin Tablets. Journal of Pharmacy Research., 2010; 3(7): 1594-1597.
310. Park j et al. An Alternative to The USP Disintegration for Orally Dissolving Tablet. Pharm tech., 2008; 32: 1-3.
311. Badgujar BP, Mundada AS. The Technologies Used for Developing Orally Disintegrating Tablets: A Review. Acta Pharmaceutica., 2011; 61(2): 117-139.
312. Amal S, Abu el-enin. Flurbiprofen Fast Disintegrating Tablets. Int J Pharm Sci., 2014; 6(2): 499-505.
313. Jha K, Geethalakshmi A, Bhatia V, Shukla T. Orally Disintegrating Tablets-Technology for Mankind. J Global Pharm Tech., 2011; 74: 11-17.
314. David Brown. Orally Disintegrating Tablets- Taste Over Speed. Drug Delivery Technology., 2003; 3(6).
315. Parakh S R et.al. A Review of Mouth Dissolving Tablet Technologies. Pharm Technol., 2003; 27(11): 92–100.
316. Gupta A, Mishra K, Gupta V. Recent Trends of Fast Dissolving Tablet-An Overview of Formulation Technology. Int J Pharm Bio., 2010; 42: 1-10.
317. Hypertension, Federal Bureau of Prisons - Clinical Practice Guidelines., May 2005.
318. Sudarshan K Singh, Agham A Sameer. Development and Characterization of Sublingual

Tablet of Lisinopril. Asian Pacific Journal of Tropical Biomedicine., 2012; S1711-S1719.
319. Panigrahi R, Chowdary KA, Mishra G, Bhowmik M. Effect of Combination of Natural Superdisintegrants on Fast Dissolving Tablets of Lisinopril. Int J Pharma Res Allied Sci., 2012; 1(3): 73-8.
320. Rajeshree P, et.al. Formulation of Fast Dissolving Tablets of Lisinopril Using Combination of Synthetic Superdisintegrants. Asian J Pharm Tech., 2012; 2(3): 94-98.
321. Malpani A, Panda B, Bhojani R. Formulation of Lisinopril Dehydrate Tablet and Study Effect of Granulation on Response Variables. Int J Pharm sci., 2009; 12: 132-39.
322. Pandey S, Goyani M. Formulation and Evaluation of Taste Masked Fast Disintegrating Tablets of Lisinopril. Int J Pharm Tech Res., 2010; 148: 1639- 43.
323. Dandagi PM, Gayakwad VM. Taste Masked Ofloxacin Mouth Disintegrating Tablets. Indian drugs., 2005; 17: 52-54.
324. Vijay S, Himanshu C. Role of Taste and Taste Masking of Bitter Drugs in Pharmaceutical Industries an Over view. Int J Pharm Sci., 2010; 74: 14-18.
325. Gohel MC. A Review of Co-processed Directly Compressible Excipients. J Pharm Sci., 2005; 102:76- 93.
326. Suresh S, Pandit V. Preparation and Evaluation of Mouth Dissolving Tablets of Salbutamol Sulphate. Int J Pharm sci., 2007; 12: 54-57.
327. Arora V, Gupta B, Advances in direct compression technology. Pharma times 2007; 74: 26-27.
328. Bhupendra G P, Nayan R. A Review on Recent Patents on Fast Dissolving Drug Delivery System. Pharm Tech., 2009; 1(3): 790- 798.
329. Bhavanam, Pamula R. Formulation and Evaluation of Levofloxacin Using Different Types and Concentrations of Superdisintegrants. J Pharm Sci and Res., 2010; 1: 1-5.
330. Setty CM, Prasad DV, Gupta V. Development of Fast Dispersible Tablets: Effect of Functionality of Superdisintegrants. Ind J Pharma Sci., 2008; 180- 185.
331. Chakraborty S, Khandai M, Singh PS. Comparative Study of Effect of Natural and Synthetic Superdisintegrants in Formulation of Fast Dissolving Tablets. Int J Green Pharmacy., 2008; 2(1): 22-28.
332. Nitin M, Adhikrao Y, Vaishali K. Novel Approaches in Development of Metronidazole Orodispersible Tablets. Res J Pharm Tech., 2009; 44: 283-86.
333. Saroha K, Kumar G, Paul Y. Formulation and Evaluation of Fast Dissolving Tablets of Amoxicillin Trihydrate Using Synthetic Superdisintegrants. Int J Pharm Bio Sci., 2013; 4(1): 254-62.
334. Pratibha, Nagendrakumar D, Keshavshetti G. Design and Evaluation of Fast Dissolving Tablets of Metoclopramide Hydrochloride Using Synthetic and Natural Superdisintegrants. Unique J Pharma & Bio Sci., 2014; 2(01): 16-24.
335. Patil A, Kumar S. Formulation and Evaluation of Solid Dispersions of an Anthelmintic Drug for Enhancement of Dissolution Rate. JIPBS., 2017; 4(3): 71-74.
336. AppaRao B, Shivalingam MR, Kishore Reddy YV, Rao S, Rajesh K, Sunitha N. Formulation and Evaluation of Aceclofenac Solid Dispersions for Dissolution Rate Enhancement. International Journal of Pharmaceutical Sciences and Drug Research., 2010; 2(2): 146-150.
337. Enose AA, Dasan P, Sivaramakrishanan H, Kakkar V. Formulation Characterization and Pharmacokinetic Evaluation of Telmisartan Solid Dispersions. J Mol Pharm Org Process Res., 2016; 4(1): 131.
338. Knutter I, Wollesky C, Kottra G, Hahn MG, Fischer W, Zebisch K, Neubert RH, Daniel H, Brandsch M. Transport of Angiotensin-Converting Enzyme Inhibitors by H+/Peptide Transporters Revisited. J Pharmacol Exp Ther., 2008; Nov; 327(2): 432-41.
339. Song JC, White CM. Clinical Pharmacokinetics and Selective Pharmacodynamics of New Angiotensin Converting Enzyme Inhibitors: an Update. Clin Pharmacokinet., 2002; 41(3): 207-24.
340. Nagarajan K, Rao MG. Formulation and Dissolution Studies of Solid Dispersions of Nifedipine. Indian Journal of Novel Drug Delivery., 2010; 2: 96-98.
341. Par KC, Lee BJ. Current Trends and Future Prospective of Solid Dispersions Containing Poorly Water-Soluble Drugs. European Journal of Pharmaceutics and Biopharmaceutics., 2013; 85: 799-813.
342. Sapkal SB, Adhao VS, Thenge RR, Darakhe RA, Shinde SA, Shrikhande VN. Formulation and Characterization of Solid Dispersions of Etoricoxib Using Natural Polymers. Turkish Journal of Pharmaceutical Sciences., 2020; Feb 17(1): 7.
343. Klecia MDS, Raquel MB, Fernanda GAV, Eduardo PA, Antonio CSL, Celso AC, et al. Development of Solid Dispersions of β-Lapachone in PEG and PVP by The Solvent Evaporation Method. Drug Dev Ind Pharm., 2018; 44: 750-6.
344. Deepak K, Narender S. Enhancement of Dissolution profile of Gliclazide by Solid dispersion adsorbates. Lat Am J Pharm., 2011; 30: 2057-2060.
345. Dua K, Ramana MV, Sara UVS, Himaja M, Garg V, Agrawal A. Dissolution Enhancement of Aceclofenac Through Solid Dispersions. Indian Pharmacist., 2006; 70-72.
346. Subramanyam CVS. Textbook of Physical Pharmaceutics. 3rd Ed. Vallabh Prakashan: Delhi, 2001; 181-234.
347. Brahmankar D M, Jaiswal S B. Biopharmaceutis and Pharmacokinetics: A Tretise, Vallabh Prakashan, New Delhi, 1 st Edition., 2006; 335-357.
348. S.Jacob, Shirwaikar A, Joseph A, Srinivasan K. Novel Co-Processed Excipients of Mannitol and

Microcrystalline Cellulose for Preparing Fast Dissolving Tablets of Glipizide. Indian J Pharm Sci., 2007; 69(5): 633-39.
349. Galey WR, Lonsdale HK and Nacht S. The In -Vitro Permeability of Skin and Buccal Mucosa to Selected Drugs and Tritiated Water. Journal Investigative Dermatol., 1976; 67(6): 713- 717.
350. Sharma S, Gupta G, Bala R, Sharma N, Seth N, Goswami J. Orodispersible Tablet A Review. Pharmainfo.net.html., 2008.
351. Rishikesh et al. Immediate Release Drug Delivery System (Tablets): An Overview. (IRJPAS); Int. Res J Pharm. App Sci., 2012; 2(5): 88-94.
352. Patel N, Naruka PS, Chauhan CS, Modi J. Formulation Development and Evaluation of Immediate Release Tablet of Topiramate Anti-Epileptic Drug. Journal of Pharmaceutical Science and Bioscientific Research., 2013; 3(2): 58 – 65.
353. Bansal M, Bansal S, Garg G. Formulation and Evaluation of Immediate Release Tablets of Zaltoprofen. Scholars Academic Journal of Pharmacy., 2013; 2(5): 398 - 405.
354. Nyol Sandeep et al. Immediate Drug Release Dosage Form: A Review. Journal of Drug Delivery & Therapeutics., 2013, 3(2): 155-161.
355. Rathod VG, Kadam V, Jadhav SB, Zamiruddin M, Bharkad VB and Biradar SP. Immediate Release Drug Delivery System: A Review. World Journal of Pharmacy and Pharmaceutical Sciences., 2014; 3(6): 545-58.
356. Rajesh M, Nagaraju K, SH Seyed MB. Formulation and Evaluation of Clarithromycin Immediate Release Film Coated Tablets. International journal of pharmacy and pharmaceutical sciences., 2012; 4 (5): 352-357.