WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 13, Issue 16, 59-111. Research Article ISSN 2277–7105

LISINOPRIL-EXCIPIENT COMPATIBILITY STUDIES FOR ADVANCED DRUG DELIVERY SYSTEMS DEVELOPMENT

Mahmoud Mahyoob Alburyhi[1]*, Maged Alwan Noman[1], Abdalwali Ahmed Saif,[1] Yahya A. S. Mohamed[2], Mohammed Abbas Hamidaddin[3], Tawfeek A. A. Yahya[4], Mokhtar Abd-hafiz Al-Ghorafi[5] and Jalal H. Abdullah[4]

[1]Professor Dr. of Pharmaceutics and Industrial Pharmacy, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[2]Associate Professor Dr. of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[3]Assistant Professor Dr. of Pharmaceutical Analytical Chemistry, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[4]Professor Dr. of Medicinal Chemistry and Drug Design, Department of Medicinal Chemistry, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
[5]Associate Professor Dr. of Pharmaceutical Chemistry and Pharmaceutical Organic Chemistry Department, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.

Article Received on
06 July 2024,
Revised on 27 July 2024,
Accepted on 16 August 2024
DOI: 10.20959/wjpr202416-33678

***Corresponding Author**
Prof. Dr. Mahmoud Mahyoob Alburyhi
Professor Dr. of Pharmaceutics and Industrial Pharmacy, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Sana'a University, Sana'a, Yemen.
alburyhi2020@gmail.com

ABSTRACT

The safety, efficacy, quality and stability of a formulation are major concepts of any API development process. In API development process, a detailed characterization of the API and other formulation components is usually carried out during the preformulation stage. The main objective of the present study was to the preformulation studies were performed to know the physico-chemical and mechanical properties of Lisinopril dihydrate for formulation development of Lisinopril ODTs. The drug-excipient compatibility studies were conducted to characterize the drug Lisinopril present in Orally Disintegrating Tablets Delivery System ODDS. Preformulation, formulation and evaluation of Lisinopril to avoid problems associated with conventional delivery system such as limited permeation, low dissolution and bioavailability and also to improve bioavailability and antihypertensive 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 Lisinopril dihydrate and various excipients as mannitol, microcrystalline cellulose as diluents, and

sodium starch glycolate, croscarmellose sodium, and crospovidone as superdisintegrants and sodium lauryl sulfate as wetting agent were evaluated for preformulation studies parameters. It was concluded that the drug Lisinopril dihydrate was found to be compatible with various excipients which were selected for the formulation development of the Lisinopril 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: Lisinopril, Compatibility, Excipients, Development, Preformulation, Formulation.

INTRODUCTION

Preformulation Studies[1-190]

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

One of the objectives of this study is to development of drug delivery systems by building scientific pharmaceutical research information depend on formulation scientists to join the knowledge and experience as well as experimental and practical results of this study with regard to information in previous studies, and approved references. It was found to be that the most important concepts and basics of preformulation studies such as definitions, methods, conclusion, idea, and types of pharmaceutical analysis techniques using in evaluation of preformulation studies parameters, in this study that we focused on developing drug delivery systems and linking the formulation development to establish the basics of pharmaceutical research in studying the drug-excipient compatibility, dug with various excipients, which is

important for the safety, effectiveness, quality, formulation, stability, bioavailability, and pharmacokinetics of the drug etc.

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.

Table 1: Biopharmaceutical Classification System (BCS).

BCS -Class	Solubility	Permeability
Class-I	High	High
Class-II	Low	High
Class-III	High	Low
Class-IV	Low	Low

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. As shown in Table 1.

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

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

Importance of Drug-Excipient Compatibility

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

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

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

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

Evaluation of Drug-Excipient Compatibility

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

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

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

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

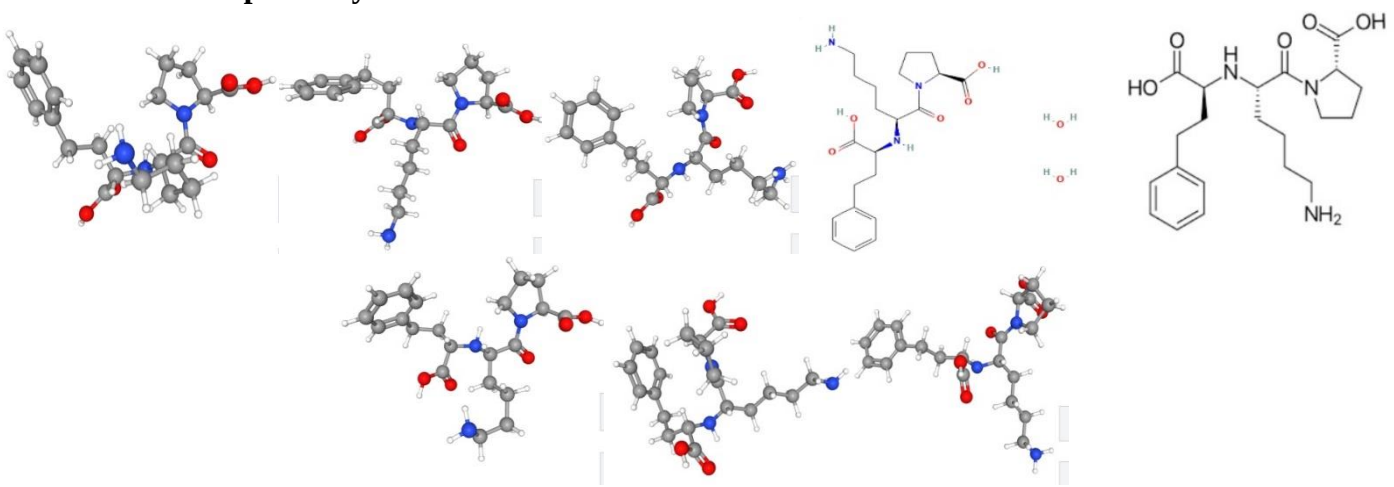
In the present study, it was proposed to drug-excipient compatibility studies of Lisinopril, with commonly different excipients using for formulation development of orally disintegrating tablets ODTs.

MATERIALS AND METHODS

Lisinopril dihydrate was obtained as a gift from (Yemen-Egyptian Pharmaceutical Industry Company - Yemen). While Talc, Mannitol, Microcrystalline Cellulose (Avicel), Croscarmellose Sodium, Crospovidone, Sodium Starch Glycolate, Aspartame, Magnesium Stearate, Sodium Lauryl Sulfate, Saccharin Sodium, Aerosil, Polyvinylpyrrolidone PVP K30, Roseberry Flavor, Methanol, Ethanol, Buffer Solutions, and other materials were obtained as a gift from (Shaphaco Pharmaceutical Industry Company-Yemen).

Evaluation of Drug-Excipient Compatibility Studies Methods[50-323]

Table 2: Lisinopril Dihydrate Data.

<table>
<tr><td colspan="4">Characterization of Lisinopril Dihydrate
 
Lisinopril Structure and 3D Conformer</td></tr>
<tr><td>Chemical Structure</td><td>(2S)-1-[(2S)-6-amino-2-[[(1S)-1-carboxy-3 phenyl propyl] amino] hexanoyl] pyrrolidine-2- carboxylic acid dihydrate.</td><td>Appearance</td><td>Is a white to off-white, crystalline powder.</td></tr>
<tr><td>Chemical Formula</td><td>C21H31N3O5</td><td>Solubility</td><td>Soluble in water and sparingly soluble in methanol and practically insoluble in ethanol.</td></tr>
<tr><td>Molecular Weight</td><td>405.5 g/mol</td><td>BCS</td><td>Class-III Drug</td></tr>
<tr><td>Action and Use</td><td>the long-acting angiotensin-converting enzyme (ACE) inhibitor, used in treatment of hypertension, heart failure and myocardia infraction</td><td>Duration of Treatment</td><td>Chronic</td></tr>
<tr><td colspan="4">Pharmacokinetics of Lisinopril</td></tr>
<tr><td></td><td>Bioavailability: with an average drug is 6-60%</td><td></td><td>Lisinopril has not been binding to</td></tr>
</table>

Drug Absorption	orally bioavailable of 25% bioavailability. Lisinopril reaches a Cmax of 58ng/ml with a Tmax of 6-8h. Lisinopril s absorption is not affected by food.	**Drug Distribution**	albumin or other proteins. The apparent volume of distribution of lisinopril is 124L.
Drug Metabolism	Lisinopril is not metabolized and is excreted as the unchanged drug.	**Drug Excretion**	Lisinoprril is entirely eliminated exclusively in the urine. A 30kg child has atypical clearance of 10L /h, which increases with renal function. The mean renal clearance of lisinopril in healthy adult males is 121mL/min.
The Elimination Half-Life (T1/2)	Lisinopril has an effective half life of accumulation of 12.6h and a terminal half life of 46.7h.	**Availability**	Tablets: 5mg,10mg, 20mg.

Table 3: Pharmaceutical Excipients Data.

Nonproprietary Name	Chemical Name	Functional Category	Concentration%	Solubility	Incompatibilities	Notes
Croscarmellose Sodium (Ac-Di-Sol)	Cellulose, carboxymethyl ether, sodium salt, crosslinked	Tablet and capsule disintegrant.	0.5-5% 10-25%	Insoluble in water	Incompatible with strong acids or with soluble salts of iron and some other metals such as aluminum, mercury, and zinc.	White or grayish-white powder
Sodium Starch Glycolate (Explotab)	Sodium carboxymethyl starch	Tablet and capsule disintegrant.	2–8%	Gives a translucent suspension in water	Incompatible with ascorbic acid.	Very hygroscopic
Microcrystalline Cellulose (Avicel PH)	Cellulose	Adsorbent, suspending agent, tablet and capsule diluent; tablet	5–20% 20–90%	Practically insoluble in water	Incompatible with strong oxidizing agents.	Crystalline powder

		disintegrant.				
Crospovidone (PVPP)	1-Ethenyl-2-pyrrolidinone homopolymer	Tablet disintegrant.	2–5%	Practically insoluble in water	Compatible with most organic and inorganic pharmaceutical ingredients.	Hygroscopic powder
Mannitol (Emprove)	Mannitol	Diluent, plasticizer, sweetening agent, tablet and capsule diluent, therapeutic agent, tonicity agent.	10–90%	Freely soluble in water	Incompatible with may be salted out by potassium chloride or sodium chloride. Sodium cephapirin. xylitol infusion and may form complexes with some metals 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
Aspartame	3-Amino-N-(a carboxyphenethyl) succinamic acid N-methyl ester; 3-Amino-N-(a methoxycarbony lphenethyl) succinamic acid;	Sweetening agent.			incompatible with dibasic calcium phosphate and also with the lubricant magnesium stearate.	
Talc	Altalc, E553b, hydrous magnesium calcium silicate, hydrous magnesium silicate, Luzenac Pharma, magnesium hydrogen metasilicate.	Anticaking agent; glidant, diluent, lubricant.			Incompatible with quaternary ammonium compounds.	
Aerosil	Aerosil; Cab-O-Sil, Cab-OSil M-5P, colloidal silica, fumed	Adsorbent; anticaking agent	0.1–1.0% 2.0–10.0%	Practically insoluble in	Incompatible with diethylstilbestrol	A submicroscopic

	silica, fumed silicon dioxide, SAS, silica colloidalis anhydrica	glidant; viscosity-increasing agent	widely used in oral and topical pharmaceutical products and is generally regarded as an essentially nontoxic and nonirritant excipient.	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.	preparations.	fumed silica with a particle size of about 15 nm. It is a light, loose, bluish-white-colored, odorless, tasteless, amorphous powder.
Saccharin Sodium	1,2-Benzisothiazolin-3-one 1,1-dioxide, sodium salt, Crystallose, E954, gendorf 450, sucaryl sodium	Sweetening agent.			Saccharin sodium does not undergo Maillard browning.	
PVP K30	E1201, Kollidon, Plasdone, polyvidone, polyvinylpyrrolidone, PVP;1vinyl-2- pyrrolidinone polymer.	Disintegrant, tablet binder.	2.0–5.0	Greater than 10% solubility in water, methanol, PG….	compatible in solution with a wide range of inorganic salts, natural and synthetic resins, and other chemicals.	White to yellowish-white amorphous powder.
Sodium Lauryl Sulfate	Dodecyl alcohol hydrogen sulfate, sodium salt, dodecyl sodium sulfate, dodecyl sulfate sodium salt, Elfan 240	Detergent; lubricant; wetting agent.			incompatible with salts of polyvalent metalions, such as aluminum, lead, tin or zinc	

According to Lisinopril and excipients data as shown in Tables 2 and 3, it was selected that the different excipients to preformulation study with Lisinopril in the present study, the equipments used as shown in Table 4.

Table 4: The Equipment's Used.

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

Determination of The Organoleptic Properties

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

Solubility Test: Solubility of Lisinopril dihydrate in water, methanol and ethanol was determined by using Sonicator at room temperature. Approximate solubility of drugs as per B.P was indicated in Table 5.

Table 5: Solubility Specification of Drugs.

Solubility	Approximate Volume of Solvent in ml per gm of Solute
Excellent	Less than 1
Very soluble	1 to 10
Freely soluble	10 to 30
Soluble	30 to 100
Sparingly soluble	30 to 100
Slightly soluble	1000 to 10000
Very slightly soluble	1000 to 10000
Practically insoluble/ Insoluble	More than 10000

UV-Visible Spectrophotometric Method

Determination of λ Max for Lisinopril Dihydrate

The standard solution of Lisinopril was scanned in the range of 200-400 nm and the λ max was determined UV scanning of Lisinopril in phosphate buffer at pH 6.8, the absorption spectra of Lisinopril in phosphate buffer at pH 6.8 were studied. A preliminary scanning of Lisinopril in phosphate buffer to determine the ʎ max by screening a 5µg/ml solution of Lisinopril in phosphate buffer these between 200- 400 nm.

Preparation of Calibration curve Solutions

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

Calibration curve: 50 mg of Lisinopril was weighed accurately and dissolved in 50 ml of phosphate buffer (pH 6.8) in a 50 ml of volumetric flask to obtain a stock solution. aliquots of 5 ml ,10 ml, 15 ml, 20 ml and 25ml were taken and transferred to 100ml volumetric flask and volume was made up to 100 ml phosphate buffer (PH,6.8). The absorbance of these solutions was measured at 216 nm against a blank of phosphate buffer. The calibration curve was plotted between concentration and absorbance.

Calibration Curve of Lisinopril Dihydrate

The standard calibration curve graph was obtained by preparing aliquots of standard solution of Lisinopril in phosphate buffer (pH 6.8) and the absorbance at 216nm was measured after suitable dilution using UV/Visible spectrophotometer.

appropriate aliquots were pipette out from standard stock solution into the series of volumetric flask and the volume was made up to the mark with concentration range 5-25 µg/ml of Lisinopril. Solutions of different concentrations were analyzed 216 nm against blank solution and absorbance were recorded. The calibration curve was plotted between concentration and absorbance.

Preformulation Studies

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

Melting Point Determination of Lisinopril Dihydrate

Melting Point: Melting point of the lisinopril dihydrate 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 lisinopril dihydrate 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 lisinopril dihydrate 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·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 lisinopril dihydrate in room condition as shown in table 6.

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 6.

Table 6: Samples of Lisinopril and Different Excipients for Compatibility Studies.

No	Component(s)	Amount(5mg:5mg)
1	Lisinopril	1
2	Lisinopril and MCC	(1:1)
3	Lisinopril and SSG	(1:1)
4	Lisinopril and SLS	(1:1)
5	Lisinopril and Crospovidone	(1:1)
6	Lisinopril and Talc	(1:1)
7	Lisinopril and Rose berry flavor	(1:1)
8	Lisinopril and Saccharin Sodium	(1:1)
9	Lisinopril and Aspartame	(1:1)
10	Lisinopril and CCS	(1:1)
11	Lisinopril and Mannitol	(1:1)
12	Lisinopril and Mg. Stearate	(1:1)
13	Lisinopril and PVP K30	(1:1)
14	Lisinopril and Aerosil	(1:1)

Preparation of Lisinopril Formulations

Mixing and Compression Processes: Mixing was done by using geometric mixing, in where all excipients accurately weighed then all of them except silicon dioxide, magnesium stearate and Roseberry flavor, were blended with specified quantity of lisinopril for 15minutes, whereas the other excipients were blended for 5 minutes and added to the former excipients. Then all formulae were passed through sieve # 18 for particle size uniformity. This method of ordering mixing of excipients with lisinopril in first sex formulae then testing powder properties that will be shown in Preformulation tests as shown in Table 7.

Table 7: Preparation of Lisinopril Dihydrate Formulations.

Ingredients	Formulation Amount %					
	Formulation Code					
	F1	F2	F3	F4	F5	F6
Lisinopril Dihydrate	3.8	3.8	3.8	3.8	3.8	3.8
Avicel PH 101	76	75.62	---	76	---	37.62
Mannitol	---	---	70.42	---	75.62	37.62
Sodium Starch Glycolate	9.6	---	---	4.81	4.81	---
Crospovidone	---	9.6	4.81	4.81	---	4.81
Croscarmellose Sodium	---	---	9.6	---	4.81	4.81
Aspartame	0.77	0.77	0.77	0.77	0.77	0.77
Talc	0.77	0.77	0.77	0.77	0.77	0.77
Aerosil	0.77	0.77	0.77	0.77	0.77	0.77
Sodium Lauryl Sulfate	0.77	1.15	1.54	0.77	1.15	1.54
PVP K30	3.076	3.076	3.076	3.076	3.076	3.076
Saccharin Sodium	0.77	0.77	0.77	0.77	0.77	0.77
Mg Stearate	0.77	0.77	0.77	0.77	0.77	0.77
Roseberry Flavor	2.8	2.8	2.8	2.8	2.8	2.8

Evaluation of Pre-Compression Parameters of Formulations

Bulk Density

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

$\rho b = M/Vb$.

Tapped Density

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

Angle of Repose

Angle of repose (**θ**) was determined using funnel method. The drug excipients mixture was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of the pile (r) was measured and the angle of repose was calculated. $\theta = \tan^{-1}(h/r)$. As shown in Table 7.

Carr's Index

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

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

Hausner's Ratio

Hausner's ratio is an index of ease of powder flow; it is calculated by the following formula. Hausner's ratio = ρt\ ρb Where, ρt - Tapped density ρb - Bulk density. As shown in Tables 8 and 9.

Table 8: Powder Flow Properties.

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

Table 9: Powder Flow Properties.

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

RESULTS AND DISCUSSION

Preformulation Studies

Characterization of Lisinopril Dihydrate

The organoleptic properties like color, odor and taste of the API were evaluated. The color of Lisinopril dihydrate was found to be white or almost white powder, no characteristic odor was observed in the study and the taste was found to be bitter. Lisinopril dihydrate showed similar color, taste and odor as per IP specification.

Physical Identification of Lisinopril Dihydrate

Lisinopril is white powder.

Solubility Test

The solubility profile of Lisinopril dihydrate was present in Table 10.

Table 10: Solubility Analysis of Lisinopril Dihydrate (API).

Raw Material (API)	Solubility
Lisinopril dihydrate	Soluble in water
	Sparingly soluble in methanol
	Insoluble in ethanol

Characterization of Lisinopril by UV Spectroscopy

The solubility studies of drug (API) revealed that Lisinopril was soluble in water, sparingly soluble in methanol and insoluble in ethanol.

The absorption maximum (λmax) of Lisinopril was observed to be 216 nm in phosphate buffer (pH 6.8) as shown in Figure 1.

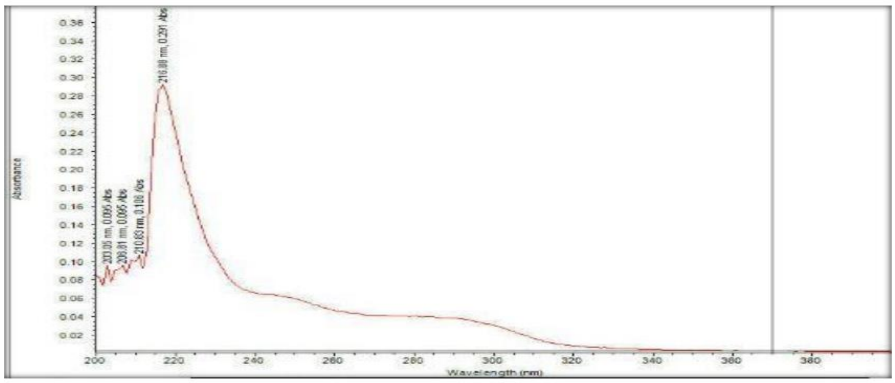


Fig. 1: UV Scanning of Lisinopril in Phosphate Buffer (pH 6.8).

Calibration Curve of Lisinopril Dihydrate

The calibration curve of Lisinopril was prepared in phosphate buffer (pH 6.8). The plot of different concentrations of Lisinopril versus absorbance was found linear at 216 nm in calibrations. The absorbance at different concentrations as shown in Table 11 The data of standard curve was linearly regressed. The slope and correlation coefficient values of phosphate buffer calibration were found 0.0221and 0.9992 respectively. The intercept on Y-axis was found 0.0084. The calibration curve is shown in Figure 2.

Table 11: Calibration Curve of Lisinopril in Phosphate Buffer (pH 6.8).

No	Concentration µg/ml	Absorbance
1	0.00	0.00
2	5	0.0958
3	10	0.2073
4	15	0.3197
5	20	0.4375
6	25	0.5454

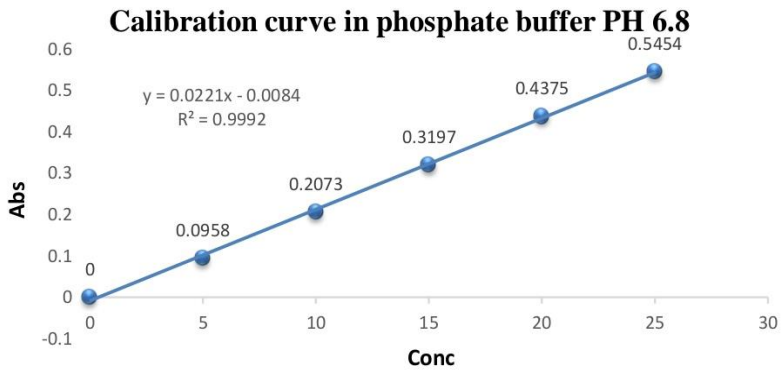


Fig. 2: Standard Calibration Curve of Lisinopril Dihydrate in Phosphate Buffer (pH 6.8).

Melting Point Determination of Lisinopril Dihydrate

Melting point of Lisinopril dihydrate was observed to be 160℃. Reported melting point of Lisinopril is (140-165 °C). The melting point range of Lisinopril dihydrate was identical to reference melting point stated in BP (140-165 °C).The sample started to melt at 155C°, and turned into liquid at 160 °C, as shwon in Table 12, indicating that the sample used is pure. That reading has stated in melting point apparatus.

Table 12: Results of Melting Point of Lisinopril Dihydrate.

Test	Temp Rang Analyzed (Melting)	Results
Test I Lisinopril	(140-165 °C)	160 °C
Test II Lisinopril	(140-165 °C)	160 °C

Characterization of Lisinopril 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 Lisinopril dihydrate, thus conforming that no interaction of drug occurred with the components of the formulation excipients as shown in Figures (3-16) and Tables (13-24).

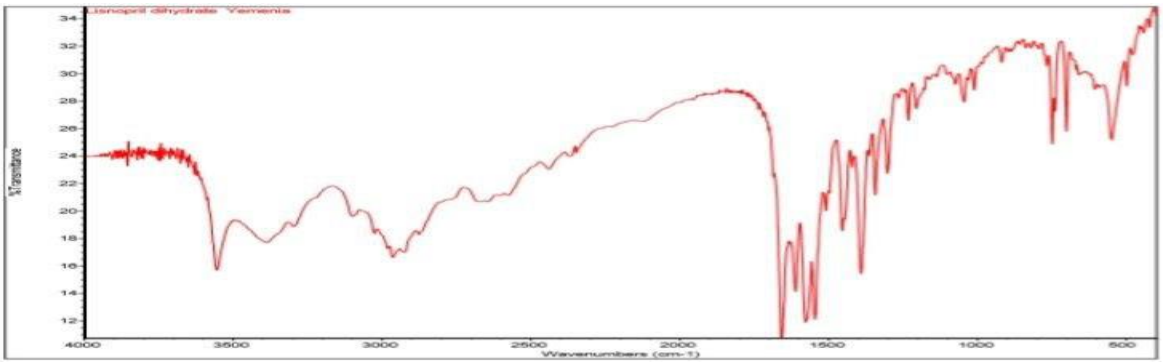


Fig. 3: FTIR Spectrum of Pure Lisinopril.

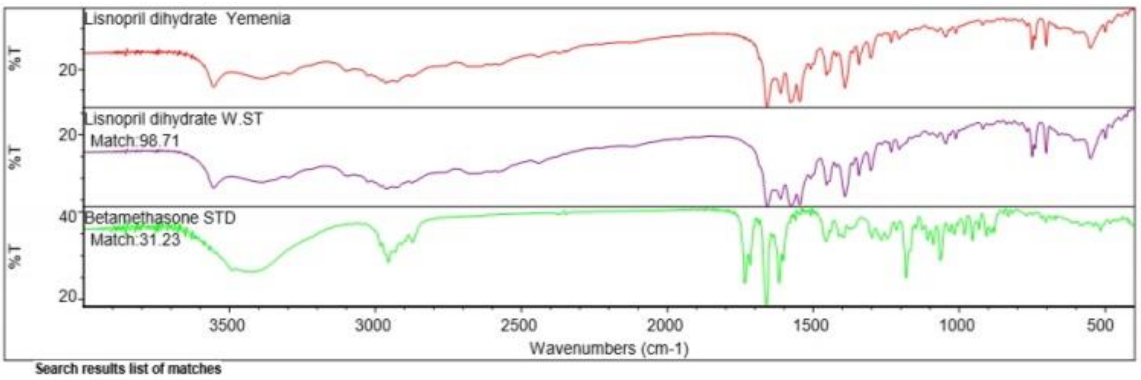


Fig. 4: FTIR Spectrum of Pure Lisinopril with STD.

Table 13: Results of IR Spectra Studies.

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	**2850-3000**	**670-900**	**1300-1420**	**1630-1680**	**1550-1610**
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample ST	2964	704	1390	1659	1577

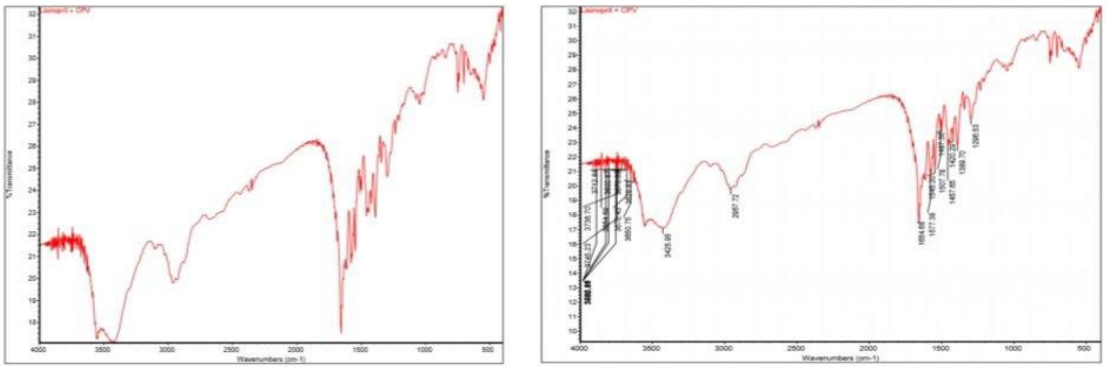


Fig. 5: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Crospovidone.

Table 13: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Crospovidone.

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	**2850-3000**	**670-900**	**1300-1420**	**1630-1680**	**1550-1610**
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with Crospovidone	2957.72	----	1389.7	1654.68	1577.38
After Stored	2957.72	----	1389.7	1656.68	1577.38

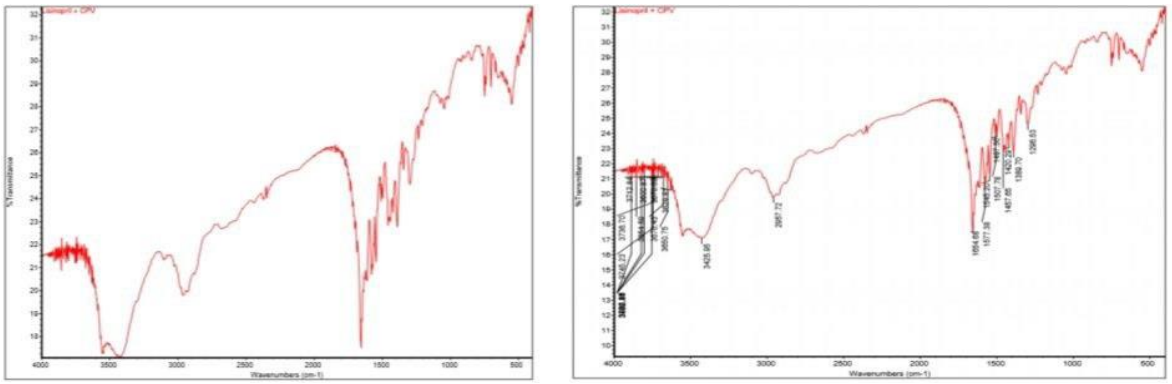


Fig. 6: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and CCS.

Table 14: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and CCS.

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	2850-3000	670-900	1300-1420	1630-1680	1550-1610
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with CCS	2964.39	----	1390.1	1655.56	1577.44
After Stored	2964.39	----	1390.1	1655.56	1577.44

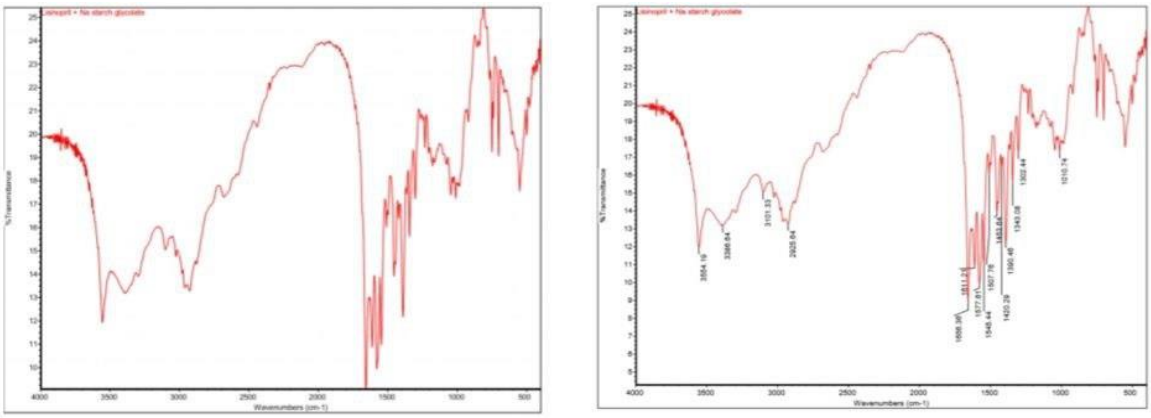


Fig. 7: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and SSG.

Table 15: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and SSG.

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	2850-3000	670-900	1300-1420	1630-1680	1550-1610
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with SSG	2925.64	----	1390.46	1656.36	1577.61
After Stored	2925.64	----	1390.46	1656.36	1577.61

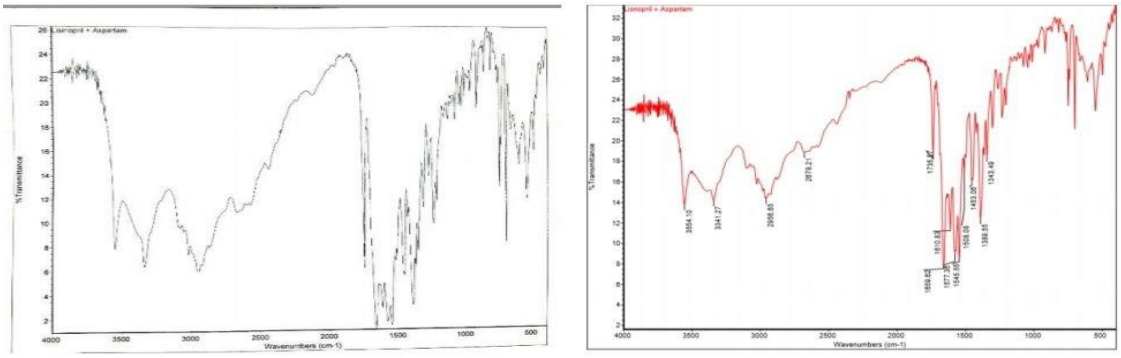


Fig. 1: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Aspartame.

Table 16: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Aspartame.

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	2850-3000	670-900	1300-1420	1630-1680	1550-1610
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with Aspartame	2956.65	----	1389.55	1659.62	1577.36
After Stored	2956.65	----	1389.55	1659.62	1577.36

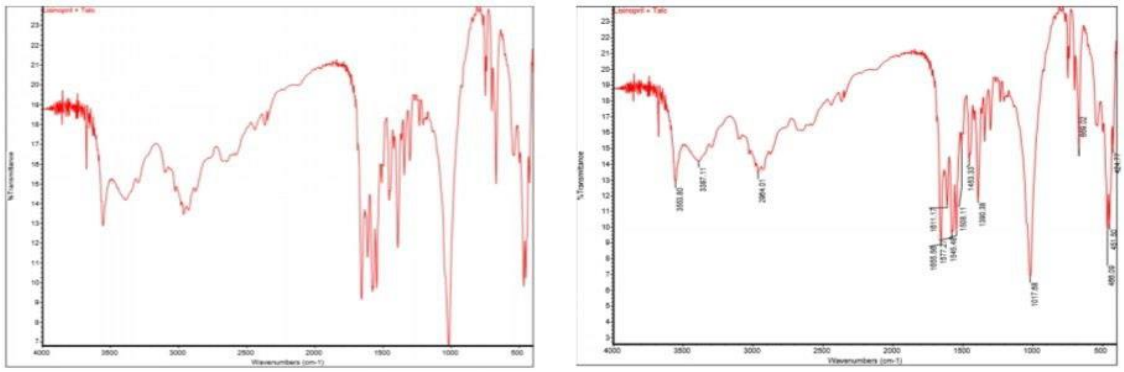


Fig. 8: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Talc.

Table 17: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Talc.

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	2850-3000	670-900	1300-1420	1630-1680	1550-1610
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with Talc	2964.01	----	669.02	1390.38	1577.27
After Stored	2964.01	----	669.02	1390.38	1577.27

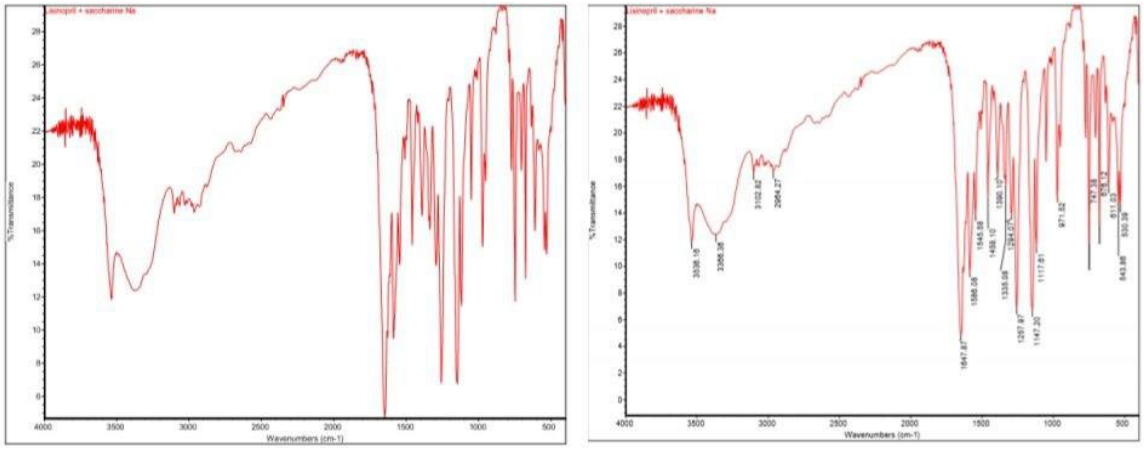


Fig. 9: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Saccharin Sodium.

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

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	2850-3000	670-900	1300-1420	1630-1680	1550-1610
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with Saccharin Sodium	2964.27	747	1335.08	1647.87	1586.08
After Stored	2964.27	747	1335.08	1647.87	1586.08

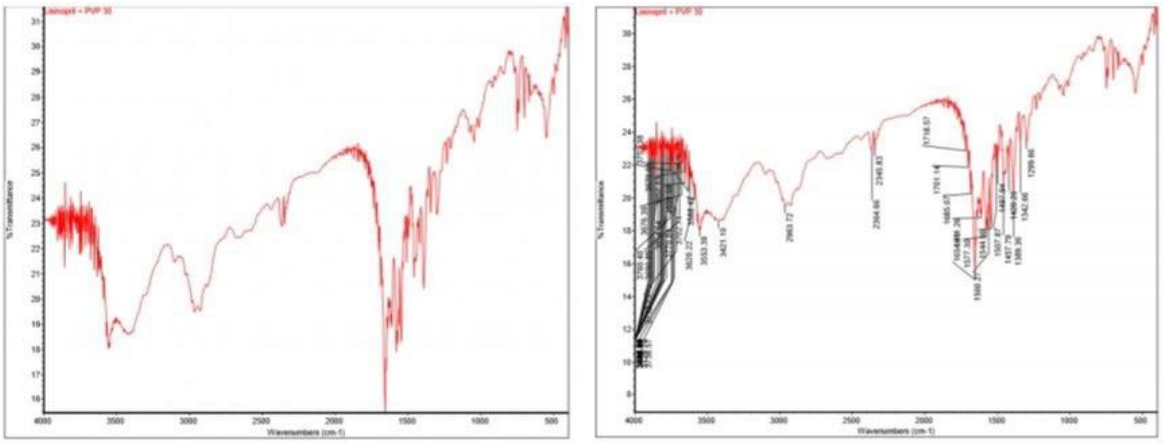


Fig. 10: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and PVP K30.

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

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	2850-3000	670-900	1300-1420	1630-1680	1550-1610
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with PVP K30	2963.72	----	1389.36	1651.46	1577.30
After Stored	2963.72	----	1389.36	1651.46	1577.30

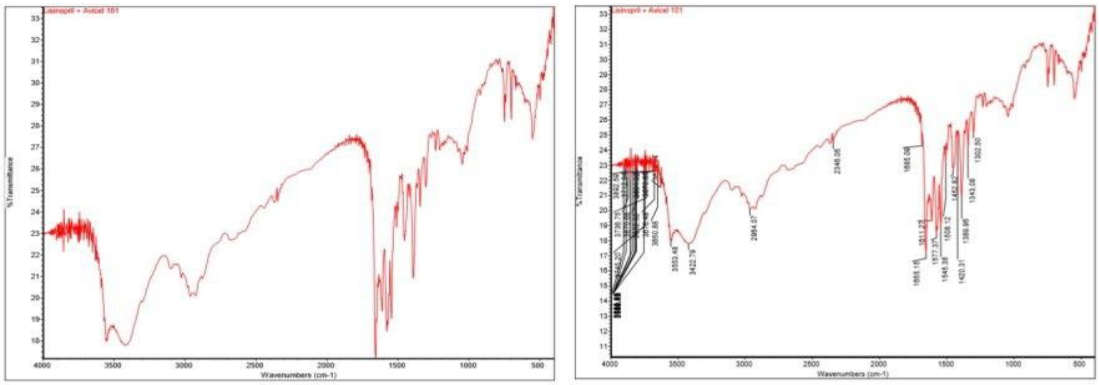


Fig. 11: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Avicel 101.

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

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	**2850-3000**	**670-900**	**1300-1420**	**1630-1680**	**1550-1610**
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with Avicel 101	2964.07	----	1389.96	1655.15	1577.37
After Stored	2964.07	----	1389.96	1655.15	1577.37

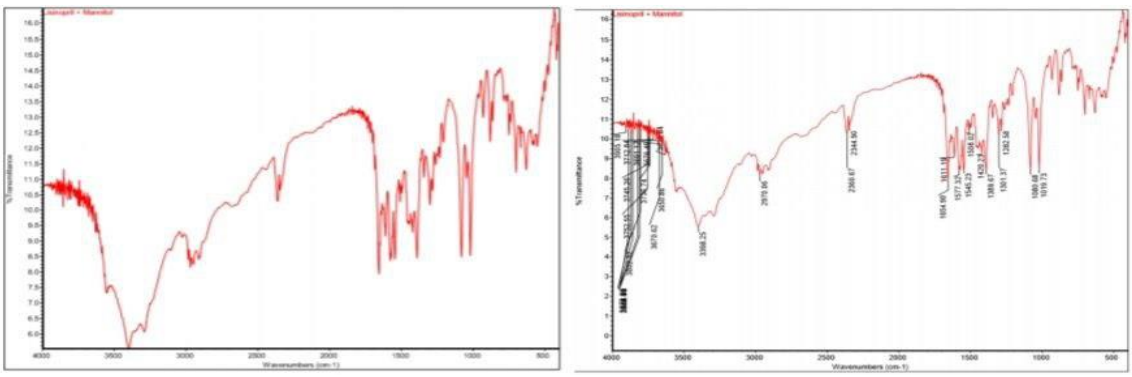


Fig. 12: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Mannitol.

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

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	**2850-3000**	**670-900**	**1300-1420**	**1630-1680**	**1550-1610**
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with Mannitol	2970.06	----	1389.67	1654.90	1577.32
After Stored	2970.06	----	1389.67	1654.90	1577.32

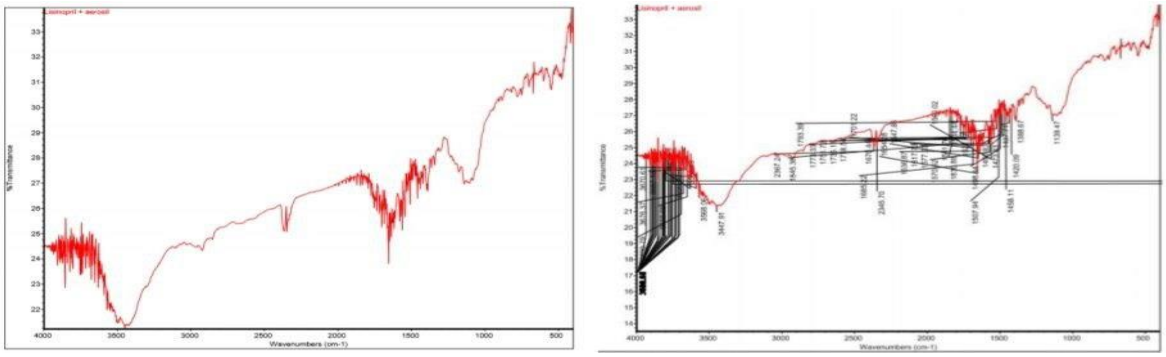


Fig. 13: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Aerosil.

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

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	**2850-3000**	**670-900**	**1300-1420**	**1630-1680**	**1550-1610**
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with Aerosil	----	----	1388.67	1654.28	1577.33
After Stored	----	----	1388.67	1654.28	1577.33

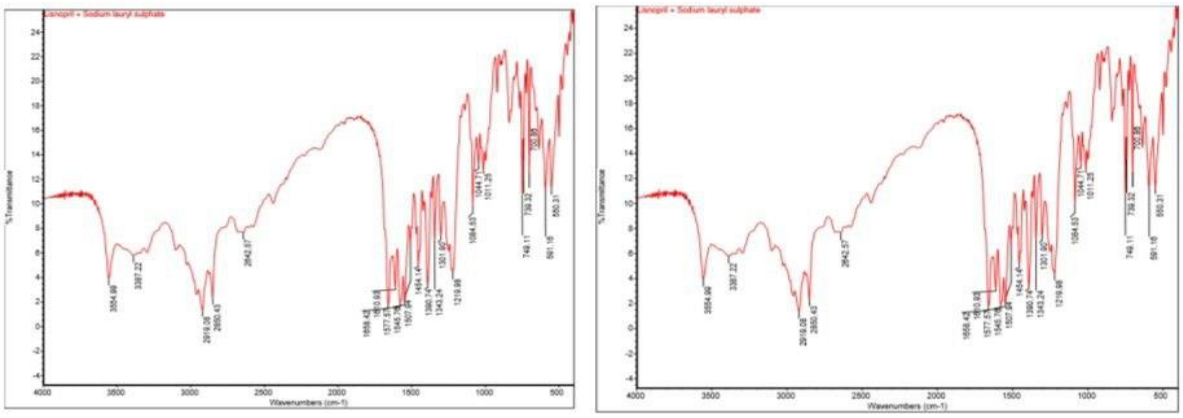


Fig. 14: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and SLS.

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

Function Group	CH-alkane	CH-aromatic	C=O phenol	C=O amid	C=C aromatic
Range	2850-3000	670-900	1300-1420	1630-1680	1550-1610
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with SLS	2850.43	749.11	1390.74	1658.42	1577.57
After Stored	2850.43	749.11	1390.74	1658.42	1577.57

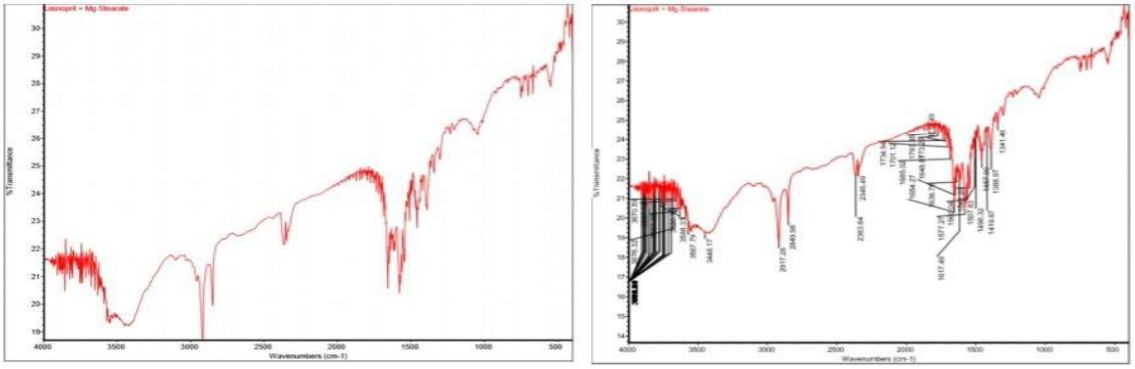


Fig. 15: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and Mg. Stearate.

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

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	**2850-3000**	**670-900**	**1300-1420**	**1630-1680**	**1550-1610**
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with Mg. Stearate	2917.28	----	1388.97	1654.27	1577.27
After Stored	2917.28	----	1388.97	1654.27	1577.27

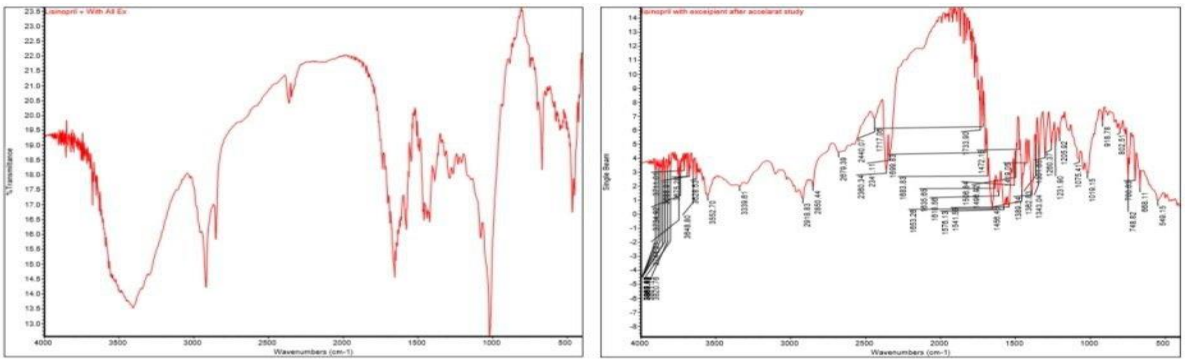


Fig. 16: FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and All Excipients.

Table 24: Results of FTIR Spectrum of Physical Mixture Fresh and Stored of Lisinopril and All Excipients.

Specific Functional Groups	CH-Alkane	CH-Aromatic	C=O Phenol	C=O Amid	C=C Aromatic
The Mid-IR Region (cm^{-1})	2850-3000	670-900	1300-1420	1630-1680	1550-1610
Pure Drug STD	2925.3	749.27	1395	1656.38	1590
Lisinopril Sample Test	2964	704	1390	1659	1577
Lisinopril ST with All Excipients	2918.77	774	1389.67	1654.94	1577.51
After Stored	2918.77	774	1389.67	1654.94	1577.51

Micromeritic Properties of Lisinopril

The powder of Lisinopril dihydrate was evaluated for the following parameters such as angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The results were shown in Table 25.

Table 25: Micromeritics properties of Lisinopril Dihydrate.

Raw Material (API)	App vol	Tapp vol	App D(g/cm3)	Tapp D (g/cm3)	Bulk vol	Bulkiness
Lisinopril	260ml	170ml	0.18	0.304	90	5.26

Table 26: Micromeritics properties of Lisinopril Dihydrate.

Raw Material (API)	Voids	Porosity (%)	Compressibility Index (%)	Hausner Ratio	Carr's Index	Angle of Repose(θ)	Evaluation of angle of Repose
Lisinopril	0.346	34.6%	34.5%	1.5	0.34	38.4	Fair

The angle of repose of Lisinopril was found to be 38.4% which indicates Fair flow property. The bulk density was found to be 0.18 g/cm3, the tapped density was found to be 0.304 g/cm3, the compressibility index was found in 34.5% which indicates very poor flowability and the Hausner's ratio was 1.5 as shown in Table 26.

Evaluation of Precompression Parameters

The powder blends were evaluated for the following parameters such as angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The results were shown in Table 27.

Table 27: Preformulation Parameters of Powder Flow Properties.

Formulation code	Angle of Repose (θ)	Bulk Density (g/cm3)	Tapped Density (g/cm3)	Compressibility index (%)	Hausner's ratio	Evaluation of angle of repose
F1	37.59	0.43	0.57	24.56	1.3	Fair
E2	34.99	0.39	0.53	26.4	1.35	Good
F3	37.95	0.51	0.72	29.16	1.41	Fair
F4	35.37	0.42	0.58	27.58	1.38	Good
F5	34.2	0.42	0.58	27.58	1.38	Good
F6	42.6	0.42	0.56	25	1.3	Passable

The angle of repose of formulation F6 was found to be 42.6 which indicates passable flow property. Angle of repose of all the other formulations were found to be between 34.2 to 37.95 which indicates good and fair flow property. The bulk density was found to be between 0.39 to 0.51 g/cm3, the tapped density was found to be between 0.53 to 0.72 g/cm3, the compressibility index was found in the range of 24.56 to 29.16 % and the Hausner's ratio lies between 1.3 to 1.41. The above results in terms of micromeritics properties revealed that the flow property of formulation F6 was passable and other formulations were good.

CONCLUSION

The compatibility studies of physical mixtures of Lisinopril dihydrate 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 Lisinopril formulations prepared were evaluated for precompression parameters and powder flow properties which were found to be within limits. It was concluded that the drug Lisinopril dihydrate was found to be compatible with various excipients which were selected for the formulation development of the Lisinopril 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 Yemen-Egyptian Pharmaceutical Industry Company -Yemen and Shaphaco Pharmaceutical Industry Company-Yemen for their support and facilities.

REFERENCES

1. 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.
2. 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.
3. 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.
4. Chadha R, Bhandari S. Drug–Excipient Compatibility Screening—Role of Thermoanalytical and Spectroscopic Techniques. J Pharm Biomed Anal., 2014; 87: 82-97.
5. 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.
6. O'Neill MA, Gaisford S. Application and Use of Isothermal Calorimetry in Pharmaceutical Development. Int J Pharm., 2011; 417: 83-93.
7. 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.
8. 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.
9. 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.
10. 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.
11. 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.
12. 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.

13. 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.
14. 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.
15. 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.
16. 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.
17. 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.
18. 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.
19. 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.
20. 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.
21. 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.
22. 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.

23. 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.
24. 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.
25. 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.
26. 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.
27. 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.
28. 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.
29. 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.
30. 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.
31. 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.
32. Gupta A, Kar HK. Solid State Compatibility Studies of Miconazole Using Thermal and Spectroscopic Methods. Adv Anal Chem., 2015; 5: 51-55.
33. 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.
34. 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.

35. 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.
36. 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.
37. 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.
38. 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.
39. 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.
40. 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.
41. 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.
42. 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.
43. 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.
44. Prasanna Kumar et al. An Overview on Preformulation Studies. Indo Am J Pharm Sci., 2015; 2(10).
45. Allen L, Ansel H. Pharmaceutical Dosage Forms and Drug Delivery Systems by Ansel (10th Edition). Lippincott Williams & Wilkins, Philadelphia., 2014.
46. Beringer P, Gupta PK, Felton L. Stability of Pharmaceutical Products. Remington: The Science and Practice of Pharmacy., 2005; 01: 1029-30.

47. 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.
48. 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.
49. Crowely P, Martini LG. Drug Excipient Interactions. Pharmaceutical Technology., 2001; 3: 0582.
50. 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.
51. 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.
52. Stephenson GA, Forbes RA, Reutzel-Edens SM. Characterization of the Solid State: Quantitative Issue. Advanced Drug Delivery Reviews., 2001; 48: 67-90.
53. Tishmack PA, Bugay DE, Byrn SR. Solid-State Nuclear Magnetic Resonance Spectroscopy-Pharmaceutical Applications. J Pharm Sci., 2003; 92: 441-474.
54. 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.
55. Deokate U, Gorde AM. Forced Degradation and Stability Testing: Strategies and Analytical Perspectives. Int J Pharm Sci Rev and Res., 2014; 42: 242-250.
56. Lena Ohannesian, Antony J. Streeter. Handbook of Pharmaceutical Analysis, Marcel Dekker, Inc., 2002.
57. Banker G, Rhodes CT. Modern Pharmaceutics, Marcel Dekker, Inc., 2000.
58. Harry G Britain. Spectroscopic Methods for the Characterization of Drug Substances, Marcel Dekker, Inc., 2008.
59. Lewis IR, Edwards HGM. Handbook of Raman Spectroscopy, New York: Marcel Dekker., 2001.
60. Blachere JR, Harry G. Brittain. X-Ray Diffraction Methods for the Characterization of Solid Pharmaceutical Materials, Marcel Dekker, Inc., 2008.
61. US Pharmacopoeia 30, National Formulary 25, USP Convention, Rockville., 2007.

62. 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.
63. 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.
64. 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.
65. 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.
66. 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.
67. USFDA, Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach., 2004.
68. USFDA, Guidance for Industry - ICH Q8 (R2) Pharmaceutical Development, C. CDER, Editor. USFDA: Silver Spring, MD., 2009; 1-20.
69. Wu Y, et al. Reactive Impurities in Excipients: Profiling, Identification and Mitigation of Drug-Excipient Incompatibility. AAPS PharmSciTech., 2011; 12(4): 1248-1263.
70. Narang A, et al. Impact of Excipient Interactions on Solid Dosage Form Stability. Pharm Res., 2012; 29(10): 2660-2683.
71. Rowe RC, Sheskey PJ, Quinn ME. Handbook of Pharmaceutical Excipients. Sixth Edition. London. APhA/Pharmaceutical Press., 2009.
72. Sims J, et al. A New Approach to Accelerated Drug-Excipient Compatibility Testing. Pharm Dev Technol., 2003; 8(2): 119.
73. 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.
74. Liltorp K, et al. Solid-State Compatibility Studies with Tablet Excipients Using Non-Thermal Methods. J Pharm Biomed Anal., 2011; 55(3): 424-428.
75. Épshtein NA. Compatibility of Medicinal and Excipient Substances in the Development of Medicinal Formulations. Pharm Chem J., 2018; 52(7): 648–57.
76. ICH Topic Q8 (R2). Pharmaceutical development., 2009; 8.
77. Thomas VH, Naath M. Design and Utilization of the Drug-Excipient Chemical Compatibility Automated System. Int J Pharm., 2008; 359(1– 2): 150–7.

78. Michael E Aulton, Pharmaceutics- The Sciences of Dosage Form Design, 4rth International Edition, Churchill Livingstone, USA., 2013; 367-389.
79. Leon Lachman, Lieberman's. The Theory and Practice of Industrial Pharmacy. Indian 4rth Edition, CBS Publisher, Reprint., 2020; 217-251.
80. Mark Gibson. Pharmaceutical Preformulation and Formulation. HIS Health Group, CRC, United state of America., 2004; 20- 45.
81. WHO. Annex (3). Pharmaceutical Development of Multisource (Generic) Finished Pharmaceutical Products.
82. 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.
83. 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.
84. 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.
85. Brough C, Williams RO. Amorphous Solid Dispersions and Nanocrystal Technologies for Poorly Water-Soluble Drug Delivery. Int J Pharm., 2013; 453: 157–66.
86. Samal HB, Debata. Solubility and Dissolution Improvement of Aceclofenac Using β-Cyclodextrin. Int J Drug Dev Res., 2012; 4: 326-33.
87. Zingone G, Rubessa F. Preformulation Study of the Inclusion Complex Warfarin-β-Cyclodextrin. Int J Pharm., 2005; 291: 3-10.
88. 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.
89. 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.
90. 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.
91. Alburyhi MM. Doctor Thesis, Faculty of Pharmacy, Cairo University., 2009.
92. 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.

93. 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.
94. 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.
95. 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.
96. 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.
97. 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.
98. 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.
99. 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.
100. 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.
101. Saif AA, Alburyhi MM, Noman MA. Formulation and Evaluation of Ketoprofen Fast Dissolving Tablets. International Journal of Sciences., 2018; 7(09): 27- 39.
102. 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.
103. 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.

104. 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.
105. 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.
106. 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.
107. 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.
108. 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.
109. 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.
110. 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.
111. 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.
112. 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.
113. 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.

114. 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.
115. 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.
116. 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.
117. Patel PA, Ahir K, Patel VB et al. Drug-Excipient Compatibility Studies: First Step for Dosage form Development. Pharm Innov., 2015; 4: 14-20.
118. Panakanti R, Narang AS. Impact of Excipient Interactions on Drug Bioavailability from Solid Dosage Forms. Pharm Res Dordr., 2012; 29: 2639-2659.
119. 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.
120. Cortese F, Gesualdo M, Cortese A, et al. Rosuvastatin: Beyond the Cholesterol-Lowering Effect. Pharm Res-Dordr., 2016; 107: 1-18.
121. McTaggart F. Comparative Pharmacology of Rosuvastatin. Atherosclerosis Supp., 2003; 4: 9-14.
122. 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.
123. Berthomieu C, Hienerwadel R. Fourier Transform Infrared (FTIR) Spectroscopy. Photosynth Res., 2009; 101: 157-170.
124. Krishna BJ, Satyanarayana J, Rao NR. Rivaroxaban: Compatibility with Pharmaceutical Excipients using DSC and FTIR Spectrophotometry. J Pharm Res Int., 2022; 43-50.
125. Bele AA, Khale A. An Overview on Thin Layer Chromatography. Int J Pharm Pharm Sci., 2011; 6: 256-267.
126. 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.

127. 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.
128. Bozal-Palabiyik B, Uslu B, Ozkan Y, et al. In-Vitro Drug Dissolution Studies in Medicinal Compounds. Curr Med Chem., 2018; 25: 4020-4036.
129. 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.
130. 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.
131. 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.
132. Aulton's Pharmaceutics: Pharmaceutics-the Science of Dosage Forms Design. Churchill Livingstone Elsevier.3rd Edition., 2007; 322-538.
133. 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.
134. Chavda HV, Patel CN, Anand IS. A Review Article on Biopharmaceutics Classification System: Published by Systematic Reviews in Pharmacy, January-June., 2010; 1(1).
135. 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.
136. Verma S, Rawat A, Kaul M, Saini S. Solid Dispersion: A Strategy for Solubility Enhancement. Int J Pharm Technol., 2011; 3: 1062-99.
137. 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.
138. 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.
139. 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.

140. 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.
141. 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.
142. 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.
143. www.drugbank.com.
144. 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).
145. 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.
146. 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).
147. 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.
148. 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).
149. 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.
150. 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.

151. 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.
152. Golla C. Design and Evaluation of Press Coated Pulsatile Delivery of Doxofylline Tablets. Acta Scientific Pharmaceutical Sciences., 2018; 2(11), 58- 62.
153. 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.
154. 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.
155. 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.
156. 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.
157. 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.
158. 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.
159. 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.
160. Karaźniewicz-Łada M, Bąba K, Dolatowski F. The Polymorphism of Statins and its Effect on Their Physicochemical Properties. Polim Med., 2018; 48: 77–82.
161. Tannebaum EJ. Oral Solid Dosage Facilities. in: Good Design Practices for GMP Pharmaceutical Facilities, 2nd Ed.; New York, NY, USA., 2005.
162. 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.

163. 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.
164. Sachin TV, Deodhar MN, Prakya V. Advances in Analytical Techniques Used in Predicting Drug-Excipient Interactions. Int J Pharm Tech., 2014; 6: 6388-6417.
165. 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.
166. Davies P. Oral Solid Dosage Form. in: Pharmacetuical Preformulation and Formulation, 2nd Ed., Gibson M, Ed. Informa HealthCare: New York, NY, USA., 2009.
167. Creekmore JR, Wiggins NA. Pharmaceutical Composition Comprising an HMG COA Reductase Inhibitor. European Patent Office. Patent No. EP1223918., 2002.
168. 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.
169. 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.
170. 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.
171. Schwartz JB. Scale Up of the Compaction and Tableting process. in Pharmaceutical Process Scale Up; Marcel Dekker Inc.: New York, NY, USA., 2002.
172. Zhou C, Gao W, Lu G. Preparation, Characterization, and InVitro Release of Microparticles Based on Dextran-Rosuvastatin Conjugate. Carbohydrate Polymers., 2013; 96: 156–162.
173. 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.
174. Hariharan M, Gupta VK. A Novel Compression Coated Tablet Dosage Form. Pharm Tech., 2001; 14–19.
175. 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.

176. 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.
177. ICH Guidelines Q1A (R2), Guidelines for Industry, Stability Testing of New Drug Substance and Product. Availale online: http: //www.ICH.org.
178. 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.
179. 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.
180. 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.
181. 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.
182. 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.
183. 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.
184. Indian Pharmacopoeia, The Indian Pharmacopoeia Commission, Ghaziabad, 6th Ed., 2010; 2: 806, 1337, 2071.
185. Martindale. The Extra Pharmacopoeia, The Complete Drug Reference, edited by Sean C Sweetman, Pharmaceutical press, 34th Ed., 2005; 862,915,966,968,996-997.
186. Herbert A Lieberman, Leon Lachman, Joseph B, Schwartz. Pharmaceutical dosage forms tablets. Marcel Dekker, New York, USA, 2 nd Edition., 2009.
187. Leon Lachman, Lieberman H A.The Theory and Practice of Industrial Pharmacy, Lea and Febiger, Philadelphia, USA, 3 rd Edition., 2003.

188. Markl D, Zeitler JA. A Review of Disintegration Mechanisms and Measurement Techniques, Pharmaceutical research.,2017; 34(5): 890.
189. Seo KS, Bajracharya R, Lee SH, Han HK. Pharmaceutical Application of Tablet Film Coating, Pharmaceutics.,2020; 12(9): 853-862.
190. 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.
191. 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.
192. 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.
193. Alburyhi MM, Saif AA, Noman MA. Formulation and Evaluation of Ticagrelor Orodispersible Tablets. World Journal of Pharmaceutical Research., 2024; 13(5): 26-55.
194. 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.
195. 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.
196. 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.
197. 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.
198. 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.

199. 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.
200. 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.
201. 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.
202. 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.
203. 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.
204. 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.
205. Patel MA, Pingale PL. High Functionality Coprocessed Excipients: A Review. World J Pharm Sci.,2014; 3(3): 795-806.
206. World Health Organization. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials, Good Manufacturing Practices and Inspection., 2007.
207. Sreenivas S A, Gadad AP, Patil MB. Formulation and Evaluation of Ondansetron Hydrochloride Directly Compressed Mouth Disintegrating Tablets. Indian Drug., 2006; 43: 35-37.
208. Mishra B, Panigrahi D. Mouth Dissolving Tablets an Overview of Preparation Techniques, Evaluation and Patented Technologies', Indian Journal of Pharmaceutical Sciences., 2005.
209. 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.
210. Goyal P, et al. Liposomal Drug Delivery Systems: Clinical Applications. Acta Pharm., 2005; 55: 1–25.

211. 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.
212. 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.
213. 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.
214. 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.
215. Tabbouche OS. Validation of a UV-Spectrophotometeric Method for the Assay Paracetamol in Solutions. Int J Pharm., 2013; 3(1): 24-7.
216. Biradar S S, Bhagavati S T, Kuppasad I J. Fast Dissolving Drug Delivery Systems: A Brief Overview. Int J Pharmacol., 2006; 4(2).
217. 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.
218. 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.
219. 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.
220. 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.
221. 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.
222. Allen LV, Ansel HC, Popovich NG. Pharmaceutical Dosage Forms and Drug Delivery Systems. Evaluation., 2011: 56: 44.
223. Aulton ME, Summers M. Tablets and compaction. Aulton's Pharmaceutics: The Design and Manufacture of Medicines., 2013; 5: 520-530.

224. Chang RK, Guo X, Burnside BA, Couch RA. Fast-Dissolving Tablets. Pharmaceutical Technology., 2000; 24(6): 52-52.
225. 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.
226. Seyda A. A Non-Steroidal Anti-Inflammatory Drug, Aceclofenac. FABAD Journal of Pharmaceutical Science., 2010; 35: 105-118.
227. Chandel N. Co-Crystalization of Aceclofenac and Paracetamol and Their Characterization. International Journal of Pharmacy & Life Science., 2011; 2(8): 1020-1028.
228. Jayanthi B, Madhusudhan S. Preformulation Characterization, Designing and Formulation of Aceclofenac Loaded Microparticles. International Journal of Drug Development & Research., 2012; 4(3): 186-196.
229. 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.
230. 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.
231. Bansal SY. Effect of Aceclofenac on Pharmacokinetic of Phenytoin. Pakistan Journal of Pharmaceutical Science., 2012; 25(2): 295-299.
232. 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.
233. 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.
234. Sona PS, Muthulingam C. Formulation and Evaluation of Taste Masked Orally Disintegrating Tablets of Diclofenac Sodium. International Journal of Pharm Tech Research., 2011.
235. Jagadeesh Induruand, Padmaja Bookya. Excipient Screening and Development of Formulation Design Space for Diclofenac Sodium Fast Dissolving Tablets. International Journal Pharmaceutical, Pharmaceutical sciences., 2011.

236. 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.
237. United States Pharmacopoeia. 30th edition NF 25, The Official Compendia of Standards., 2007.
238. 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.
239. 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.
240. 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.
241. 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.
242. 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.
243. 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.
244. 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.
245. 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.
246. 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.

247. Bolhuis GK, Armstrong NA. Excipients for Direct Compaction - an Update. Pharma Dev and Tech., 2006; 11(1): 111-124.
248. 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.
249. 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.
250. Ravichandiran V. Modern Pharmaceutics. Rev J Pharm Res., 2011; 4(8): 2590–2.
251. 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.
252. Alford N, Martin PJ. Martin's Physical Pharmacy and Pharmaceutical Sciences. and Others, Editor., 2006.
253. Treatise DM. Biopharmaceutics and Pharmacokinetics -A Treatise. and Others, Editor., 2009.
254. 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.
255. 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.
256. Patil PB, Datir SK, Saudagar RB. Journal of Drug Delivery and Therapeutics., 2019; 9 (3-S),989-994.
257. 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.
258. Remington, The Science and Practice of Pharmacy. Lippincott Williams & Wilkins, 20th Edition., 2002.
259. 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.
260. 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.

261. 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.
262. 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.
263. 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.
264. 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), p.360.
265. Savale SK. Formulation and Evaluation of Diclofenac Sustained Released Tablet. Asian Journal of Pharmaceutical Analysis and Medicinal Chemistry., 2015; 3(4).
266. 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.
267. 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.
268. Martindale: The Complete Drug Reference, 37Th Edn. The Pharmaceutical Press, London., 2011.
269. 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.
270. Wagh MP. Formulation and Evaluation of Fast Dispersible Tablets of Aceclofenac Using Different Superdisintegrant. Int J Pharm Pharm Sci., 2010; 2(1): 154–7.
271. Debjit B, et al. Fast Dissolving Tablet: An Overview. Journal of Chemical and Pharmaceutical Research., 2009; 1(1): 163-177.
272. Mizumoto T, et al. Formulation Design of a Novel Fast Disintegrating Tablet. Int J Pharm., 2008; 306: 3- 9.

273. 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.
274. Park j et al. An Alternative to The USP Disintegration for Orally Dissolving Tablet. Pharm tech., 2008; 32: 1-3.
275. Badgujar BP, Mundada AS. The Technologies Used for Developing Orally Disintegrating Tablets: A Review. Acta Pharmaceutica., 2011; 61(2): 117-139.
276. Amal S, Abu el-enin. Flurbiprofen Fast Disintegrating Tablets. Int J Pharm Sci., 2014; 6(2): 499-505.
277. Jha K, Geethalakshmi A, Bhatia V, Shukla T. Orally Disintegrating Tablets-Technology for Mankind. J Global Pharm Tech., 2011; 74: 11-17.
278. David Brown. Orally Disintegrating Tablets- Taste Over Speed. Drug Delivery Technology.,2003; 3(6).
279. Parakh S R et.al. A Review of Mouth Dissolving Tablet Technologies. Pharm Technol., 2003; 27 (11): 92–100.
280. 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.
281. Hypertension, Federal Bureau of Prisons - Clinical Practice Guidelines., May 2005.
282. Sudarshan K Singh, Agham A Sameer. Development and Characterization of Sublingual Tablet of Lisinopril. Asian Pacific Journal of Tropical Biomedicine., 2012; S1711-S1719.
283. 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.
284. 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.
285. 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.
286. Pandey S, Goyani M. Formulation and Evaluation of Taste Masked Fast Disintegrating Tablets of Lisinopril. Int J Pharm Tech Res., 2010; 148: 1639- 43.
287. Dandagi PM, Gayakwad VM. Taste Masked Ofloxacin Mouth Disintegrating Tablets. Indian drugs., 2005; 17: 52-54.
288. 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.

289. Gohel MC. A Review of Co-processed Directly Compressible Excipients. J Pharm Sci., 2005; 102: 76- 93.
290. Suresh S, Pandit V. Preparation and Evaluation of Mouth Dissolving Tablets of Salbutamol Sulphate. Int J Pharm sci., 2007; 12: 54-57.
291. Arora V, Gupta B, Advances in direct compression technology. Pharma times 2007; 74: 26-27.
292. Bhupendra G P, Nayan R. A Review on Recent Patents on Fast Dissolving Drug Delivery System. Pharm Tech., 2009; 1 (3): 790- 798.
293. Bhavanam, Pamula R. Formulation and Evaluation of Levofloxacin Using Different Types and Concentrations of Superdisintegrants. J Pharm Sci and Res., 2010; 1: 1-5.
294. Setty CM, Prasad DV, Gupta V. Development of Fast Dispersible Tablets: Effect of Functionality of Superdisintegrants. Ind J Pharma Sci., 2008; 180- 185.
295. 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.
296. Nitin M, Adhikrao Y, Vaishali K. Novel Approaches in Development of Metronidazole Orodispersible Tablets. Res J Pharm Tech., 2009; 44: 283-86.
297. 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.
298. 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.
299. 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.
300. 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.
301. 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.

302. 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.
303. Song JC, White CM. Clinical Pharmacokinetics and Selective Pharmacodynamics of New Angiotensin Converting Enzyme Inhibitors: an Update. Clin Pharmacokinet., 2002; 41(3): 207-24.
304. Nagarajan K, Rao MG. Formulation and Dissolution Studies of Solid Dispersions of Nifedipine. Indian Journal of Novel Drug Delivery., 2010; 2: 96-98.
305. 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.
306. 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.
307. 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.
308. Deepak K, Narender S. Enhancement of Dissolution profile of Gliclazide by Solid dispersion adsorbates. Lat Am J Pharm., 2011; 30: 2057-2060.
309. Dua K, Ramana MV, Sara UVS, Himaja M, Garg V, Agrawal A. Dissolution Enhancement of Aceclofenac Through Solid Dispersions. Indian Pharmacist., 2006; 70-72.
310. Subramanyam CVS. Textbook of Physical Pharmaceutics. 3rd Ed. Vallabh Prakashan: Delhi, 2001; 181-234.
311. Brahmankar D M, Jaiswal S B. Biopharmaceutis and Pharmacokinetics: A Tretise, Vallabh Prakashan, New Delhi, 1 st Edition., 2006; 335-357.
312. 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.
313. 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.
314. Sharma S, Gupta G, Bala R, Sharma N, Seth N, Goswami J. Orodispersible Tablet A Review. Pharmainfo.net.html., 2008.

315. Rishikesh et al. Immediate Release Drug Delivery System (Tablets): An Overview. (IRJPAS); Int. Res J Pharm. App Sci., 2012; 2(5): 88-94.
316. 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.
317. 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.
318. Nyol Sandeep et al. Immediate Drug Release Dosage Form: A Review. Journal of Drug Delivery & Therapeutics., 2013, 3(2), 155-161
319. 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.
320. 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.
321. Natarajan R, Vaishnani R, Rajendra NN. Formulation and Evaluation of Immediate Release Tablets of Paroxetine HCL Using Different Superdisintegrants. International Journal of Research in Pharmaceutical and Biomedical Sciences., 2011; 2 (3): 1095-1099.
322. Ratnaparkhi M, Dhage K, Chaudhari S, Salvankar S. Formulation and Evaluation of Immediate Release Tablets of Metformin HCL and Glibenclamide Using Different Superdisintegrants. PharmaTech Medica., 2012; 1(3): 8085.
323. Pande V, Karale P, Goje P and Mahanavar S. An Overview on Emerging Trends in Immediate Release Tablet Technologies. Austin Therapeutics., 2016; June 28.