“Compatibility Study of Albendazole, Levofloxacin and Pregabalin with Various Excipients and their Subsequent Formulation Optimization”

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A thesis Paper submitted to the Department of Pharmacy, East West University, Bangladesh, in partial fulfillment of the requirements for the degree of Masters of Pharmacy.

Declaration by the Research Candidate

I, **Mahjabin Haque,** hereby declare that the dissertation entitled "**Compatibility Study of Albendazole, Levofloxacin and Pregabalin with Various Excipients and their Subsequent Formulation Optimization**" submitted by me to the Department of Pharmacy, East West University and in the partial fulfillment of the requirement for the degree of Masters of Pharmacy, is a confide record of original research work carried out by me under the supervision and guidance of **Shamsun Nahar Khan**, PhD., Post Doc Harvard USA, MRSC, Associate Professor, Department of Pharmacy, East West University.

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Certificate by the Supervisor

This is to certify that the thesis entitled **"Compatibility Study of Albendazole, Levofloxacin and Pregabalin with Various Excipients and their Subsequent Formulation Optimization"** submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the degree of Masters of Pharmacy, was carried out by **Mahjabin Haque**, ID: 2015-1-79-012, during the period of her research in the Department of Pharmacy, East West University, under the supervision and guidance of me. The thesis has not formed the basis for the award of any other degree/diploma/fellowship or other similar title to any candidate of any university.

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Certificate by the Chairperson

This is to certify that the thesis entitled **"Compatibility Study of Albendazole, Levofloxacin and Pregabalin with Various Excipients and their Subsequent Formulation Optimization"** submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the degree of Masters of Pharmacy, was carried out by **Mahjabin Haque**, ID No.: 2015-1-79-012, under the supervision of **Shamsun Nahar Khan**, PhD., Post Doc Harvard USA, MRSC, Associate Professor, Department of Pharmacy, East West University.

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Dedication

This Research Paper is dedicated
To
My Beloved Parents

Abstract

This work was proposed to assess the compatibility of Actives viz. Albendazole, Levofloxacin and Pregabalin with different functional excipients like fillers/diluents, disintegrants, binders and lubricants which are commonly used in solid dosage formulation. Samples were made by mixing active and excipients in different ratio and put in stability chamber at different stability conditions. Samples were withdrawn at different time intervals and tested accordingly. Assay, Impurity and IR spectrum were chosen as testing parameter to determine the compatibility of actives with particular excipient. This research work has demonstrated the relationship between active and excipients and their compatibility in dosage form formulation. Tentative formula of the dosage forms viz. Albendazole Chewable Tablets, Levofloxacin Film Coated Tablets and Pregabalin Capsules were also established and evaluated.

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1.1 Introduction

Drug-excipient interactions/incompatibilities are major concerns in formulation development. Selection of the proper excipient during preformulation studies is of prime importance. Many stability problems encountered during development and post-commercialization can be ascribed to inadequate matching of the ingredients in dosage forms, lack of awareness of the complexities of chemical and physical interactions, or the unheralded presence of a residue in one of the excipients. Many such issues concern low levels of novel entities formed by drug– excipient interactions that pose questions concerning safety or tolerance.

Knowledge of drug–excipient interactions is a necessary prerequisite to the development of dosage forms that are stable and of good quality. Drug-excipient interactions may take a long time to be manifested in conventional stability testing studies, and are not always predicted by stress and pre-formulation studies.

They can complicate and compromise a development program or the viability of a commercial product. It is possible to reduce the probability of such undesirable and costly scenarios by allying knowledge of the propensity of a drug to undergo degradation reactions with awareness of excipient reactivity and of the residues that they may contain.

Thermo analytical and spectroscopic techniques have played a pivotal role in characterization of solid state interactions and early detection of drug–excipient compatibility. The in-depth knowledge and appropriate use of these analytical techniques have brought forth extraction of valuable information concerning the drug–excipient interactions that aid in the selection of appropriate excipients for stable and an efficacious solid dosage form (Patel *et al.*,2015).

Compatibility studies are usually the last activity done during pre-formulation profiling. All pre-formulation studies, except compatibility studies, are carried out on pure drug substance. Compatibility studies are aimed at studying the interactions of drug substance with other excipients. Selection of excipients is vital for development of a quality drug product. Choice of excipients is guided by the type of proposed dosage form. For example, for a tablet dosage form, excipients belonging to categories of diluent, binder, disintegrant, lubricant, glidant are usually included in the compatibility studies. Based on the need, optionally solubilizer, stabilizing agent, buffer and rate controlling polymer can also be included.

1.2 Mechanisms for incompatibility

Studies of drug-excipient compatibility represent an important phase in the preformulation stage of the development of all dosage forms. The potential physical and chemical interactions between drugs and excipients can affect the chemical, physical, therapeutical properties and stability of the dosage form.

Compatibility studies aim at identifying potential physical and chemical incompatibility between drug substance and excipients. Excipients may contribute to incompatibility by (i) altering the moisture content, (ii) altering the micro-environment pH, (iii) acting as a catalyst for degradation or (iv) contributing an impurity that causes degradation.

1.3 Role of compatibility studies in formulation development

A complete characterization and understanding of physicochemical interactions of an active pharmaceutical ingredient (API) in the dosage forms is an integral part of preformulation stage of new dosage form development as it is most desirable for consistent efficacy, safety and stability of a drug product. In a dosage form, an API comes in direct contact with other components (excipients) of the formulation that facilitate the administration and release of an active component as well as protect it from the environment. Although excipients are pharmacologically inert, they can interact with drugs in the dosage form to affect drug product stability in physical aspects such as organoleptic properties, or chemically by causing drug degradation. Careful selection of the excipients is required for a robust and effective formulation of dosage forms that make administration easier, improve patient compliance, promote release and bioavailability of the drug and increase its shelf life.

Thus, compatibility screening of an API with excipients or other active ingredients is recognized as one of the mandatory factors and is at the fore front of drug product science and technology research.

A complete understanding of the physicochemical interactions in dosage forms is expected under quality by design prototype of drug development. The analytical methods into the initial steps of preformulation studies have contributed significantly to early prediction, monitoring and

characterization of the API incompatibility to avoid costly material wastage and considerably reduce the time required to arrive at an appropriate product formulation.

Compatibility studies thus allow in systematic selection of excipients, for formulation development. Early detection of incompatibilities also helps in developing strategies to mitigate stability related problems in the dosage forms (Bansal, 2012).

1.4 Mechanism of drug excipient interaction

Exact mechanism of drug excipients interaction is not clear. However, there are several well documented mechanisms in the literature. Drug excipients interaction occurs more frequently than excipient-excipient interaction. Drug excipients interaction can either be beneficial or detrimental, which can be simply classified as-

- Physical interactions
- Chemical interactions
- Biopharmaceutical interactions

1.4.1 Physical interactions

Physical interactions are very common in dosage form and also difficult to detect. Physical interactions may or may not involve chemical changes thus permitting the components in the formulation to retain their molecular structure. Physical interactions involve change in a dissolution, solubility, sedimentation rate etc. Physical interactions can be either beneficial or detrimental to the product performance which is dependent on its application.

1.4.2 Chemical interactions

Active pharmaceutical ingredients and excipients react with each other to form unstable compounds. Several chemical drugs excipient interactions have been reported in literature. Generally chemical interactions have a deleterious effect on the formulation hence such kind of interactions must be usually avoided.

1.4.3 Biopharmaceutical interactions

These are the interactions which are observed after administration of the medication. Interaction of medicine with body fluid influences the rate of absorption. All excipients interact in physiological way when they are administered along with active pharmaceutical ingredients.

1.5 Study design for compatibility studies

In this study design, three actives were chosen for compatibility study with different excipients used in solid oral dosage forms. Albendazole (Broad spectrum Anthelmintic), Levofloxacin (Antibiotic, fluoroquinolones) and Pregabalin (Calcium Channel Blocker) were selected for this study design. Excipients like fillers/diluents, disintegrants, binders, lubricants were considered from different classes.

The test samples would be divided into 3 major categories such as:

(i) 1 part of Drug : 1 Part of Filler

For high dose drugs, compatibility study of active and fillers like Microcrystalline Cellulose, Lactose Monohydrate and Maize Starch can be performed as 1:1 ratio.

(ii) 1 part of Drug : 0.5 Parts of Functional Excipient

The functional excipients considered for compatibility study can be Hypromellose, Hydroxypropyl Cellulose, Povidone (K 30), Crospovidone, Magnesium Stearate, Sodium Starch Glycolate, Croscarmellose Sodium, Sodium Lauryl Sulfate, Colloidal Silicon Dioxide and Purified Talc. The ratio between active and functional excipients will be 1:0.5.

(iii) 1 part of Drug : Actual usage of Functional Excipients

The ratio of API to Excipients as actual usage for study purpose.

Pure API as well as samples of API and excipients were mixed in different ratio and charged on stability under stability conditions of 40ºC/75%RH (open & closed), 25ºC/60%RH (open & closed) and 2º - 8ºC. Samples were tested at different time intervals such as 1 week, 2 week, 3 week and 4 week. First samples of 40ºC/75%RH (open condition) were evaluated. If it fails, then only other samples will be tested. Assay, Impurity and IR spectrum were the testing parameters which are selected to evaluate the compatibility of a particular API with a definite excipient.

General information of the actives considered for this study are given below-

1.5.1 ALBENDAZOLE

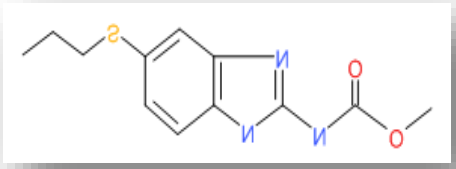
Albendazole is a benzimidazole broad-spectrum Anthelmintic. It is used for the treatment of intestinal nematodes such as Neurocysticercosis, Hydatid disease etc.

Smith Kline & French Animal Health were working on Albendazole, which was first marketed as Valbazen, an animal anthelminth, in the UK in November, 1977. Albendazole was found to be considerably more active than other benzimidazoles. This was because it was metabolized to Albendazole Sulphoxide which was also an active anthelminthic, while almost all the other benzimidazoles were metabolized to inactive compounds. It was eventually approved for human use and marketing in 1987.

Systematic (IUPAC) Name:

Methyl [5-(propylthio)-1*H*-benzoimidazol-2-yl]carbamate

Chemical Structure:



Molecular Formula: $C_{12}H_{15}N_3O_2S$

Molecular Mass: 265.333 g/mol

Partition Co – efficient: LogP 3.2

pKa:

Strongest Acidic: 9.51

Strongest Basic: 4.27

Appearance: White or slightly yellowish powder

Hygroscopicity: Hygroscopic

Melting Point: 207 °C - 209 °C

Light Sensitivity: It is not light sensitive.

Bioavailability: < 5%

Protein Binding: 70% bound to plasma protein

Biological Half-life: Elimination half life ranges from 8-12 hours

Solubility:

- Practically insoluble in Water, Ethanol(96 percent)
- Freely soluble in Anhydrous Formic Acid
- Very slightly soluble in Methylene Chloride

Albendazole exhibits pH dependent solubility.

In pH 1.2, its solubility is 900 µg / mL and in pH 6.8 the solubility is 1 µg / mL.

Polymorphism:

Two polymorphic forms have been observed such as –

- Form I
- Form II

Albendazole is commercialized in Form I which is metastable but the most soluble form. Form II is obtained by the re-crystallization of form I. Both forms proved to be physically quite stable under storage condition, likely due to high energy barrier for the activation of the interconversion. However, care is required to control undesirable polymorphic phase conversion in this API.

BCS Classification:

Considering solubility, permeability and dissolution characteristic, Albendazole is considered as BCS Class IV (Low Solubility and Low Permeability) Drug.

1.5.2 LEVOFLOXACIN

Levofloxacin is in a group of antibiotics called fluoroquinolones. Levofloxacin fights bacteria in the body.

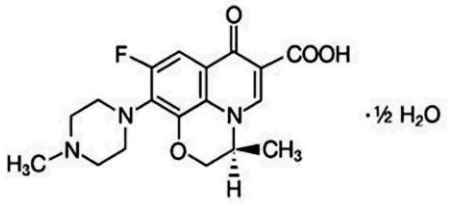
Levofloxacin is used to treat bacterial infections of the skin, sinuses, kidneys, bladder, or prostate. Levofloxacin is also used to treat bacterial infections that cause bronchitis or pneumonia, and to treat people who have been exposed to anthrax or plague.

Chemically, Levofloxacin is a chiral fluorinated Carboxyquinolone. Levofloxacin is the pure (-)-(S)- enantiomer of the racemic drug substance Ofloxacin.

Systematic (IUPAC) Name:

(-)-(S)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1 piperazinyl)-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine 6-carboxylic acid hemihydrate

Chemical Structure:



Molecular Formula: $C_{18}H_{20}FN_3O_4$. 1/2 H_2O

Molecular Mass: 370.38 g/mol

pKa:

Strongest Acidic: 5.45

Strongest Basic: 6.20

Partition Co – efficient: Levofloxacin is lipophilic in nature (LogP is 0.60)

Appearance: Light yellowish white to yellow white crystalline powder

Hygroscopicity: Non - Hygroscopic

Melting Point: (225 – 227) °C

Optical Rotation: -92 ° to -106 °

Water Content: 2 – 3 %

Light Sensitivity: Solution of Levofloxacin is unstable in light.

Bioavailability: 99%

Protein Binding: (24 – 38) %

Biological Half-life: 6 to 8 hours

Solubility:

Levofloxacin is soluble in DMSO and Acetic Acid. It is sparingly soluble in water, acetone and methanol. It is practically insoluble in glycerin and n-octanol.

- Levofloxacin exhibits pH dependent solubility
- Between pH 0.56 to 5.84, solubility profile of Levofloxacin is flat (73-108 mg/mL).
- Above pH 5.84, solubility of Levofloxacin gradually increases with the increasing pH (Up to pH 6.74)
- The solubility of Levofloxacin is maximum at pH 6.74 (272 mg/mL)

- Above pH 6.74, solubility of Levofloxacin gradually decreases. It exhibits minimum solubility at pH 7-8 (< 50 mg/mL)

Polymorphism:

Levofloxacin exhibits polymorphism. US patent journal 7629458 B2 and data sheets describe the following polymorphic forms of Levofloxacin –

Three Polymorphic forms – Anhydrous α, Anhydrous β, and Anhydrous γ

Two Pseudopolymorphic forms – Hemihydrate and Monohydrate

Six Solvate forms - A, B, C, G, F, H

Data sheets and journals clearly state that the hemihydrate form is the most desirable due to the following reasons –

- The hemihydrate form is consistently obtained by ensuring the process parameters
- The monohydrate form is not found as impurity in hemihydrate form
- Hemihydrate is stable crystal form and does not get converted to the Monohydrate form, both during storage and upon exposure to humidity.

BCS Classification:

Considering that the highest dose (750 mg) of Levofloxacin is soluble in 250 mL of less volume of water over a pH range of 1.2 – 6.8, Levofloxacin can be considered as a highly soluble drug.

Caco – 2 Permeability of Levofloxacin was found to be $28.36 \pm 1.93 \times 10^{-6}$ cm/s, which is more than the highly permeable internal standard Labetalol ($18.05 \pm 1.90 \times 10^{-6}$ cm/s)

WHO prequalification reports and data sheets, it has been stated that Levofloxacin Tablets undergo rapid dissolution, (> 85% in 15 minutes).

Considering the above facts regarding solubility, permeability and rapid dissolution, Levofloxacin can be considered as BCS Class I (High Solubility and High Permeability) Drug.

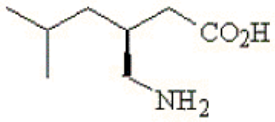
1.5.3 PREGABALIN

Pregabalin is a 3-isobutyl derivative of the inhibitory neurotransmitter γ-aminobutyric acid (GABA) that functions as a calcium channel blocker.

Systematic (IUPAC) Name:

(S)-3-(aminomethyl)-5-methylhexanoic acid

Chemical Structure:



Molecular Formula: $C_8H_{17}NO_2$

Molecular Mass: 159.23 g/mol

pKa1 : 4.2

pKa2: 10.6

(pKa for the Carboxylic Acid group is 4.2 and the pKa for the amine group is 10.6. Therefore, Pregabalin exist as zwitter ion at environmental condition.)

Appearance: Pregabalin is a white to off-white, crystalline solid

Hygroscopicity: Non – Hygroscopic

Melting Point: 186 °C – 188 °C

Optical Rotation: +10 ° to +12 °

Water Content: NMT 0.5%

Light Sensitivity: Not Sensitive

Solubility:

Freely soluble in water and both basic and acidic solutions.

The saturation solubility of pregabalin in aqueous media at room temperature is >30 mg/mL in the pH range 1 to 13.

Polymorphism:

- Pregabalin shows polymorphism. According to the literature, pregabalin can exist in different polymorphic forms: amorphous, hemihydrate form, Form I, II, III & IV and alpha form.
- Polymorphic form I (anhydrous crystalline form) is thermodynamically stable with respect to conversion to other polymorphs. This form is also present in the reference medicinal product.

Enantiomeric Purity:

Pregabalin exhibits stereoisomerism due to the presence of one chiral center.

The (R)-(−)-enantiomer of pregabalin has been found to be about 40 times less active when compared with the (S)-(+)-enantiomer.

Therefore, (R)-(−)-enantiomer is considered as impurity and which is controlled in API Specification (Limit: NMT 0.15%).

Partition Coefficient (Log P): N-Octanol/Water partition co-efficient (log Kow) at pH 7.4 = -1.78

Bioavailability: ≥ 90 %

Volume of Distribution: Approximately 0.56 l/kg

Elimination half-life: 6.3 hour

BCS Classification:

Considering that the highest dose (300 mg) of Pregabalin is soluble in 250 mL of less volume of water over a pH range of 1.2 – 6.8, Pregabalin can be considered as a highly soluble drug.

In an-situ rat intestinal perfusion model, pregabalin is perfused at the proximal end and measured what came out from the distal end. Beside's perfusing the drug, an internal standard metoprolol also perfused as well as water transport marker.

It shows that permeability of pregabalin is pretty high. It is fairly comparable to the permeability of Metoprolol, the high-permeability internal standard. So, from the figure it can be told that Pregabalin is a highly permeable compound.

2.1 Literature Review

In the year of 2017, Oliveira and his group (Oliveira *et al.*, 2017) studied antipyretic and analgesic effect of Paracetamol (PAR), phenylephrine hydrochloride (PHE) and chlorpheniramine maleate (CPM). The work described the use of thermal analysis for the characterization of the physicochemical compatibility between drugs and excipients during the development of solid dosage forms. Thermogravimetric analysis (TGA) and Differential Scanning Calorimetry (DSC) were used to study the thermal stability of the drug and of the physical mixture (drug/excipients) in solid binary mixtures (1:1). DSC thermograms demonstrated reproducible melting event of the prepared physical mixture. Starch, Mannitol, Lactose and Magnesium Stearate influence thermal parameters. Information recorded from the derivative thermogravimetric (DTG) and TGA curves demonstrated the decomposition of drugs in well-defined thermal events, translating the suitability of these techniques for the characterization of the drug/excipients interactions.

In the year of 2016, Silva and the group (Silva *et. al.*, 2016) worked in the aim of characterization of Atorvastatin and evaluate interactions between Atorvastatin and various excipients by DSC and FTIR, using Pearson's correlation as a tool to corroborate possible interactions that it was not possible to evidence in visual analyses. The DSC curves were obtained using a Shimadzu calorimeter, Model DSC-60, in the aluminum crucible under heating rate of 20 °C min^{-1} at a temperature of 25–400 °C. The spectra of the samples were obtained on a FTIR–ATR model IR prestige-21 Shimadzu spectrophotometer at a wavelength of 700–4000 cm^{-1} on average of 20 scans. The theoretical spectrum was obtained using an ad hoc algorithm. From the analysis of DSC and evaluation of Pearson's correlation, it observed physical interactions with excipients: starch glycolate, pre-gelatinized starch, croscarmellose, sodium lauryl sulfate, magnesium stearate and mannitol. There is no interaction with lactose. Then, the Pearson's correlation was so important tool to evaluate possible interactions between IPAs and excipients, using FTIR data to corroborate DSC results.

A Study has been performed by Bharate and other two scientists (Bharate *et. al.,* 2010) to identify drug-excipient compatibility which represent an important phase in the pre-formulation stage for the development of all dosage forms. The potential physical and chemical interactions between drugs and excipients can affect the chemical nature, the stability and bioavailability of drugs and, consequently, their therapeutic efficacy and safety. The present review covers the literature reports of incompatibilities of commonly used pharmaceutical excipients with different active pharmaceutical ingredients. Examples of drug-excipient interactions, such as transacylation, the Maillard browning reaction, acid base reactions and physical changes are discussed for different active pharmaceutical ingredients belonging to different therapeutic areas viz. antiviral, anti-inflammatory, antidiabetic, antihypertensives, CNS drugs, anti-convulsants, antibiotics, bronchodialators, antimalarial, amtiemetic, vitamins, antiamoebics, antipsychotics, antidepressants, anticancer, anticoagulants and sedatives/ hypnotics. Once solid-state reactions are understood in a pharmaceutical system, the necessary steps can be taken to prevent reactivity and improve the stability of drug substances and products.

A comparative study was performed by Patel and group (Patel *et al*., 2015) about drug-excipient compatibility, an important phase in the preformulation stage of the development of all dosage forms. The potential physical and chemical interactions between drugs and excipients can affect the chemical, physical, therapeutical properties and stability of the dosage form. The present review contains a basic mode of drug degradation, mechanism of drug- excipient interaction like physical, chemical and biopharmaceutical. Different Thermal and Non-thermal method of analysis, Tools and software for incompatibility is also discussed. Once the type of interaction is determined we can take further steps to improve the stability of drug and dosage form. From review, we conclude that consequent use of thermal and non-thermal method provide data for drug- excipient interaction which can further help in selection of excipient for the development of stable dosage form.

Fathima and her co-workers (Fathima *et. al.,* 2011) explained that Excipients are included in dosage forms to aid manufacture, administration or absorption. Although considered pharmacologically inert, excipients can initiate, propagate or participate in chemical or physical interactions with drug compounds, which may compromise the effectiveness of a medication. Excipients are not exquisitely pure. Even for the most commonly used excipients, it is necessary to understand the context of their manufacture in order to identify potential active pharmaceutical ingredients interactions with trace components. Chemical interactions can lead to degradation of the active ingredient, thereby reducing the amount available for therapeutic effect. Physical interactions can affect rate of dissolution, uniformity of dose or ease of administration.

Gao and other scientists (Gao *et. al*., 2014) Studied compatibility of Medroxyprogesterone Acetate and pharmaceutical excipients through thermal and spectroscopy techniques. In this article they described that active drug-excipient compatibility is considered as an important phase in the preformulation stage of the development of all dosage forms. For the development of conjugation estrogens and medroxyprogesterone acetate (MPA) double-layer tablets, techniques of thermal, isothermal stress testing (IST), and molecular vibrational spectroscopy analysis were performed to access the compatibility. Differential scanning calorimetry (DSC) studies were used as an important and complementary tool during preformulation to determine drug-excipient compatibility. On the basis of DSC results, MPA was found to be compatible with polyethylene glycol 6000. However, the results of Raman and IST studies showed that all the excipients defined in the prototype formula were found to be compatible with MPA. Overall, the compatibility of selected excipients with MPA was successfully evaluated using a combination of thermal and IST methods, and the formulations developed using the compatible excipients were found to be stable.

Stulzer along with other scientists (Stulzer et. al., 2008) demonstrated compatibility study between Piroxicam and other pharmaceutical excipients used in solid dosage forms. Differential scanning calorimetry (DSC) with the support of Fourier transform infrared spectroscopy (FT-IR)

was used as a screening technique for testing the compatibility of piroxicam (4-hydroxy-2-methyl-N-(2-pyridyl)-2H-1,2-benzothiazine-3carboxamide-1,1-dioxide) with various pharmaceutical excipients for solid dosage forms. Based on the results, magnesium stearate, stearic acid, and mannitol were found to show interaction with piroxicam. In conclusion, tools of DSC and FT-IR were successfully employed to evaluate the compatibility of piroxicam and selected excipients.

Active pharmaceutical ingredients (APIs) containing primary and secondary amine moieties have been extensively studied for their potential incompatibility with monosaccharides and disaccharides containing a reducing end such as glucose, lactose, and maltose because of the undesirable interaction between the amine and aldehyde functionalities. This study was conducted by Alexei (Alexei *et. al.*, 2013) who found out that compatibility studies of these APIs with olysaccharides such as starch are much less common. During a recent compatibility study between starch and desloratadine, an API that contains a secondary amine functional group, we observed a novel degradant formed between desloratadine and a previously unidentified starch impurity in addition to an Amadori degradant formed between desloratadine and maltose, a known starch impurity. An approach that combines liquid chromatography–tandem mass spectrometry ($LC–MS^n$) analysis, stress studies, and comprehensive nuclear magnetic resonance (NMR) analyses was used to identify this novel degradant. On the basis of the structure determined by NMR spectroscopy and the results from the stress studies, a degradation mechanism is proposed to account for the formation of this novel degradant through the reaction of desloratadine with an isomer of acetylformoin, an impurity of polysaccharide origin. Because starch is a very common excipient used in solid dosage formulations, the results of this compatibility study should facilitate pharmaceutical development involving secondary amine APIs and starch.

A drug–excipient compatibility screening model was developed by Ajit and group (Ajit *et. al.*, 1999) in which it demonstrated that potential stability problems due to interactions of drug substances with excipients in solid dosage forms can be predicted. The model involved storing

drug–excipient blends with 20% added water in closed glass vials at 50 °C and analyzing them after 1 and 3 weeks for chemical and physical stability. The total weight of drug–excipient blend in a vial was usually kept at about 200 mg. The amount of drug substance in a blend was determined on the basis of the expected drug-to-excipient ratio in the final formulation. Potential roles of several key factors, such as the chemical nature of the excipient, drug-to-excipient ratio, moisture, microenvironmental pH of the drug–excipient mixture, temperature, and light, on dosage form stability could be identified by using the model. Certain physical changes, such as polymorphic conversion or change from crystalline to amorphous form, that could occur in drug–excipient mixtures were also studied. Selection of dosage form composition by using this model at the outset of a drug development program would lead to reduction of "surprise" problems during long-term stability testing of drug products.

In the year of 2013, Fulias and a group of scientists (Fulias *et. al*., 2013) studied the compatibility of active substances with excipients finds an important role in the domain of pharmaceutical research, being known the fact that final formulation is the one administered to the patient. In order to evaluate the compatibility between active substance and excipients, different analytical techniques can be used, based on their accuracy, reproducibility and fastness.

Compatibility study of two well-known active substances, procaine and benzocaine, with four commonly used excipients, was carried out employing thermal analysis (TG/DTG/HF) and Fourier Transform Infrared Spectroscopy (UATR-FT-IR). The selected excipients were microcrystalline cellulose, lactose monohydrate, magnesium stearate and talc. Equal proportion of active substance and excipients (*w*/*w*) was utilized in the interaction study. The corroboration of data obtained by thermal analysis with the ones from FT-IR spectroscopy indicated that no interaction occurs between procaine and benzocaine, with microcrystalline cellulose and talc, as well for the benzocaine-lactose mixture. Interactions were confirmed between procaine and benzocaine respectively and magnesium stearate, and for procaine and lactose.

Differential scanning calorimetry (DSC) was used as a screening technique for assessing the compatibility of ibuproxam with some currently employed pharmaceutical excipients, narrated in the study performed by Mura and the group (Mura *et. al.,* 1998). The influence of processing effects (simple blending, cogrinding or kneading) on drug stability was also evaluated. On the basis of DSC results, ibuproxam was found to be compatible with corn starch, avicel and sodium carboxymethylcellulose. Some drug-excipient interaction was observed with polyethyleneglycol 4000, palmitic acid, stearic acid, Ca and Mg stearate. Actual solid-phase interactions of the drug with polyvinylpolypyrrolidone and polyvinylpirrolidone K30 were induced by mechanical treatments. Hot-stage microscopy (HSM) and scanning electron microscopy (SEM) were of help in interpreting the DSC results and excluding in all cases relevant pharmaceutical incompatibilities.

In a study performed by Shantikumar and his group (Shantikumar *et. al*., 2014) demonstrated that Differential scanning calorimetry (DSC) is a primary technique for measuring the thermal properties of materials, which reflects the physico-chemical properties of drug substances. In the present study, it is used as a screening technique for assessing the compatibility of sitagliptin with some currently employed pharmaceutical excipients. The influence of processing conditions and their effects (simple blending, co-grinding or kneading) on drug stability was evaluated. Sitagliptin showed a sharp endothermic peak at 212.1 °C with an enthalpy change of 131.5 J g^{-1} indicating melting of drug. Facile transformation of dehydrated sitagliptin to monohydrate form was observed in some mixtures, disappearance of sharp melting endothermic peak of sitagliptin was observed in some mixtures. On the basis of DSC results, sitagliptin was found to be compatible with micro crystalline cellulose, croscarmellose, and pregelatinized starch. Some excipient interaction was observed with magnesium stearate, ascorbic acid, and citric acid. X-ray diffractometry and FT-IR were used as supportive tools in interpreting the DSC results. Overall, the excipients selected were compatible with the API and the mixtures are stable within the tested conditions. These results would be useful for formulation development of the film coated tablets of Sitaglitptin.

In the year of 2015, a study regarding Thermal techniques, such as differential scanning calorimetry (DSC), thermogravimetry (TG), derivate of TG curve, differential thermal analysis, and non-thermal techniques such as fourier transform infrared (FTIR) spectroscopy and X-ray diffractometry (XRD) were used to evaluate the possible interactions between hydroquinone (HQ) and excipients commonly used in semi-solid pharmaceutical forms. No evidence of interaction was observed between HQ and cetyl alcohol (CA), cetostearyl alcohol (CTA), disodium ethylenediaminetetraacetate, and decyl oleate. However, based on the thermoanalytical trials, a physical interaction was suspected between HQ and dipropylene glycol (DPG), glycerin (GLY), hydroxypropyl methylcellulose (HPMC), imidazolidinyl urea (IMD), methylparaben (MTP), and propylparaben (PPP). The FTIR results show that for DPG, GLY, HPMC, MTP, and PPP, there were no chemical interactions with HQ at room temperature, but the heating promotes interaction between HQ and HPMC. The FTIR spectra of HQ/IMD show the chemical interaction at room temperature, which was also observed with heating. The XRD results of mixtures between HQ and DPG, HPMC, IMD, MTP, and PPP indicate no interaction between these substances at room temperature, but the heating modifies the HQ crystallinity in these mixtures. All of these methods showed incompatibility between HQ and the excipient IMD.

Skotnicki and other three scientists (Skotnicki *et. al.*, 2015) examined compatibility study between Bisoprolol and Valsartan. The objective of this study was to evaluate the thermal behavior of crystalline and amorphous bisoprolol fumarate and its compatibility with amorphous valsartan. This pharmacologically relevant drug combination is a potential candidate for fixed-dose combination formulation. The thermal behavior of physical mixtures with different concentrations of bisoprolol and valsartan were examined by DSC and TMDSC, and the observed interactions were investigated by XRPD, solution- and solid-state NMR. A combined analysis of thermal methods, solution- and solid-state NMR and XRPD experiments allowed the investigation of the conformational and dynamic properties of bisoprolol fumarate. Since bisoprolol fumarate and valsartan react to form a new amorphous product, formulation of a fixed-dose combination would require separate reservoirs for bisoprolol and valsartan to prevent interactions. Similar problems might be expected with other excipients or APIs containing carboxylic groups.

Joshi and other two scientists (Joshi *et. al*., 2002) showed that proper formulation is an important aspect of any dosage form design. As a part of preformulation studies, differential scanning calorimetry (DSC) was used to investigate the physicochemical compatibility between Carbamazepine and various excipients commonly used in tablet manufacturing, supported by Fourier transform infrared (FTIR) and x-ray powder diffraction (XRPD) studies. Compatibility studies were conducted on samples kept at room temperature and at an elevated temperature of 55 degrees C for 3 weeks. Carbamazepine was found to be compatible with all lactose-based components, such as Granulac 230, Flowlac 100, and Microcelac 100. Differential scanning calorimetry studies indicated incompatibility with mannitol, microcrystalline cellulose, starch, and stearic acid. However, XRPD and FTIR studies implied that all the above excipients are compatible with Carbamazepine. X-ray powder diffraction demonstrated incompatibility with stearic acid for samples stored at 55 degrees C for 3 weeks, indicative of formation of a solid solution. Thus, DSC being a thermal method of analysis should not be used singly to detect any inherent incompatibility. It has to be supported sufficiently by other non-thermal techniques, such as XRPD and FTIR.

3.1 MATERIALS

3.1.1 API Collection

For the research purpose, the following APIs were used.

Table 3.1 : List of APIs with their therapeutic class and supplier name

Sl. No.	Name of API	Class	Source (Supplier Name)
1.	Albendazole	Anthelmintic	Sequent Scientific Limited, India
2.	Levofloxacin Hemihydrate	Antibacterial Agent (Fluoroquinolone)	Hetero Drugs Limited, India
3.	Pregabalin	Anticonvulsant	Hetero Drugs Limited, India

3.1.2 Excipients Collection

For the research purpose, the following excipients were used.

Table 3.2: List of excipients with their class

Sl. No.	Name of Excipients	Class
1.	Microcrystalline Cellulose	Diluent, Binder, Disintegrant
2.	Lactose	Diluent
3.	Mannitol	Diluent
4.	Maize Starch	Binder
5.	Pregelatinised Starch	Binder, Disintegrant
6.	Povidone (K 30)	Binder
7.	Hypromellose 5 cps	Binder
8.	Hydroxypropyl Cellulose	Binder
9.	Crospovidone	Disintegrant
10.	Croscarmellose Sodium	Disintegrant

11.	Sodium Starch Glycolate	Disintegrant
12.	Sodium Lauryl Sulfate	Surfactant, Solubilizer
13.	Colloidal Anhydrous Silica	Glidant
14.	Purified Talc	Lubricant
15.	Magnesium Stearate	Lubricant
16.	Saccharin Sodium	Sweetener
17.	Orange Powder Flavor	Flavoring Agent
18.	Mango Powder Flavor	Flavoring Agent
19.	Vanilla Powder Flavor	Flavoring Agent

3.1.3 Reagents and Working Standards Collection

For the research purpose, the following reagents were used.

Table 3.3: List of reagents

Sl. No.	Reagents and Working Standards
1.	Monobasic Ammonium Phosphate
2.	Sulfuric Acid (≥98%)
3.	Methanol
4.	Cupric Sulfate
5.	Ammonium Acetate
6.	Acetonitrile
7.	Potassium Dihydrogen Phosphate
8.	Potassium Hydroxide
9.	Albendazole WS
10.	Levofloxacin Hemihydrate WS
11.	Pregabalin WS

3.1.4 Equipments and Instruments

For the research purpose, the following equipments were used.

Table 3.4: List of equipments

Sl. No.	Equipments
1.	Weighing Balance
2.	HPLC Machine
3.	Sonicator
4.	Mechanical Shaker
5.	Disintegrator
6.	Dissolution Tester
7.	UV Spectroscopy
8.	IR Spectrometer

3.1.5 Apparatus

For the research purpose, the following apparatus were used.

Table 3.5: List of apparatus

Sl. No.	Apparatus
1.	400 micron SS Screen (40 mesh)
2.	Glass Vial
3.	Rubber Stopper
4.	Aluminum Foil Paper
5.	Beaker
6.	Volumetric Flask
7.	Spatula
8.	Funnel
9.	Pipettes
10.	Pumper
11.	C18, 4.6 x250 cm, 5 µ Column

3.2 METHODS

3.2.1 Stability sample preparation procedure

(i) Accurately weigh API and each excipient.

(ii) Mix API and each particular excipient separately in a polybag.

(iii) Pass the above mixture through 40 mesh sieve and mix well.

(iv) Fill the mixture into Clear Glass Vials and stopper the vials with LDPE plug (Punctured and intact, as per the study design) with proper labeling.

3.2.2 Stability Testing Parameters

i) Appearance
ii) Assay
iii) Total Related Substances

3.2.3 Testing Schedule

Table 3.6: Storage condition with testing interval

Storage Condition	Duration
40 ^{O}C/ 75 % RH (Open)	1 Week
40 ^{O}C/ 75 % RH (Closed)	2 Week
25 ^{O}C/ 60 % RH (Open)	3 Week
25 ^{O}C/ 60 % RH (Closed)	4 Week
2 – 8 ^{O}C	

- Firstly test the open samples only at 40 ^{O}C/ 75 % RH (open). If the results for all the excipients are OK, the study is over. If for a particular excipient, total RS is more, then the closed 40 ^{O}C/ 75 % RH (closed) will be tested. If closed one is also not OK, then testing of samples at 25 ^{O}C/ 60 % RH (open) will be conducted for that excipient. If this result also not OK, then samples at 25 ^{O}C/ 60 % RH (closed) will be analyzed.

3.2.4 Design of experiments

3.2.4.1 Compatibility study of Albendazole with different excipients:

Sl. No.	API:Excipients	Ratio
1.	Albendazole	Control
2.	Albendazole:Mirocrystalline Cellulose	1:1
		1:0.4
3.	Albendazole:Lactose	1:1
		1:0.5
4.	Albendazole:Maize Starch	1:1
		1:0.1
5.	Albendazole:Mannitol	1:1
		1:0.15
		1:0.5
6.	Albendazole:Povidone (K 30)	1:0.5
		1:0.02
7.	Albendazole:Crospovidone	1:0.5
		1:0.2
8.	Albendazole:Sodium Starch Glycolate	1:0.5
		1:0.2
9.	Albendazole:Croscarmellose Sodium	1:0.5
		1:0.2
10.	Albendazole:Magnesium Stearate	1:0.5
		1:0.02
11.	Albendazole:Sodium Lauryl Sulfate	1:0.5
		1:0.02
12.	Albendazole:Colloidal Anhydrous Silica	1:0.5
		1:0.1
13.	Albendazole:Purified Talc	1:0.5

		1:0.05
14.	Albendazole:Saccharin Sodium	1:0.5
		1:0.01
15.	Albendazole:Orange Powder Flavor	1:0.5
		1:0.02
16.	Albendazole:Vanilla Powder Flavor	1:0.5
		1:0.02
17.	Albendazole:Passionfruit Powder Flavor	1:0.5
		1:0.02

3.2.4.2 Compatibility study of Levofloxacin with different excipients:

Sl. No.	API:Excipients	Ratio
1.	Levofloxacin	Control
2.	Levofloxacin:Microcrystalline Cellulose	1:1
		1:0.4
3.	Levofloxacin:Lactose	1:1
		1:0.4
4.	Levofloxacin:Maize Starch	1:1
		1:0.4
5.	Levofloxacin:Hypromellose 5 cps	1:0.5
		1:0.03
6.	Levofloxacin:Hydroxypropyl Cellulose	1:0.5
		1:03
7.	Levofloxacin:Povidone (K 30)	1:0.5
		1:0.1
8.	Levofloxacin:Crospovidone	1:0.5
		1:0.1
9.	Levofloxacin:Sodium Starch Glycolate	1:0.5

		1:0.1
10.	Levofloxacin:Croscarmellose Sodium	1:0.5
		1:0.1
11.	Levofloxacin:Magnesium Stearate	1:0.5
		1:0.02
12.	Levofloxacin:Sodium Lauryl Sulfate	1:0.5
		1:0.02
13.	Levofloxacin:Colloidal Anhydrous Silica	1:0.5
		1:0.02
14.	Levofloxacin:Purified Talc	1:0.5
		1:0.05

3.2.4.3 Compatibility study of Pregabalin with different excipients:

Sl. No.	API:Excipients	Ratio
1.	Pregabalin	Control
2.	Pregabalin:Pregelatinised Starch	1:1
		1:0.3
3.	Pregabalin:Maize Starch	1:1
		1:0.3
4.	Pregabalin:Purified Talc	1:0.5
		1:0.1
		1:0.03
5.	Pregabalin:Colloidal Anhydrous Silica	1:0.5
		1:0.03

3.2.5 Analytical Method

ALBENDAZOLE

Assay:

Preparation of Solvent Mixture:

1 volume of Sulfuric Acid was diluted with 99 volumes of Methanol.

Preparation of Standard Solution:

25 mg of Albendazole WS was taken in 25 mL volumetric flask. 5 mL of solvent mixture and 15 mL of Methanol were added and made it dissolved. It was diluted upto volume with Methanol. 5 mL of this solution was further diluted to 25 mL with Methanol.

Preparation of Sample Solution:

Blend was taken equivalent to 100 mg of Albendazole in a 50 mL volumetric flask. 5 mL of solvent mixture and 20 mL of Methanol were added and sonicated it for 15 minutes. Then it was diluted upto volume with Methanol. 5 mL of this solution was further diluted to 25 mL with Methanol.

Preparation of Mobile Phase:

1.67 g of Monobasic Ammonium Phosphate was dissolved in 1000 mL of water. 300 mL of this solution was then mixed with 700 mL of Methanol.

Chromatographic System:

Table 3.7: Chromatographic system for Albendazole

Column	C18, 4.6 x 250 cm, 5 µ
Temperature	Ambient
Wavelength	254 nm
Flow Rate	0.7 mL/minute
Injection Volume	20 µL

Procedure:

Separately equal volumes of standard and sample solution were injected and major peak responses for standard and sample solution were recorded. The amount of Albendazole was calculated as per the following formula-

Area of sample/Area of standard x Weight of standard/Weight of sample x Potency of standard x Average weight

LEVOFLOXACIN

Preparation of Mobile Phase:

874 mg of Cupric Sulfate, 918 mg of L-Isoleucine and 5.94 mg of Ammonium Acetate were dissolved in 700 mL of water and made it dissolve. Then 300 mL Methanol was added and mixed well.

Preparation of Diluent:

20 volume of Acetonitrile and 80 volume of water was mixed to make diluent.

Preparation of Standard Solution:

100 mg of Levofloxacin Hemihydrate WS was taken in a 50 mL volumetric flask. 30 mL of diluent was added into it and sonicate for 10 minutes. Then volume upto the mark with diluent. 5 ml of this solution was then further diluted with mobile phase upto 50 ml.

Preparation of Sample Solution:

Blend was taken equivalent to 100 mg of Levofloxacin Hemihydrate in a 50 mL volumetric flask. 30 mL of diluent was added into it and sonicate for 10 minutes. Then volume upto the mark with diluent. 5 ml of this solution was then further diluted with mobile phase upto 50 ml.

Chromatographic System:

Table 3.8: Chromatographic system for Levofloxacin

Column	C18, 4.6 x 250 mm, 5 µ
Temperature	45ºC
Wavelength	360 nm
Flow Rate	0.8 mL/minute
Injection Volume	25 µL

Procedure:

Separately equal volumes of standard and sample solution were injected and major peak responses for standard and sample solution were recorded. The amount of Levofloxacin was calculated as per the following formula-

Area of sample/Area of standard x Weight of standard/Weight of sample x Potency of standard x Average weight

PREGABALIN

Preparation of Buffer Solution:

1.36 g of Potassium Dihydrogen Orthophosphate was dissolved in 1000 mL of water. The pH of this solution was then adjusted to 6.50 ± 0.05 with Potassium Hydroxide solution.

Preparation of Mobile Phase/Diluent:

95 volume of buffer was mixed with 5 volume of Acetonitrile to make mobile phase.

Preparation of Standard Solution:

250 mg of Pregabalin WS was taken in 25 mL volumetric flask and volume upto the mark with diluent. Sonicated it for 6-8 minutes.

Preparation of Sample Solution:

Blend was taken equivalent to 250 mg of Pregabalin in a 25 mL volumetric flask and volume upto the mark with diluent. Sonicated it for 6-8 minutes.

Chromatographic System:

Table 3.9: Chromatographic system for Pregabalin

Column	C18, 4.6 x 150 mm, 5 µ
Temperature	35ºC
Wavelength	210 nm
Flow Rate	0.6 mL/minute
Injection Volume	10 µL

Procedure:

Separately equal volumes of standard and sample solution were injected and major peak responses for standard and sample solution were recorded. The amount of Pregabalin was calculated as per the following formula-

Area of sample/Area of standard x Weight of standard/Weight of sample x Potency of standard x Average weight

IR Spectrum:

IR spectrum was examined by infrared absorption spectrophotometry, comparing with the spectrum obtained with WS.

4.1 Assay Result

Different samples were withdrawn at definite time points and tested accordingly. Given below are the results-

4.1.1 Albendazole with different excipients

Assay results were calculated as per the given formula in section 3.2.5 Below are the results-

Table 4.1: % Assay results of Albendazole and different excipients at various time points

Sl. No.	API:Excipients	Ratio	Assay (%)			
			1 Week	2 Week	3 Week	4 Week
1.	Albendazole		99.9	105.0	105.1	104.8
2.	Albendazole:Mirocrystalline Cellulose (101)	1:1	99.0	101.2	100.7	100.7
		1:0.4	100.4	102.7	103.3	104.8
3.	Albendazole:Lactose	1:1	97.2	99.2	98.8	98.8
		1:0.5	101.2	102.9	102.8	102.9
4.	Albendazole:Maize Starch	1:1	98.3	104.4	104.6	103.9
		1:0.1	102.2	107.3	108.4	109.4
5.	Albendazole:Mannitol	1:1	101.1	103.7	103.3	103.2
		1:0.15	101.1	101.8	101.9	101.8
		1:0.5	97.5	97.6	97.9	98.3
6.	Albendazole:Povidone (K 30)	1:0.5	90.8	92.7	92.6	92.7
		1:0.02	100.6	101.8	103.3	104.3
7.	Albendazole:Crospovidone	1:0.5	94.9	96.6	96.9	96.9
		1:0.2	96.3	96.8	96.8	96.9
8.	Albendazole:Sodium Starch Glycolate	1:0.5	94.3	95.6	96.7	96.2
		1:0.2	99.2	99.3	99.4	99.6
9.	Albendazole:Croscarmellose Sodium	1:0.5	99.4	100.8	100.8	100.9
		1:0.2	105.5	105.7	105.9	105.9
10.	Albendazole:Magnesium Stearate	1:0.5	69.2	70.2	70.4	70.3
		1:0.02	103.1	103.4	103.2	103.4

11.	Albendazole:Sodium Lauryl Sulfate	1:0.5	100.2	101.5	101.8	101.7
		1:0.02	101.1	101.3	101.0	101.1
12.	Albendazole:Colloidal Anhydrous Silica	1:0.5	103.1	104.5	104.8	105.1
		1:0.1	113.3	113.5	113.4	113.7
13.	Albendazole:Purified Talc	1:0.05	102.5	102.6	102.4	102.6
14.	Albendazole:Saccharin Sodium	1:0.5	95.3	96.7	97.2	97.0
		1:0.01	102.3	102.4	102.3	102.3
15.	Albendazole:Orange Powder Flavor	1:0.5	101.7	103.7	102.5	102.9
		1:0.02	101.7	101.9	101.9	101.3
16.	Albendazole:Vanilla Powder Flavor	1:0.5	99.2	101.2	101.3	101.2
		1:0.02	101.5	103.5	102.6	100.9
17.	Albendazole:Passionfruit Powder Flavor	1:0.5	98.7	99.3	98.9	98.9
		1:0.02	102.4	102.4	102.7	102.0

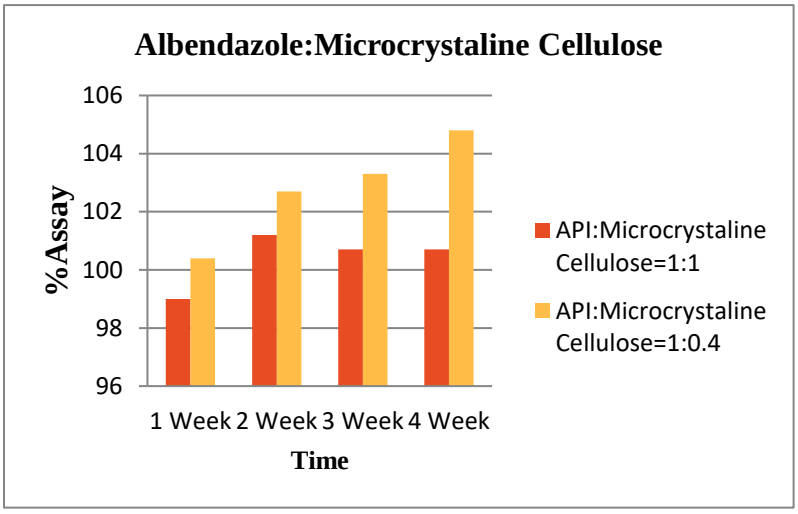


Figure 4.1: % Assay results of Albendazole with Microcrystalline Cellulose at weekly basis

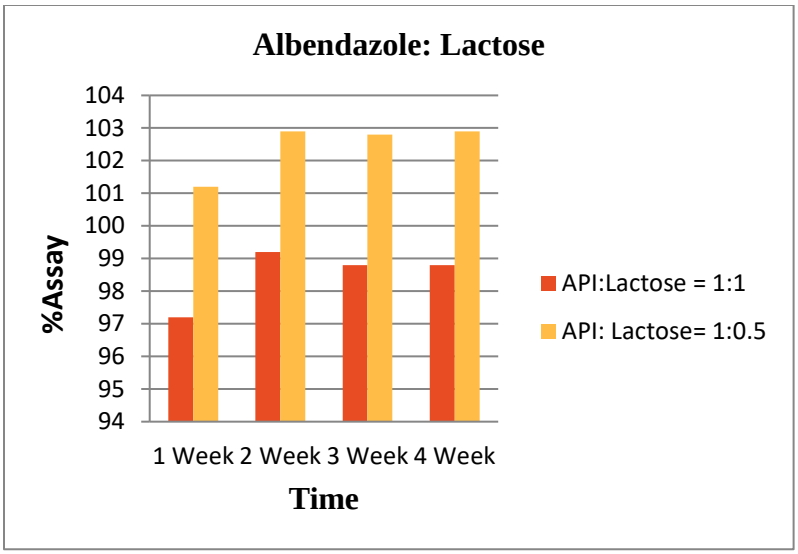


Figure 4.2: % Assay results of Albendazole with Lactose at weekly basis

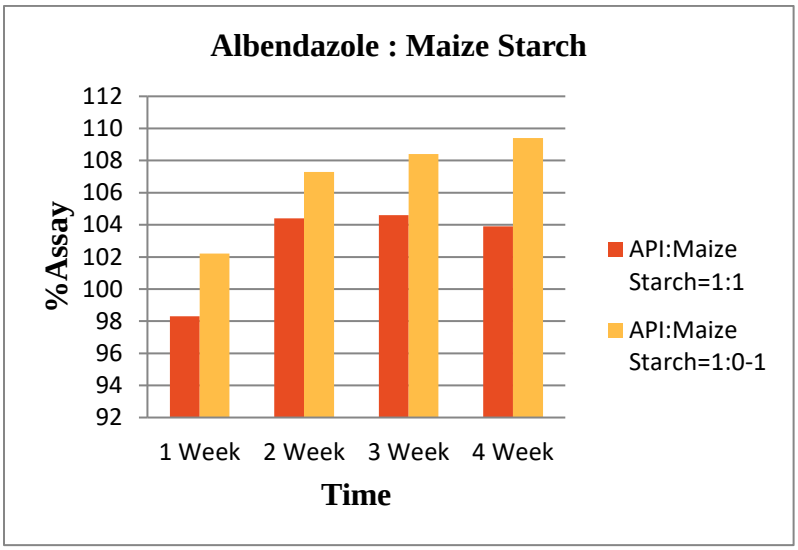


Figure 4.3: % Assay results of Albendazole with Maize Starch at weekly basis

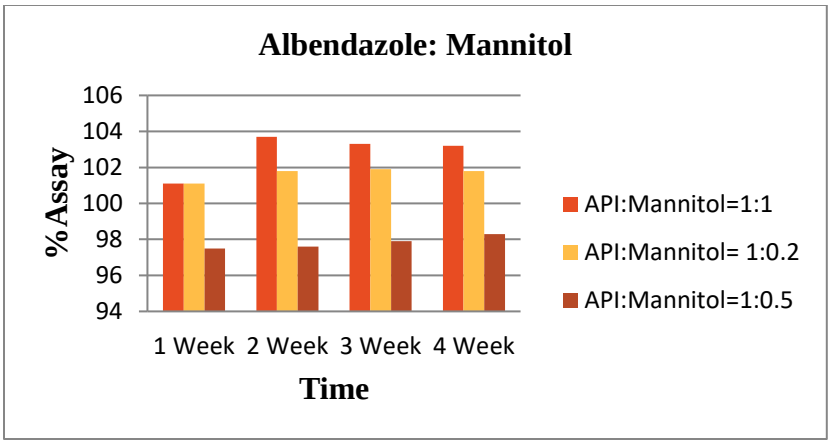


Figure 4.4: % Assay results of Albendazole with Mannitol at weekly basis

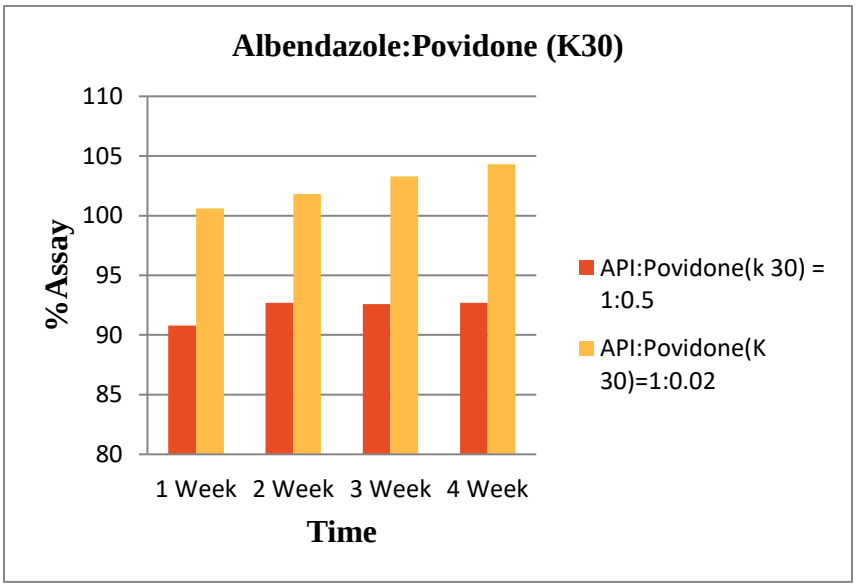


Figure 4.5: % Assay results of Albendazole with Povidone (K 30) at weekly basis

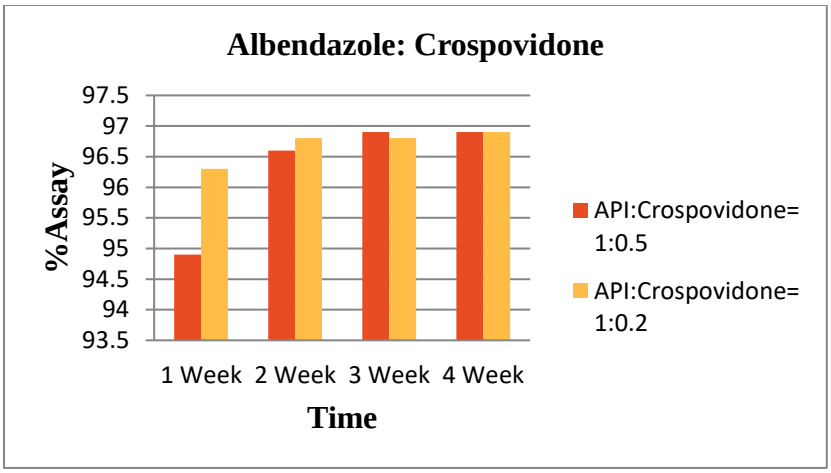


Figure 4.6: % Assay results of Albendazole with Crospovidone at weekly basis

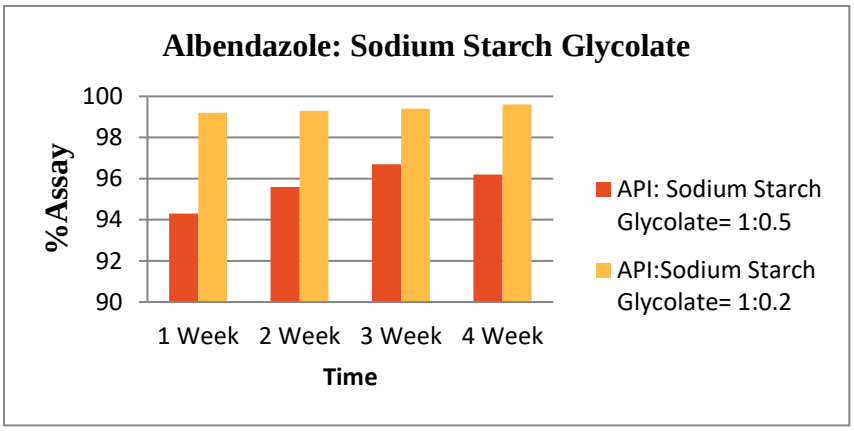


Figure 4.7: % Assay results of Albendazole with Sodium Starch Glycolate at weekly basis

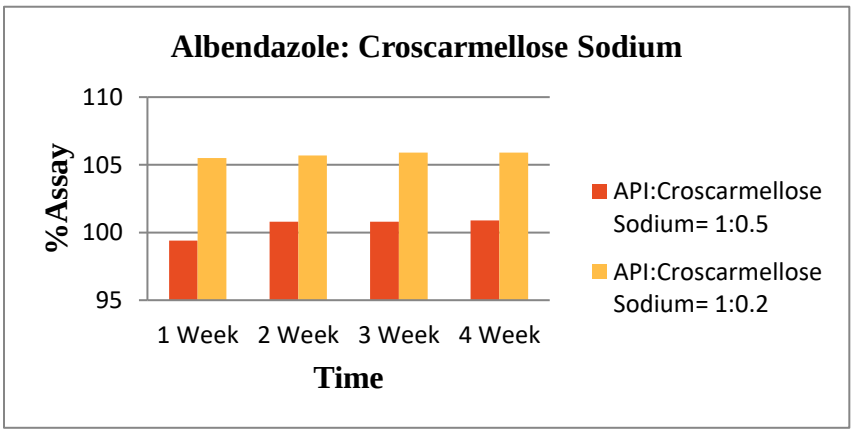


Figure 4.8: % Assay results of Albendazole with Croscarmellose Sodium at weekly basis

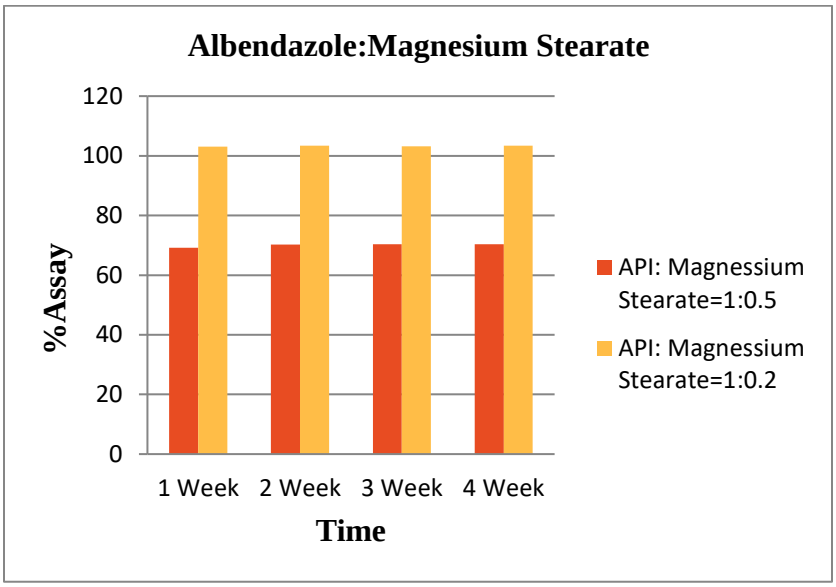


Figure 4.9: % Assay results of Albendazole with Magnesium Stearate at weekly basis

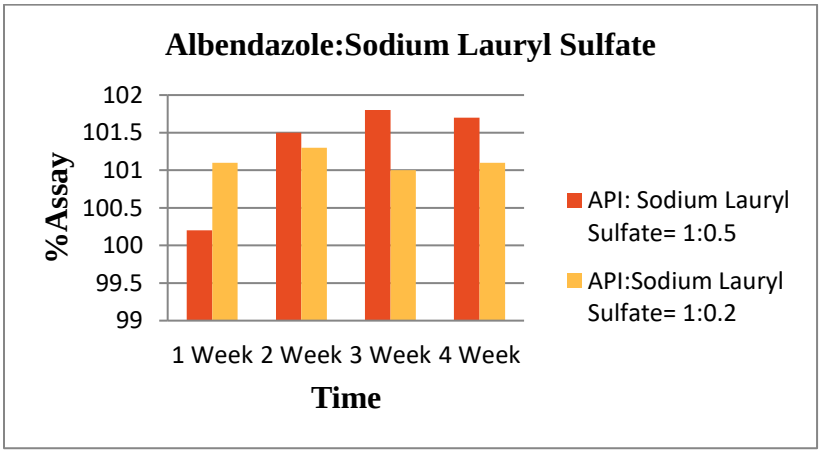


Figure 4.10: % Assay results of Albendazole with Sodium Lauryl Sulfate at weekly basis

4.1.2 Levofloxacin with different excipients

Assay results were calculated as per the given formula in section 3.2.5. Below are the results-

Table 4.2: % Assay results of Levofloxacin and different excipients at various time points

Sl. No.	API:Excipients	Ratio	Assay (%)			
			1 Week	2 Week	3 Week	4 Week
1.	Levofloxacin	Control	100.9	101.2	101.7	102.4
2.	Levofloxacin:Microcrystalline Cellulose 101	1:1	95.6	96.1	96.4	96.6
		1:0.4	100.7	100.3	100.7	101.2
3.	Levofloxacin:Lactose	1:1	101.1	101.4	101.6	101.9
		1:0.4	101.7	100.9	101.5	101.9
4.	Levofloxacin:Maize Starch	1:1	100.4	100.7	100.8	101.2
		1:0.4	99.4	98.6	99.1	99.9
5.	Levofloxacin:Hypromellose 5 cps	1:0.5	96.7	96.9	96.7	96.9
		1:0.03	100.1	99.7	99.9	100.5
6.	Levofloxacin:Hydroxypropyl Cellulose	1:0.5	98.5	98.1	97.9	98.3
		1:03	101.9	101.5	101.6	102.2
7.	Levofloxacin:Povidone (K 30)	1:0.5	91.9	92.2	91.9	92.7
		1:0.1	98.4	97.9	97.6	98.5
8.	Levofloxacin:Crospovidone	1:0.5	93.0	92.9	92.4	93.0
		1:0.1	98.5	98.2	97.9	97.9
9.	Levofloxacin:Sodium Starch Glycolate	1:0.5	97.7	97.7	97.1	97.9
		1:0.1	98.5	97.9	97.9	97.9
10.	Levofloxacin:Croscarmellose Sodium	1:0.5	97.5	98.0	98.3	99.8
		1:0.1	92.9	92.6	93.2	93.7
11.	Levofloxacin:Magnesium Stearate	1:0.5	100.1	100.0	99.9	100.6
		1:0.02	102.1	101.9	101.7	93.5
12.	Levofloxacin:Sodium Lauryl Sulfate	1:0.5	98.5	98.5	98.7	99.2
		1:0.02	100.6	100.9	100.9	102.1
13.	Levofloxacin:Colloidal	1:0.5	100.9	100.4	100.6	101.2

	Anhydrous Silica	1:0.02	99.2	99.5	99.4	99.7
14.	Levofloxacin:Purified Talc	1:0.5	100.3	99.8	99.9	100.7
		1:0.05	101.2	101.6	101.6	101.7

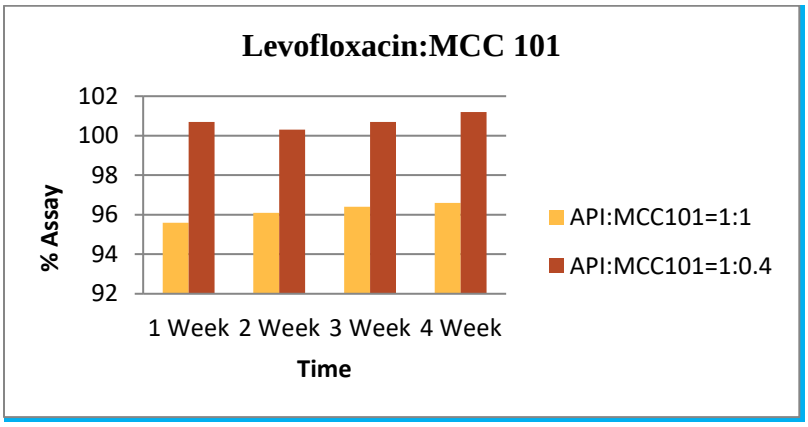


Figure 4.11: % Assay results of Levofloxacin with Microcrystalline Cellulose at weekly basis

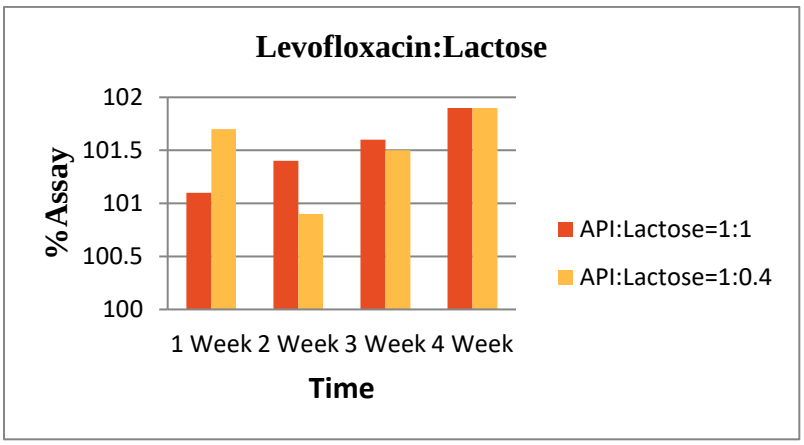


Figure 4.12: % Assay results of Levofloxacin with Lactose at weekly basis

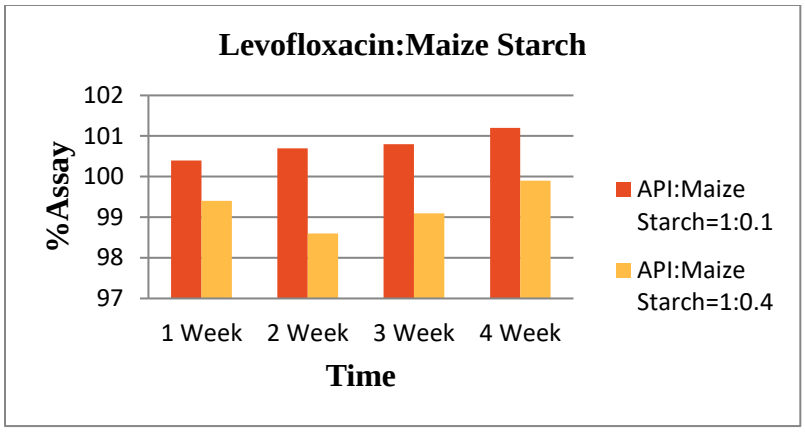


Figure 4.13: % Assay results of Levofloxacin with Maize Starch at weekly basis

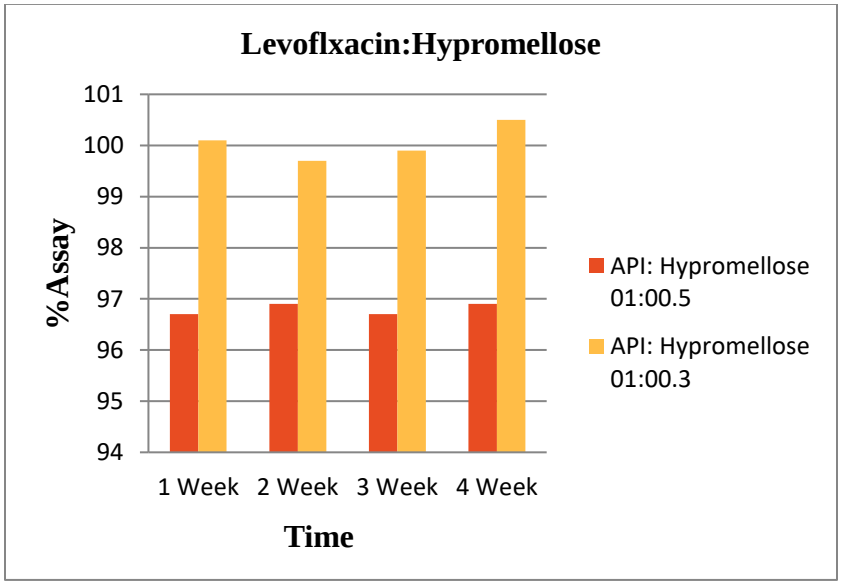


Figure 4.14: % Assay results of Levofloxacin with Hypromellose at weekly basis

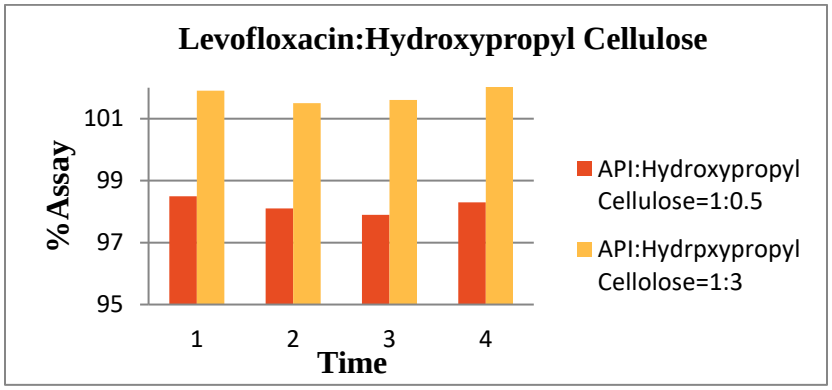


Figure 4.15: % Assay results of Levofloxacin with Hydroxypropyl Cellulose at weekly basis

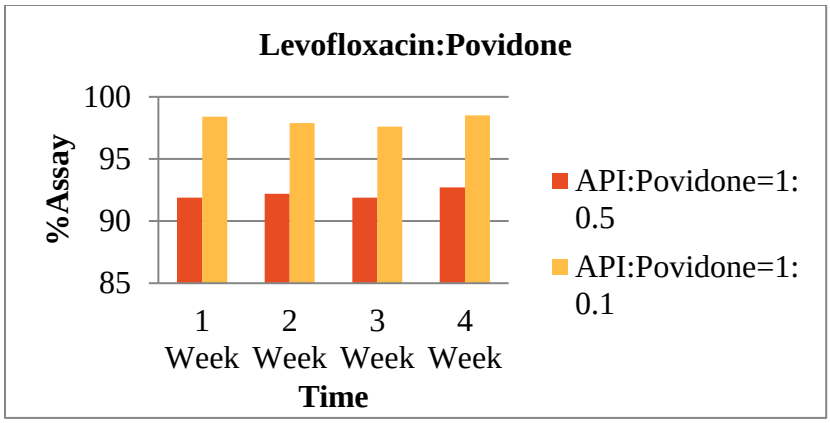


Figure 4.16: % Assay results of Levofloxacin with Povidone (K 30) at weekly basis

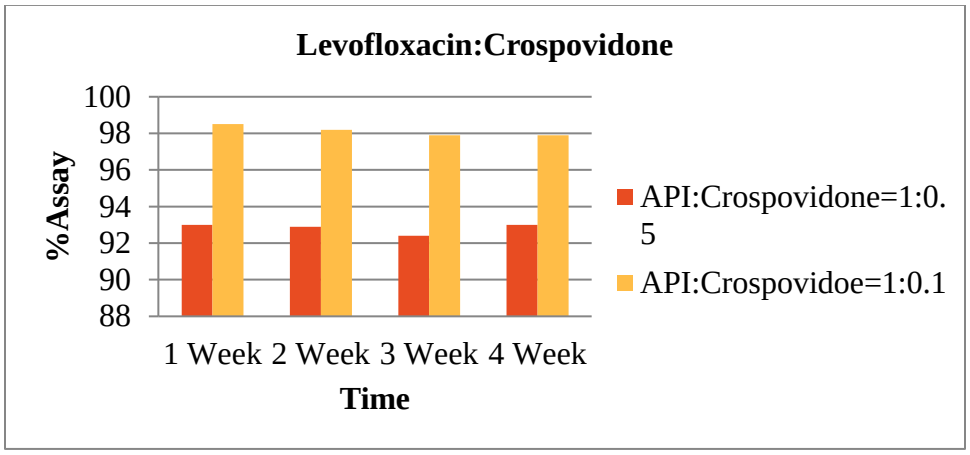


Figure 4.17: % Assay results of Levofloxacin with Crospovidone at weekly basis

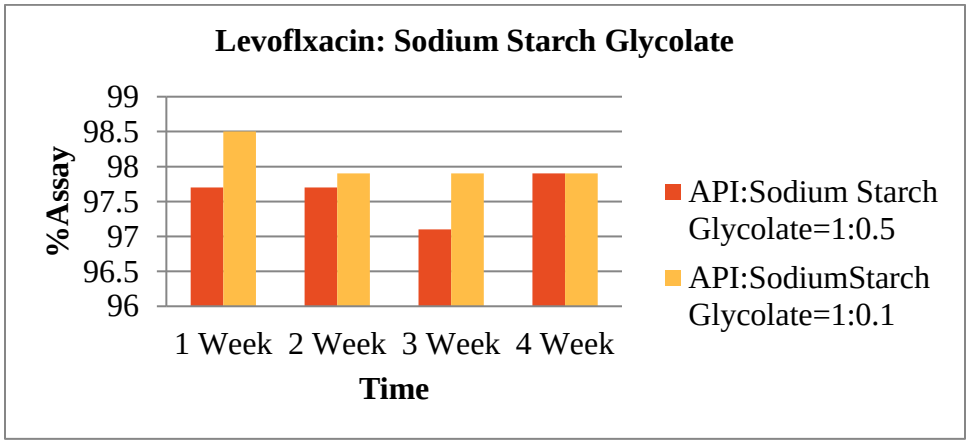


Figure 4.18: % Assay results of Levofloxacin with Sodium Starch Glycolate at weekly basis

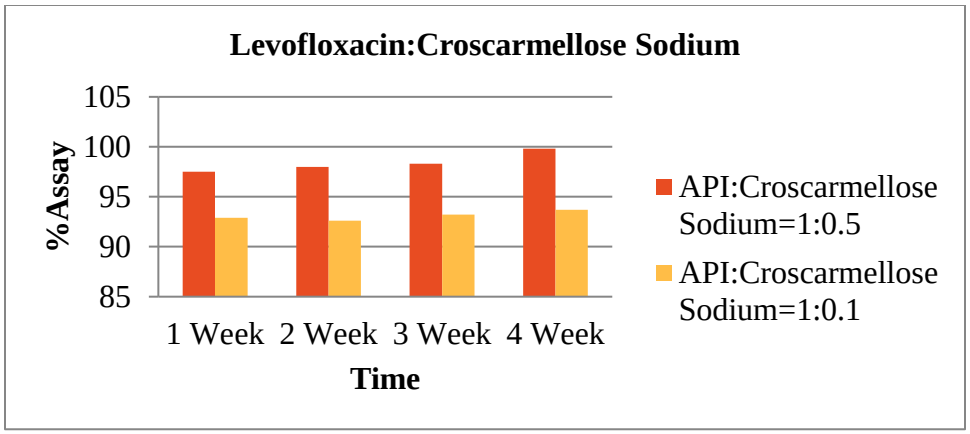


Figure 4.19: % Assay results of Levofloxacin with Croscarmellose Sodium at weekly basis

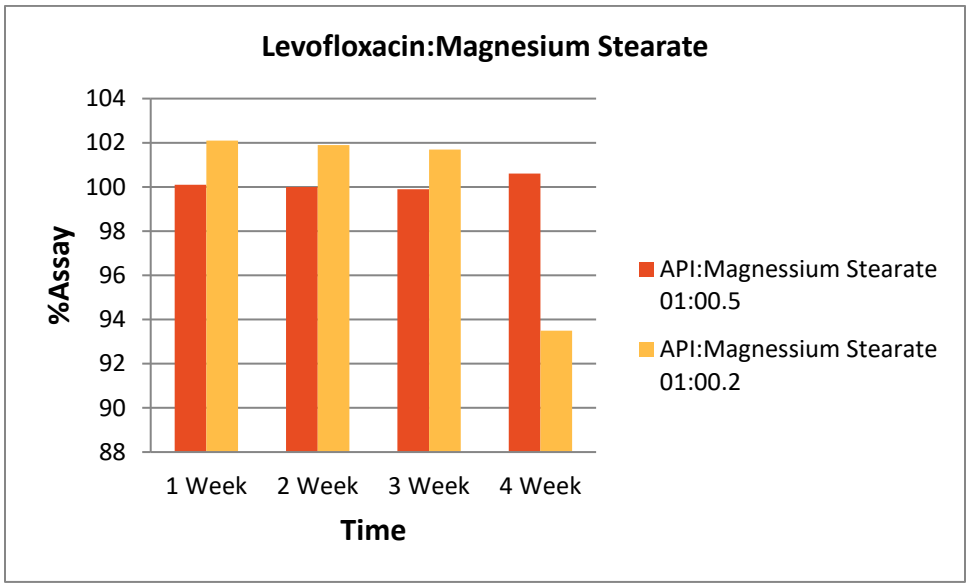


Figure 4.20: % Assay results of Levofloxacin with Magnesium Stearate at weekly basis

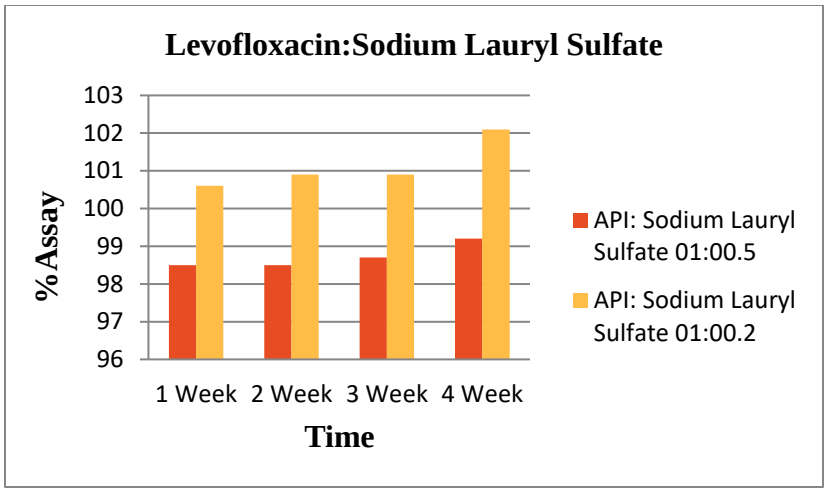


Figure 4.21: % Assay results of Levofloxacin with Sodium Lauryl Sulfate at weekly basis

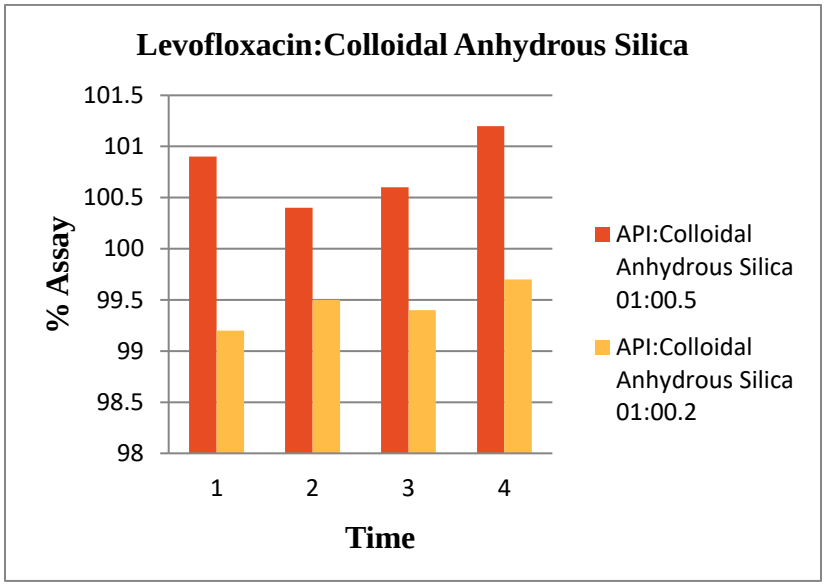


Figure 4.22: % Assay results of Levofloxacin with Colloidal Anhydrous Silica at weekly basis

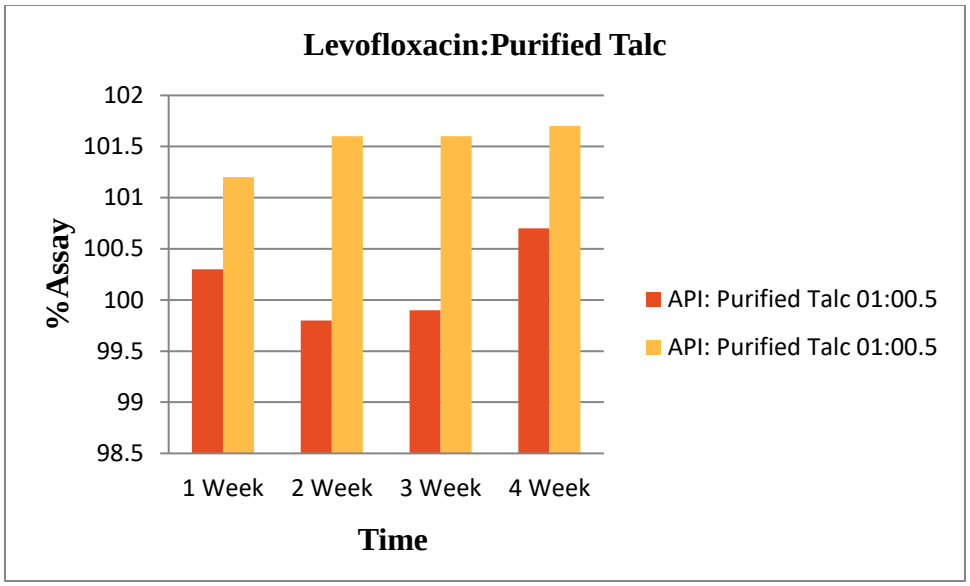


Figure 4.23: % Assay results of Levofloxacin with Microcrystalline Cellulose at weekly basis

4.1.3 Pregabalin with different excipients

Assay results were calculated as per the formula given in section 3.2.5. Below are the results-

Table 4.3: % Assay results of Pregabalin and different excipients at various time points

Sl. No.	API:Excipients	Ratio	Assay (%)			
			1 Week	2 Week	3 Week	4 Week
1.	Pregabalin		99.9	100.5	100.8	100.6
2.	Pregabalin:Pregelatinised Starch	1:1	97.9	98.4	98.4	101.8
		1:0.3	96.9	97.0	97.1	97.0
3.	Pregabalin:Maize Starch	1:1	101.3	102.1	102.0	101.8
		1:0.3	100.7	100.7	100.6	100.7
4.	Pregabalin:Purified Talc	1:0.5	100.6	102.0	101.9	102.0
		1:0.1	99.7	99.0	99.1	99.5
		1:0.03	101.1	100.6	100.8	101.2
5.	Pregabalin:Colloidal Anhydrous Silica	1:0.5	92.9	93.2	92.8	93.2
		1:0.03	99.2	98.9	98.8	99.5

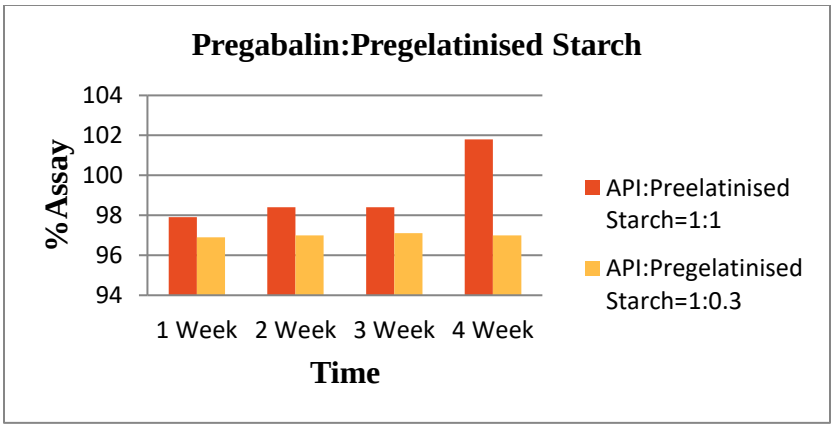


Figure 4.24: % Assay results of Pregabalin with Pregelatinized Starch at weekly basis

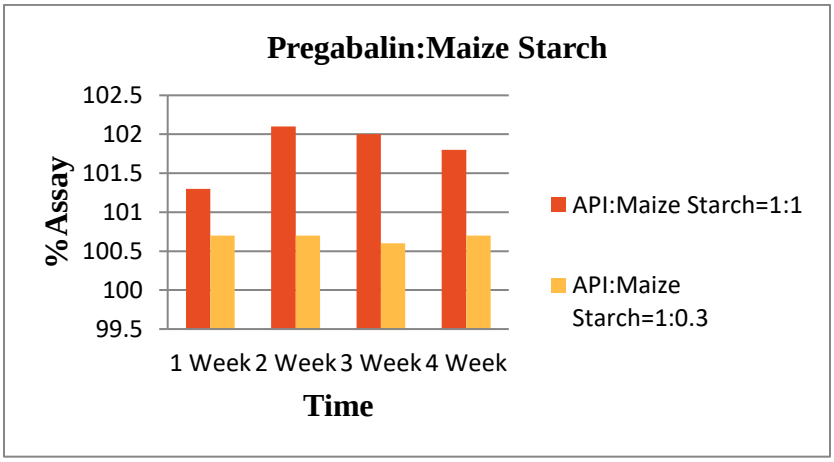


Figure 4.25: % Assay results of Pregabalin with Maize Starch at weekly basis

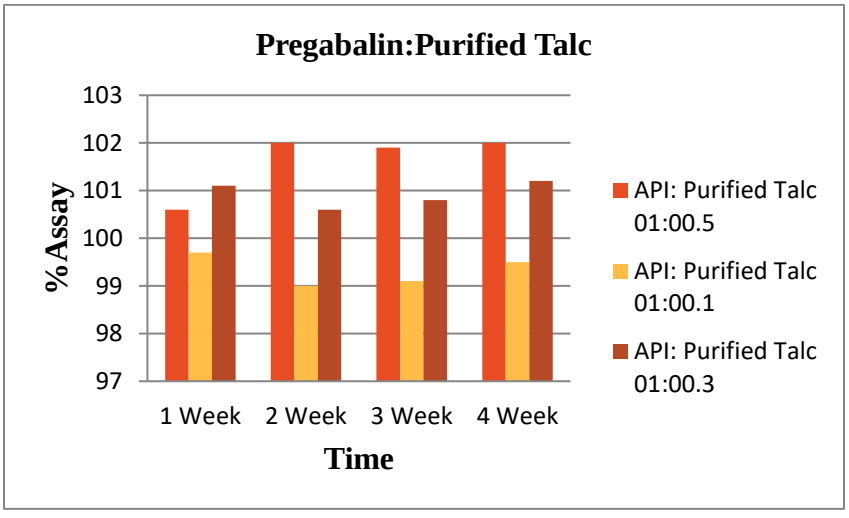


Figure 4.26: % Assay results of Pregabalin with Purified Talc at weekly basis

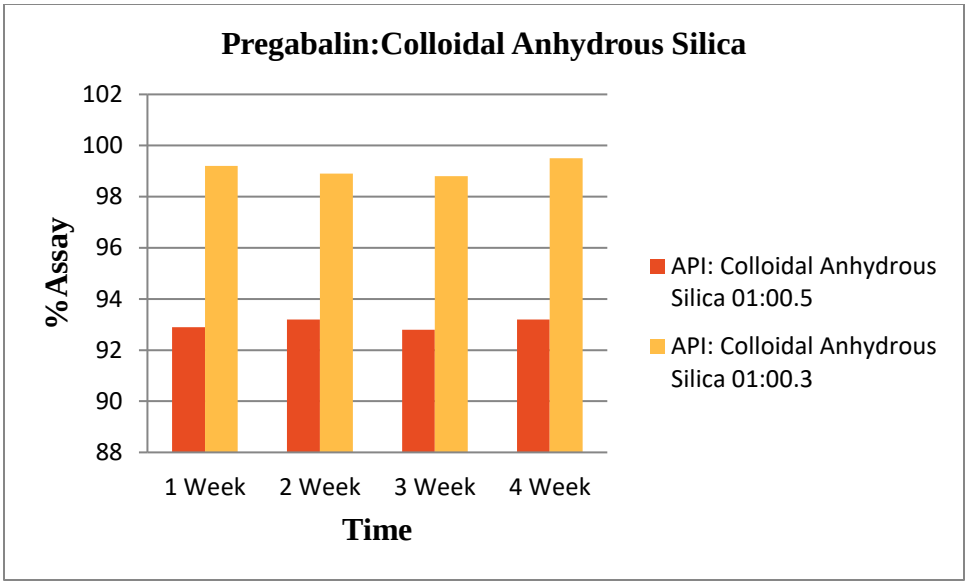


Figure 4.27: % Assay results of Pregabalin with Colloidal Anhydrous Silica at weekly basis

4.2 Impurity Results

Different samples were tested. Given below are the results-

4.2.1 Albendazole with different excipients

Impurity of Albendazole was assessed by testing of the samples taken from 40ºC/75% RH condition after 1 month. Results are obtained below-

Table 4.4: Impurity results of Albendazole and different excipients

Sl. No.	API:Excipients	Ratio	Total Impurity (%)
1.	Albendazole	Control	-
2.	Albendazole:Mirocrystalline Cellulose (101)	1:1	0.15
		1:0.4	0.08
3.	Albendazole:Lactose	1:1	0.22
		1:0.5	0.12
4.	Albendazole:Maize Starch	1:1	0.16
		1:0.1	0.09
5.	Albendazole:Mannitol	1:1	0.25

		1:0.15	0.03
		1:0.5	0.07
6.	Albendazole:Povidone (K 30)	1:0.5	0.39
		1:0.02	0.33
7.	Albendazole:Crospovidone	1:0.5	0.32
		1:0.2	0.19
8.	Albendazole:Sodium Starch Glycolate	1:0.5	0.10
		1:0.2	0.11
9.	Albendazole:Croscarmellose Sodium	1:0.5	0.15
		1:0.2	0.11
10.	Albendazole:Magnesium Stearate	1:0.5	0.39
		1:0.02	0.24
11.	Albendazole:Sodium Lauryl Sulfate	1:0.5	0.20
		1:0.02	0.16
12.	Albendazole:Colloidal Anhydrous Silica	1:0.5	0.15
		1:0.1	0.10
13.	Albendazole:Purified Talc	1:0.5	0.32
		1:0.05	0.27
14.	Albendazole:Saccharin Sodium	1:0.5	0.27
		1:0.01	0.20
15.	Albendazole:Orange Powder Flavor	1:0.5	0.32
		1:0.02	0.30
16.	Albendazole:Vanilla Powder Flavor	1:0.5	0.28
		1:0.02	0.18
17.	Albendazole:Passionfruit Powder Flavor	1:0.5	0.26
		1:0.02	0.10

4.2.2 Levofloxacin with different excipients

Impurity of Levofloxacin was assessed by testing of the samples taken from 40ºC/75% RH condition after 1 month. Results are obtained below-

Table 4.5: Impurity results of Levofloxacin and different excipients

API : Excipient	Ratio	Total Impurity (%)
Levofloxacin	Control	-
Levofloxacin : Microcrystalline Cellulose 101	1:1	0.16
Levofloxacin : Lactose Monohydrate	1:1	0.16
Levofloxacin : Maize Starch	1:1	0.15
Levofloxacin : Hypromellose 5 cps	1: 0.5	0.15
Levofloxacin : Hydroxypropyl Cellulose	1: 0.5	0.15
Levofloxacin : Povidone K 30	1: 0.5	0.22
Levofloxacin : Crospovidone	1: 0.5	0.22
Levofloxacin : Sodium Starch Glycolate	1: 0.5	0.20
Levofloxacin : Croscarmellose Sodium	1: 0.5	0.13
Levofloxacin : Magnesium Stearate	1: 0.5	0.18
Levofloxacin : Sodium Lauryl Sulfate	1: 0.5	0.12
Levofloxacin : Colloidal Silicon Dioxide	1: 0.5	0.15
Levofloxacin : Purified Talc	1: 0.5	0.15
Levofloxacin : Microcrystalline Cellulose	1: 0.4	0.15
Levofloxacin : Lactose Monohydrate	1: 0.4	0.15
Levofloxacin : Maize Starch	1: 0.4	0.13
Levofloxacin : Hypromellose 5 cps	1: 0.03	0.15
Levofloxacin : Hydroxypropyl Cellulose	1: 0.03	0.14
Levofloxacin : Povidone K 30	1: 0.1	0.16
Levofloxacin : Crospovidone	1: 0.1	0.16
Levofloxacin : Sodium Starch Glycolate	1: 0.1	0.16
Levofloxacin : Croscarmellose Sodium	1: 0.1	0.14
Levofloxacin : Magnesium Stearate	1: 0.02	0.15
Levofloxacin : Sodium Lauryl Sulfate	1: 0.02	0.14
Levofloxacin : Colloidal Silicon Dioxide	1: 0.02	0.15
Levofloxacin : Purified Talc	1: 0.05	0.20

4.2.3 Pregabalin with different excipients

Impurity of Pregabalin was assessed by testing of the samples taken from 40ºC/75% RH condition after 1 month. Results are obtained below-

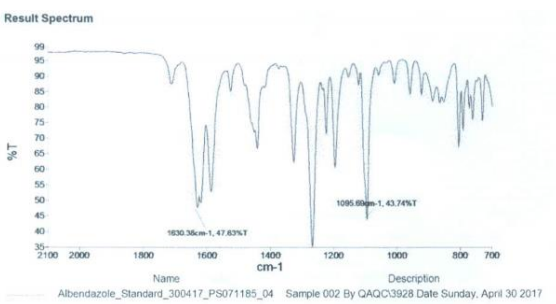
Table 4.6: Impurity results of Pregabalin and different excipients

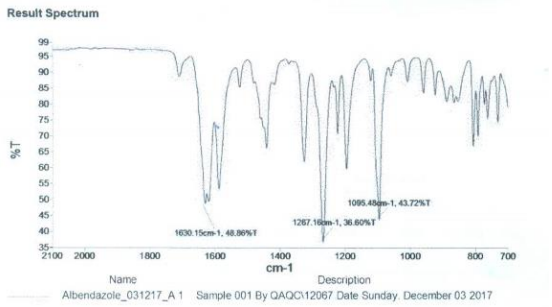
Sample Name	Ratio	Impurity %(HPGNRC01)	Impurity %(HPGNRC03)	Maximum unspecified impurity%	Total Impurity%
Pregabalin	Control	0.009	0.003	0.116	0.36
Pregabalin: Pregelatinized Starch	1:1	0.008	0.011	0.147	0.42
	1:0.3	0.002	0.010	0.050	0.20
Pregabalin : Maize Starch	1:1	0.010	0.020	0.076	0.30
	1:0.3	0.011	0.024	0.059	0.24
Pregabalin: Purified Talc	1:0.5	0.008	0.007	0.086	0.21
	1:0.3	0.005	0.010	0.050	0.15
	1:0.1	0.001	0.006	0.078	0.18
Pregabalin : Colloidal Anhydrous Silica	1:0.5	0.011	**0.757**	**0.220**	0.932
	1:0.03	0.009	0.046	**0.469**	0.87
	Limit	NMT 0.2%	NMT 0.2%	NMT 0.2%	NMT 1.0%

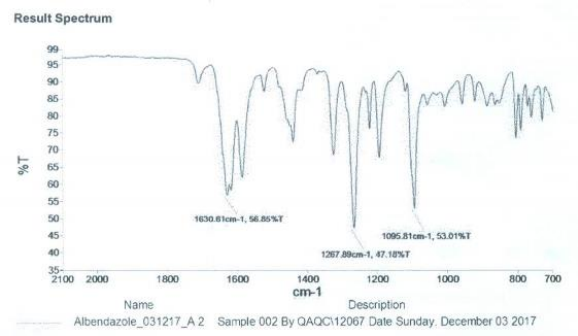
4.3 IR Spectrum

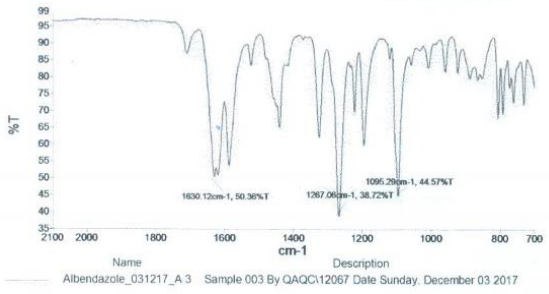
4.3.1 Albendazole with different excipients

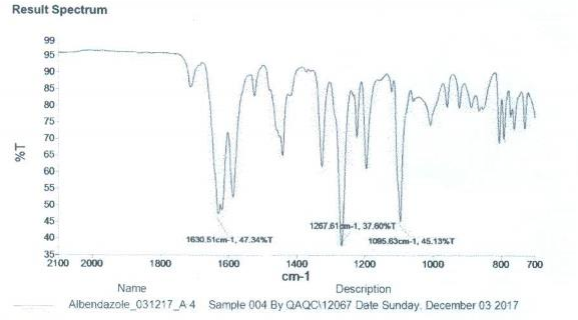
Sample Name	API:Excipients	Absorbance
Standard	Albendazole WS	1267.4
A-1	Albendazole (Pure API)	1267.2
A-2	Albendazole:Microcrystalline Cellulose	1267.9
A-3	Albendazole:Lactose	1267.1
A-4	Albendazole:Maize Starch	1267.6
A-5	Albendazole:Mannitol	1266.8
A-6	Albendazole:Povidone (K 30)	1267.2
A-7	Albendazole:Crospovidone	1266.4
A-8	Albendazole:Sodium Starch Glycolate	1266.0
A-9	Albendazole:Croscarmellose Sodium	1266.4
A-10	Albendazole:Magnesium Stearate	1268.8
A-11	Albendazole:Sodium Lauryl Sulfate	1268.2
A-12	Albendazole:Colloidal Anhydrous Silica	1268.2
A-13	Albendazole:Purified Talc	1268.0
A-14	Albendazole:Saccharin Sodium	1268.3
A-29	Albendazole:Orange Powder Flavor	1268.3
A-30	Albendazole:Vanilla Powder Flavor	1268.3
A-31	Albendazole:Passionfruit Powder Flavor	1267.1

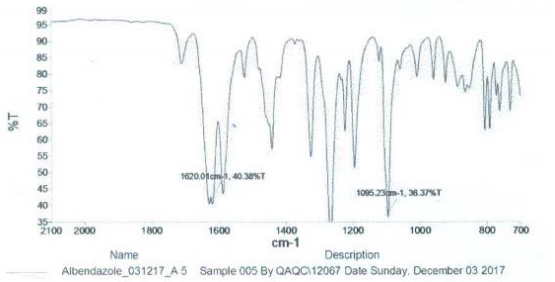


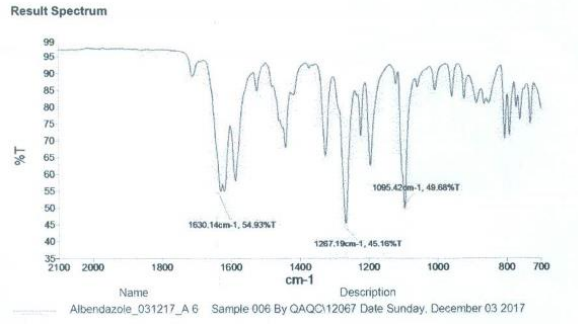


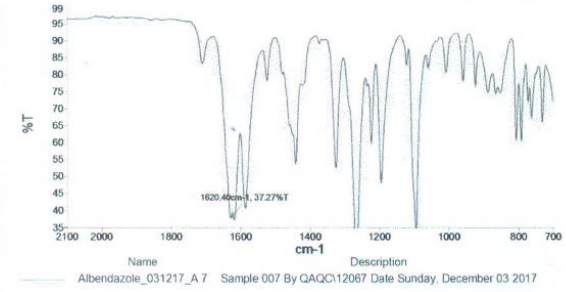

Result Spectrum
%T
1630.61cm-1, 56.85%T
1095.81cm-1, 53.01%T
1267.89cm-1, 47.18%T
cm-1
Name
Description
Albendazole_031217_A 2 Sample 002 By QAQC\12067 Date Sunday, December 03 2017

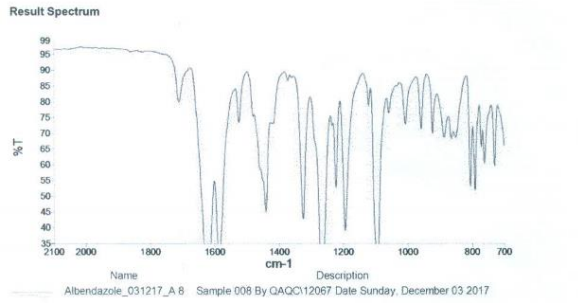

%T
1630.12cm-1, 50.36%T
1267.06cm-1, 38.72%T
1095.29cm-1, 44.57%T
cm-1
Name
Description
Albendazole_031217_A 3 Sample 003 By QAQC\12067 Date Sunday, December 03 2017

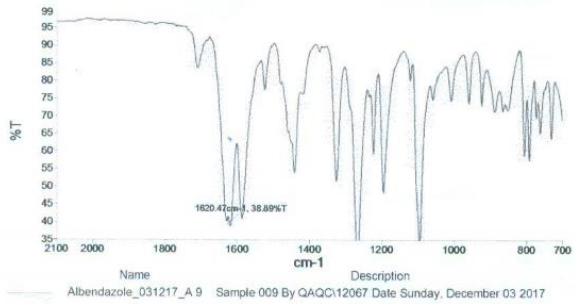

Result Spectrum
%T
1630.51cm-1, 47.34%T
1267.61cm-1, 37.60%T
1095.63cm-1, 45.13%T
cm-1
Name
Description
Albendazole_031217_A 4 Sample 004 By QAQC\12067 Date Sunday, December 03 2017

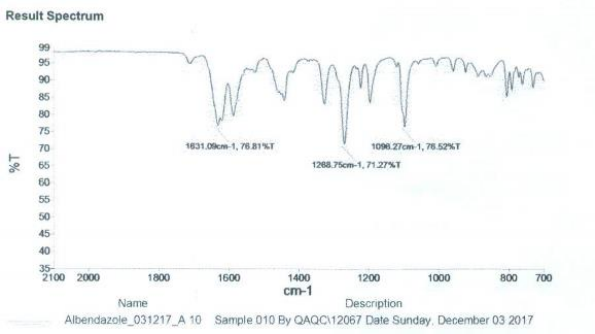

%T
1620.01cm-1, 40.38%T
1095.23cm-1, 36.37%T
cm-1
Name
Description
Albendazole_031217_A 5 Sample 005 By QAQC\12067 Date Sunday, December 03 2017

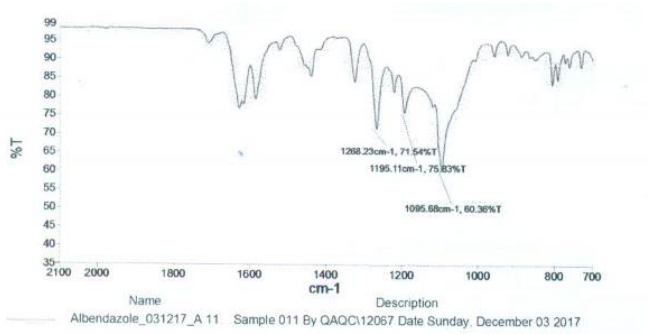

Result Spectrum
%T
1095.42cm-1, 49.68%T
1630.14cm-1, 54.93%T
1267.19cm-1, 45.16%T
cm-1
Name
Description
Albendazole_031217_A 6 Sample 006 By QAQC\12067 Date Sunday, December 03 2017

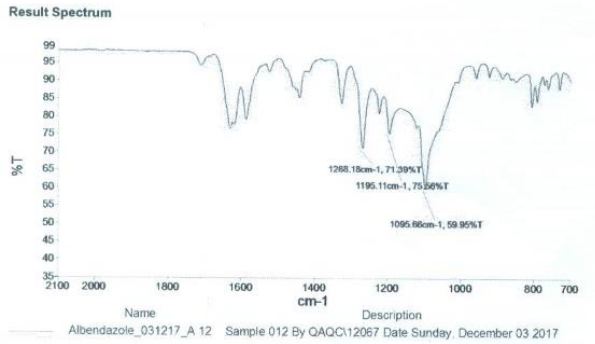

%T
1620.46cm-1, 37.27%T
cm-1
Name
Description
Albendazole_031217_A 7 Sample 007 By QAQC\12067 Date Sunday, December 03 2017

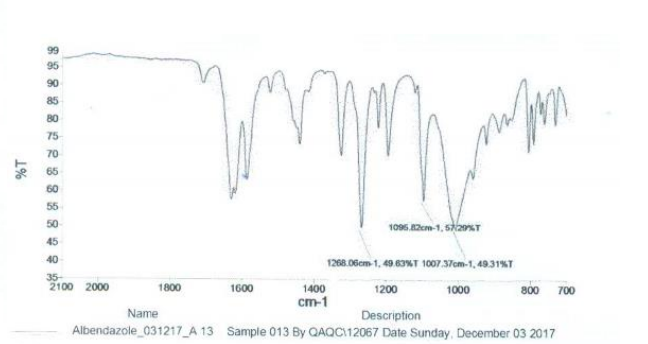

Result Spectrum
%T
cm-1
Name
Description
Albendazole_031217_A 8 Sample 008 By QAQC\12067 Date Sunday, December 03 2017

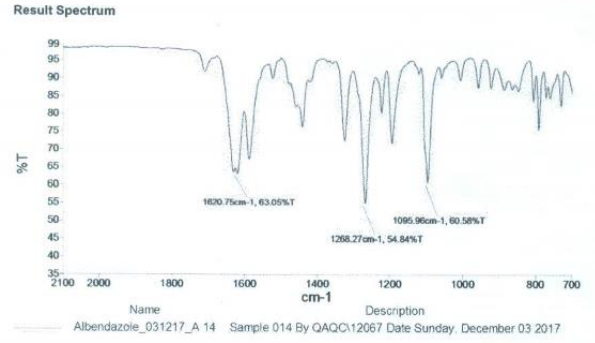

%T
1620.47cm-1, 38.89%T
cm-1
Name
Description
Albendazole_031217_A 9 Sample 009 By QAQC\12067 Date Sunday, December 03 2017

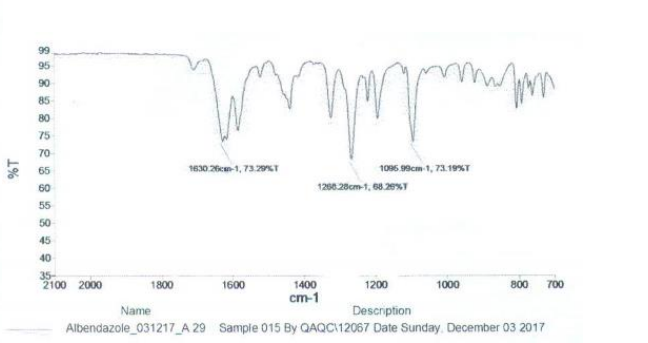

Result Spectrum
1631.09cm-1, 76.81%T
1096.27cm-1, 76.52%T
1268.75cm-1, 71.27%T
%T
cm-1
Name
Description
Albendazole_031217_A 10 Sample 010 By QAQC\12067 Date Sunday, December 03 2017

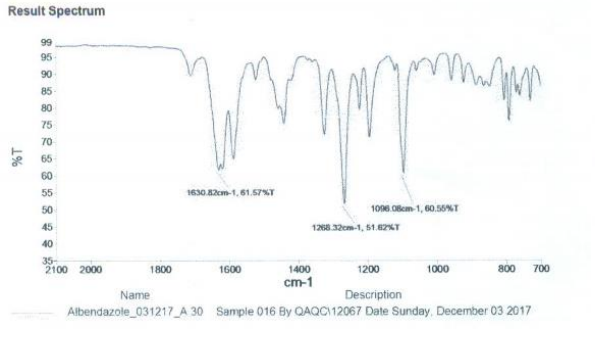

1268.23cm-1, 71.54%T
1195.11cm-1, 75.83%T
1095.68cm-1, 60.36%T
%T
cm-1
Name
Description
Albendazole_031217_A 11 Sample 011 By QAQC\12067 Date Sunday, December 03 2017

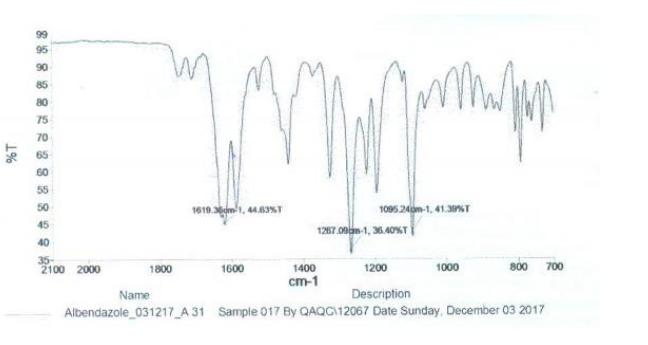

Result Spectrum
1268.18cm-1, 71.39%T
1195.11cm-1, 75.56%T
1095.68cm-1, 59.95%T
%T
cm-1
Name
Description
Albendazole_031217_A 12 Sample 012 By QAQC\12067 Date Sunday, December 03 2017


1095.82cm-1, 57.29%T
1268.06cm-1, 49.63%T 1007.37cm-1, 49.31%T
%T
cm-1
Name
Description
Albendazole_031217_A 13 Sample 013 By QAQC\12067 Date Sunday, December 03 2017


Result Spectrum
1620.75cm-1, 63.05%T
1095.96cm-1, 60.58%T
1268.27cm-1, 54.84%T
%T
cm-1
Name
Description
Albendazole_031217_A 14 Sample 014 By QAQC\12067 Date Sunday, December 03 2017

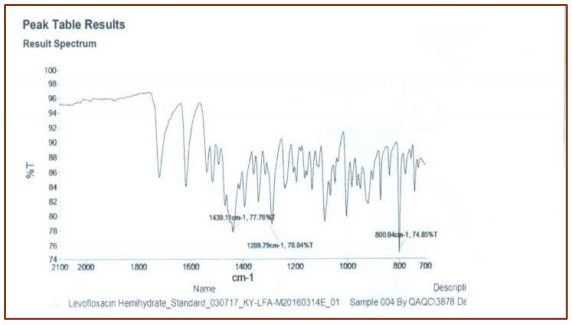

1630.26cm-1, 73.29%T
1095.99cm-1, 73.19%T
1268.28cm-1, 68.28%T
%T
cm-1
Name
Description
Albendazole_031217_A 29 Sample 015 By QAQC\12067 Date Sunday, December 03 2017

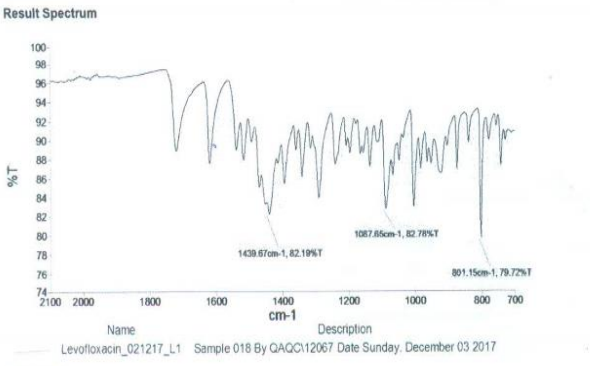

Result Spectrum
1630.82cm-1, 61.57%T
1096.08cm-1, 60.55%T
1268.32cm-1, 51.62%T
%T
cm-1
Name
Description
Albendazole_031217_A 30 Sample 016 By QAQC\12067 Date Sunday, December 03 2017

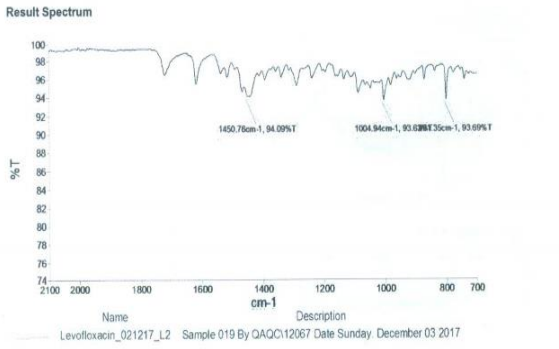

1619.36cm-1, 44.63%T
1095.24cm-1, 41.39%T
1267.09cm-1, 36.40%T
%T
cm-1
Name
Description
Albendazole_031217_A 31 Sample 017 By QAQC\12067 Date Sunday, December 03 2017

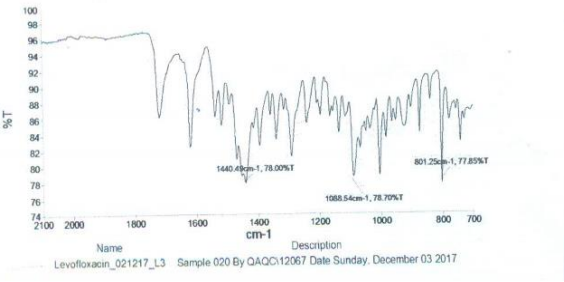
4.3.2 Levofloxacin with different excipients

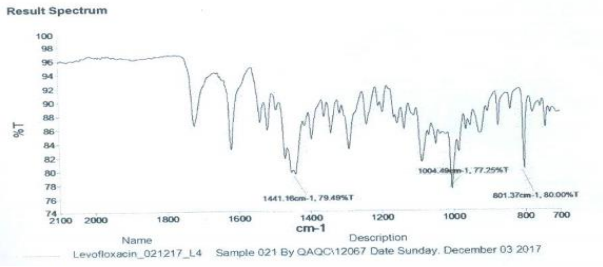
Sample Name	API:Excipients	Absorbance
Standard	Levofloxacin Hemihydrate WS	800.9
L-1	Levofloxacin (Pure API)	801.2
L-2	Levofloxacin:Microcrystalline Cellulose	801.4
L-3	Levofloxacin:Lactose	801.3
L-4	Levofloxacin:Maize Starch	801.4
L-5	Levofloxacin:Hypromellose 5 cps	1451.8
L-6	Levofloxacin:Hydroxypropyl Cellulose	801.3
L-7	Levofloxacin:Povidone (K 30)	801.2
L-8	Levofloxacin:Crospovidone	801.5
L-9	Levofloxacin:Sodium Starch Glycolate	801.6
L-10	Levofloxacin:Croscarmellose Sodium	801.2
L-11	Levofloxacin:Magnesium Stearate	801.3
L-12	Levofloxacin:Sodium Lauryl Sulfate	801.3
L-13	Levofloxacin:Colloidal Anhydrous Silica	801.2
L-14	Levofloxacin:Purified Talc	801.2

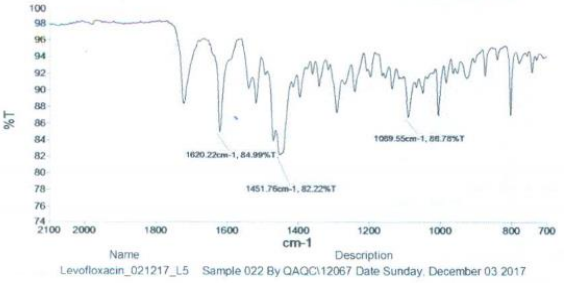

Peak Table Results
Result Spectrum
%T
cm-1
Name
Levofloxacin Hemihydrate_Standard_030717_KY-LFA-M20160314E_01 Sample 004 By QAQC\3878 De

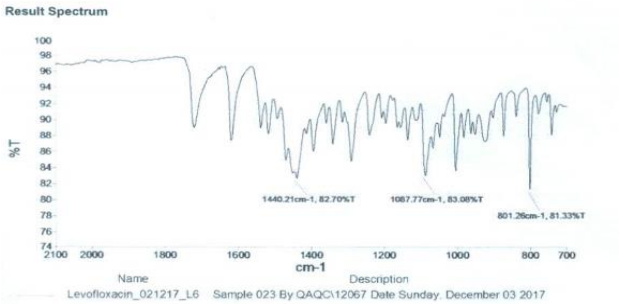

Result Spectrum
%T
1439.67cm-1, 82.19%T
1087.65cm-1, 82.78%T
801.15cm-1, 79.72%T
cm-1
Name
Description
Levofloxacin_021217_L1 Sample 018 By QAQC\12067 Date Sunday, December 03 2017

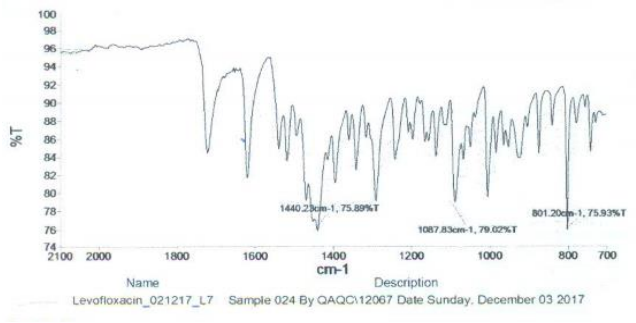

Result Spectrum
%T
1450.78cm-1, 94.09%T
cm-1
Name
Description
Levofloxacin_021217_L2 Sample 019 By QAQC\12067 Date Sunday, December 03 2017

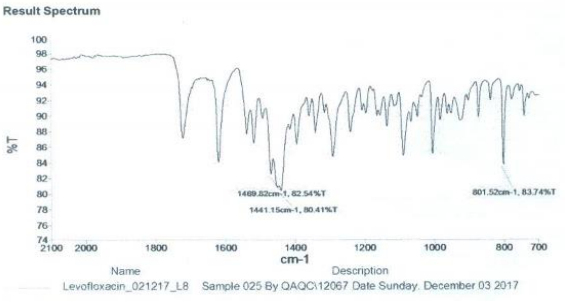

%T
1440.49cm-1, 78.00%T
1088.54cm-1, 78.70%T
801.25cm-1, 77.85%T
cm-1
Name
Description
Levofloxacin_021217_L3 Sample 020 By QAQC\12067 Date Sunday, December 03 2017

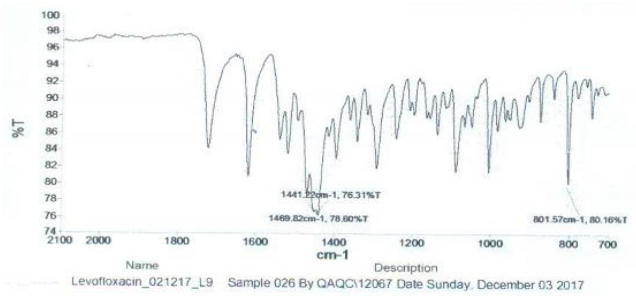

Result Spectrum
%T
1441.16cm-1, 79.49%T
1004.49cm-1, 77.25%T
801.37cm-1, 80.00%T
cm-1
Name
Description
Levofloxacin_021217_L4 Sample 021 By QAQC\12067 Date Sunday, December 03 2017

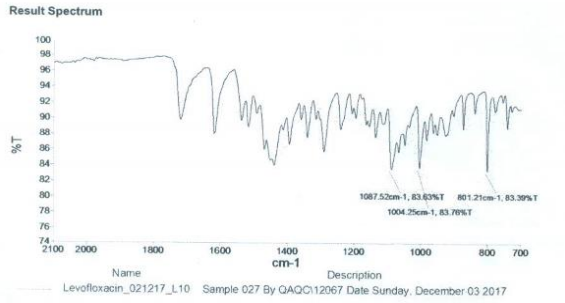

%T
1620.22cm-1, 84.99%T
1451.76cm-1, 82.22%T
1089.55cm-1, 86.78%T
cm-1
Name
Description
Levofloxacin_021217_L5 Sample 022 By QAQC\12067 Date Sunday, December 03 2017

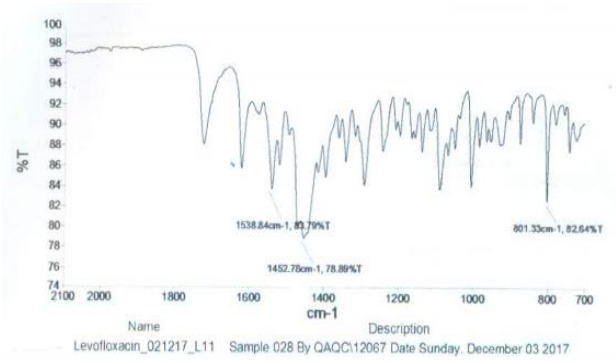

Result Spectrum
%T
1440.21cm-1, 82.70%T
1087.77cm-1, 83.08%T
801.26cm-1, 81.33%T
cm-1
Name
Description
Levofloxacin_021217_L6 Sample 023 By QAQC\12067 Date Sunday, December 03 2017

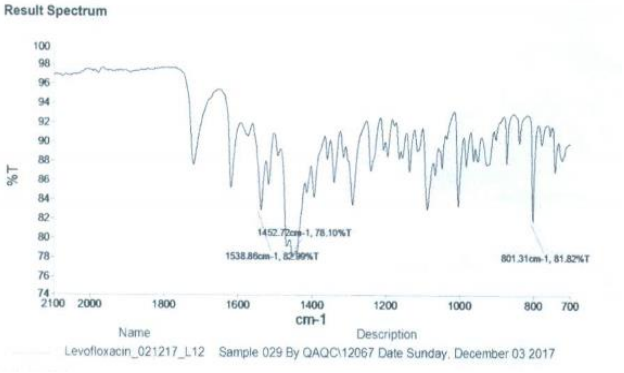

%T
1440.23cm-1, 75.89%T
1087.83cm-1, 79.02%T
801.20cm-1, 75.93%T
cm-1
Name
Description
Levofloxacin_021217_L7 Sample 024 By QAQC\12067 Date Sunday, December 03 2017

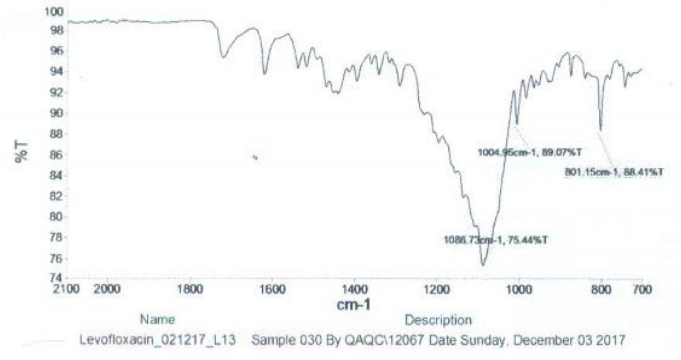

Result Spectrum
%T
1469.82cm-1, 82.54%T
1441.15cm-1, 80.41%T
801.52cm-1, 83.74%T
cm-1
Name
Description
Levofloxacin_021217_L8 Sample 025 By QAQC\12067 Date Sunday, December 03 2017

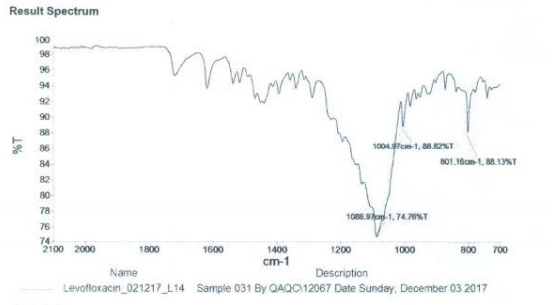

%T
1441.22cm-1, 76.31%T
1469.82cm-1, 78.60%T
801.57cm-1, 80.16%T
cm-1
Name
Description
Levofloxacin_021217_L9 Sample 026 By QAQC\12067 Date Sunday, December 03 2017


Result Spectrum
%T
1087.52cm-1, 83.63%T
801.21cm-1, 83.39%T
1004.25cm-1, 83.76%T
cm-1
Name
Description
Levofloxacin_021217_L10 Sample 027 By QAQC\12067 Date Sunday, December 03 2017


%T
1538.84cm-1, 80.79%T
1452.78cm-1, 78.89%T
801.33cm-1, 82.64%T
cm-1
Name
Description
Levofloxacin_021217_L11 Sample 028 By QAQC\12067 Date Sunday, December 03 2017

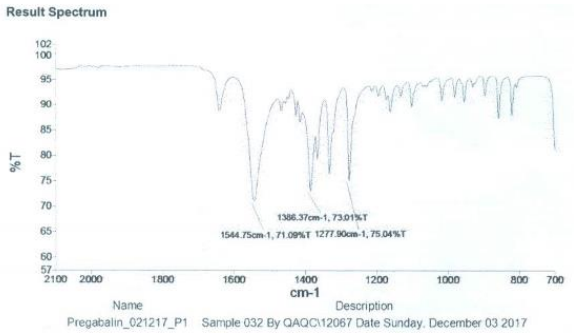

Result Spectrum
%T
1452.72cm-1, 78.10%T
1538.86cm-1, 82.96%T
801.31cm-1, 81.82%T
cm-1
Name
Description
Levofloxacin_021217_L12 Sample 029 By QAQC\12067 Date Sunday, December 03 2017

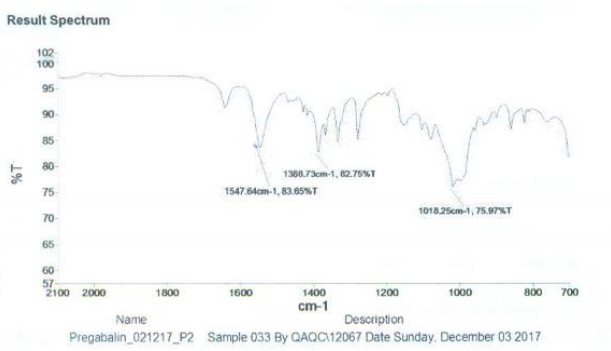

%T
1004.95cm-1, 89.07%T
801.15cm-1, 88.41%T
1086.73cm-1, 75.44%T
cm-1
Name
Description
Levofloxacin_021217_L13 Sample 030 By QAQC\12067 Date Sunday, December 03 2017

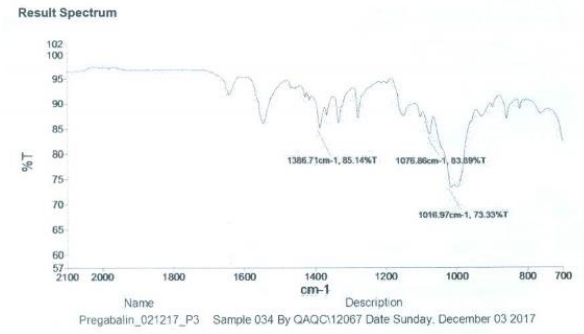

Result Spectrum
%T
1004.97cm-1, 88.82%T
801.16cm-1, 88.13%T
1086.97cm-1, 74.76%T
cm-1
Name
Description
Levofloxacin_021217_L14 Sample 031 By QAQC\12067 Date Sunday, December 03 2017

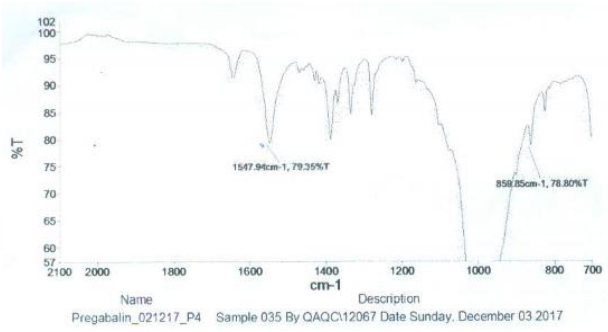
4.3.3 Pregabalin with different excipients

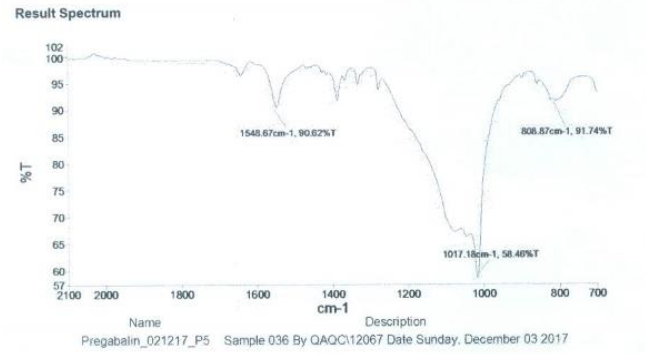
Sample Name	API:Excipients
Standard	Pregabalin WS
L-1	Pregabalin (Pure API)
L-2	Pregabalin:Pregelatinized Starch
L-3	Pregabalin:Maize Starch
L-4	Pregabalin:Purified Talc
L-5	Pregabalin:Colloidal Anhydrous Silica











4.4 Formula Optimization

In this research work, three dosage forms were chosen with three different drug molecules. These are Albendazole Chewable Tablets 400 mg, Levofloxacin Film Coated Tablets 250/500/750 mg and Pregabalin Capsules 25/50/75/100/150/200/225/300 mg.

4.4.1 Albendazole Chewable Tablets 400 mg

Raw Materials	**T-1**	**T-2**		**T-3**		**T-4**	**T-5**
KEY POINTS	Water Granl	Water Granl, Alb in slurry, Tab wt 1050 mg		IPA Granl, PVP 2.5%		IPA Granl	Water Granl
IG PART							
Albendazole	400	-		400		400	400
Lactose	354	354		380		230	230
Maize Starch	50	50		50		150	150
MCC 101	-	40		100		150	150
CCS	25	25		30		30	30
Aerosil-200	10	20		10		10	10
SLS	-	-		5		10	10
Sod Saccharin	-	-		5		5	5
BINDER SOLN							
Albendazole	-	400		-		-	-
SLS	16	16		-		-	-
Povidone K-30	20	20		25		20	20
Sod Saccharin	5	5		-		-	-
PW (at 45°C)	100%	100%		-		-	100%
IPA	-	-		100%		100%	
EG PART		**L-1**	**L-2**	**L-1**	**L-2**		
MCC 102	100	-	-	-	-	-	-
MCC 101	-	95	65	-	-	-	-
Aerosil-200	-	5	5	-	-	-	-
CCS	25	-	30	-	-	-	-
Orange Fla	10	10	10	10	10	10	10
Mg Stearate	10	10	10	10	10	10	10
TOTAL	1025	1050		1025		1025	1025
KEY OBSERVATION	Disso less at terminal point	DT faster in media but not dissolv, *CCS not use in EG **Disso check at 75 RPM**		No impact with IPA granl		No impact with IPA granl	Tab wt not coming

DT (minutes)	5:00-6:00	5:10-7:50	4:50-5:30	3:10-3:45	3:45-4:00	3:58-7:38	4:23-4:49
% Dissolution							
5 min	15	25	32	31	34	37	14
10 min	30	40	44	47	49	49	27
15 min	42	47	49	57	57	58	41
30 min	**58**	**55**	**56**	**70**	**69**	**69**	**55**

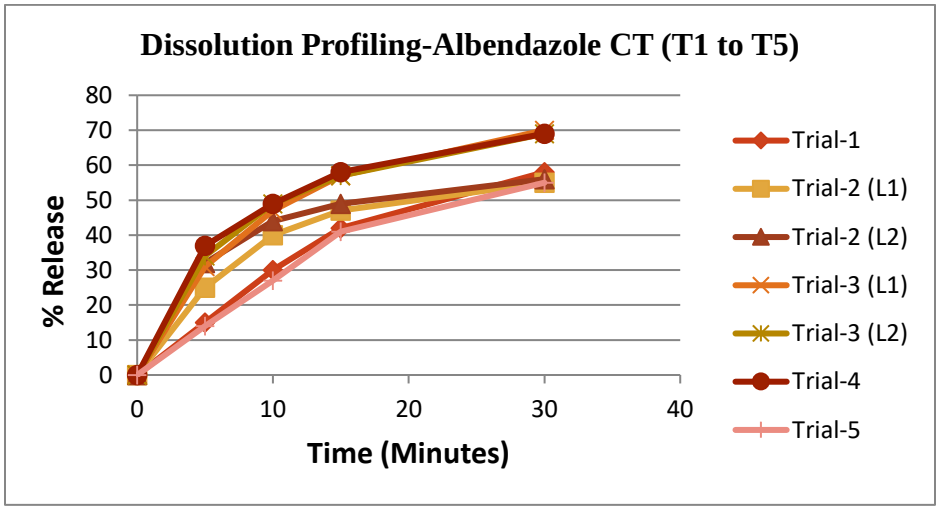


Figure 4.28: Dissolution curve of Albendazole CT (T1 to T5)

Raw Materials	**T-6**	**T-7**	**T-8**	**T-9**	**T-10**
KEY POINTS	80:20 Granl	Water Granl, Mannitol in place of Lactose	Water Granl, Mannitol used, CCS 8%	Water Granl, PVP 1%	Water Granl, Portion of Lactose in soln with SLS
IG PART					
Albendazole	400	400	400	400	400
Lactose	230	-	-	-	230
Mannitol	-	380	230	240	60
Maize Starch	150	50	50	50	50
MCC 101	150	100	200	200	150
CCS	30	30	80	80	80
Aerosil-200	10	10	10	10	10
SLS	10	-	-	-	-
Sod Saccharin	5	5	5	5	5
BINDER SOLN					

SLS	-	10	10	10	10		
Povidone K-30	20	20	20	10	10		
Aerosil-200	-	-	-	-	-		
PW (at 45°C)	80%	100%	100%	100%	100%		
IPA	20%	-	-	-	-		
EG PART					**L-1**	**L-2**	**L-3**
CCS	-	-	-	-	-	-	30
SLS	-	-	-	-	-	5	-
Orange Fla	10	10	10	10	10	10	10
Mg Stearate	10	10	10	10	10	10	10
TOTAL	1025	1025	1025	1025	1025		
KEY OBSERVATION	Tab wt not coming	Good so far, initial disso les	+60 granules less, DT increase	granules ok	Disso increase in 30 min, initially less	Additional 0.5% SLS in EG didn't help	No significance in adding 3% CCS in EG
DT (minutes)	5:30 – 6:45	7:35 – 8:05	6:50 – 7:50	6:25 – 7:40	8:34 – 8:56	7:18 – 8:10	7:32 – 8:05
% Dissolution							
5 min	20	24	18	23	24	13	24
10 min	38	43	34	40	44	31	48
15 min	35	56	46	53	60	45	63
30 min	**68**	**72**	**65**	**67**	**77**	**66**	**75**

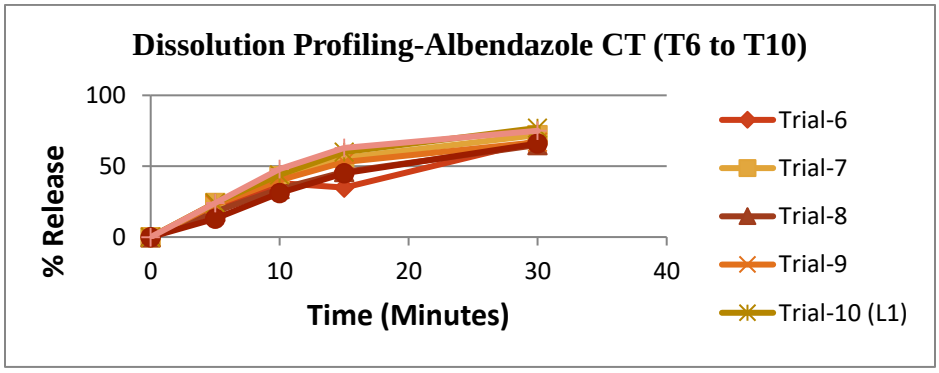


Figure 4.29: Dissolution curve of Albendazole CT (T6 to T10)

Raw Materials	**T-11**		**T-12**	**T-13**	**T-14**	**T-15**	
KEY POINTS	Water Granl, Portion of Lactose in soln with SLS, MCC (12% IG+3% EG), CCS in EG		Co-sieving	Co-milling	Aerosil 5% (co-sieved with Alb)	Aerosil 5%, MCC in EG	
IG PART							
Albendazole	400		400	400	400	400	
Lactose	205		205	205	185	185	
Mannitol	60		60	60	60	60	
Maize Starch	100		50	50	50	50	
MCC 101	120		120	120	100	-	
CCS	-		80	80	80	80	
Aerosil-200	10		10	10	50	50	
Lactose	25		25	25	25	25	
SLS	10		10	10	10	10	
Povidone K-30	10		10	10	10	10	
Sod Saccharin	5		5	5	5	5	
PW (at 45°C)	100%		100%	100%	100%	100%	
EG PART	**L-1**	**L-2**				**L-1**	**L-2**
MCC 102	-	-	-	-	-	-	130
MCC 101	30	30	30	30	30	130	-
	-	-	-	-	-	-	-
Aerosil-200	-	-	-	-	-	-	-
CCS	30	-	-	-	-	-	-
Crospovidone	-	30	-	-	-	-	-
SLS	-	-	-	-	-	-	-
Orange Fla	10	10	10	10	10	10	10
Mg Stearate	10	10	10	10	10	10	10
TOTAL	1025		1025	1025	1025	1025	1025
KEY OBSERVATION	Disso falls drastically probably because CCS is in the EG & less qty. (3%)		No diff btween co-sieving & co-milling	No diff btween co-sieving & co-milling	Infinite disso good	L-2 (MCC 102) slightly better than L-1	
DT (minutes)	5:00 – 6:25		4:30 – 5:40	4:25 – 6:20	5:20 – 6:30	4:50 – 6:25	4:50 – 5:50
% Dissolution	L1	L2					
5 min	16	21	28	14	31	19	28
10 min	35	35	41	35	54	40	52
15 min	45	44	48	50	61	56	67
30 min	**59**	**55**	**56**	**63**	**72**	**71**	**76**

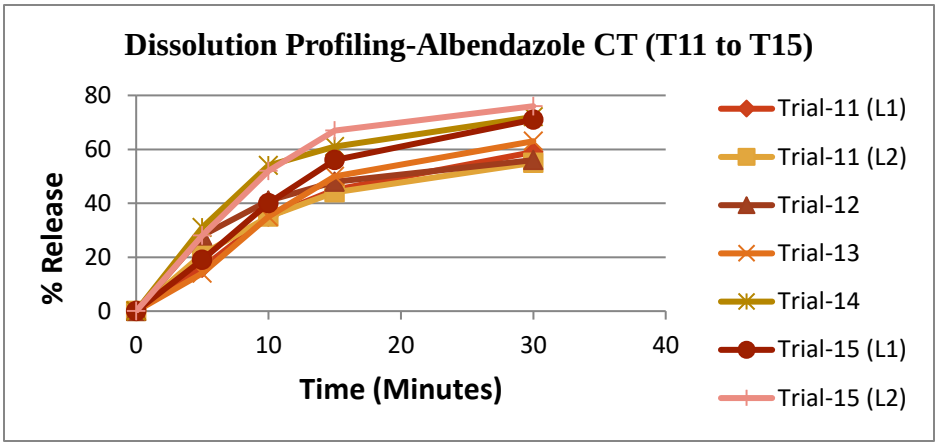


Figure 4.30: Dissolution curve of Albendazole CT (T11 to T5)

Raw Materials	**T-16**	**T-17**	**T-18**	**T-19**	**T-20**
KEY POINTS	Lactose replaced with Mannitol, PVP in binder soln	Lactose replaced with Mannitol, PVP in dry mix	co-sieved with 60 mesh	co-sieved with 40 mesh	co-sieved with 30 mesh, Aerosil in soln with lactose, SLS, Saccharin
IG PART					
Albendazole	400	400	400	400	400
Lactose	-	-	180	180	180
Mannitol	230	230	60	60	60
Maize Starch	100	100	50	50	50
MCC 101	-	-	110	110	110
MCC 105	50	50	-	-	-
CCS	30	30	80	80	80
Aerosil-200	50	50	50	50	-
Povidone K-30		20	-	-	-
BINDER SOLN					
Lactose	-	-	20	20	20
Mannitol	25	25	-	-	-
SLS	15	15	10	10	10
Povidone K-30	20	-	10	10	10
Aerosil-200	-	-	-	-	**50**
Sod Saccharin	5	5	5	5	5
PW (at 45°C)	100%	100%	100%	100%	100%
EG PART					
MCC 102	50	50	30	30	30
CCS	30	30	-	-	-

Orange Fla	10	10	10	10	10
Mg Stearate	10	10	10	10	10
TOTAL	1025	1025	1025	1025	1025
KEY OBSERVATION	No impact of using PVP in binder soln or dry mix	No impact of using PVP in binder soln or dry mix	Very promising result (matches with Zentel India)	good result (slightly less at 10 & 15 min)	initial disso less
DT (minutes)	5:30-6:15	4:39-4:50	6:52-7:10	5:30-5:52	4:39-4:41
% Dissolution					
5 min	18	23	27	30	23
10 min	35	38	52	45	34
15 min	49	48	66	58	48
30 min	**67**	**64**	**80**	**79**	76

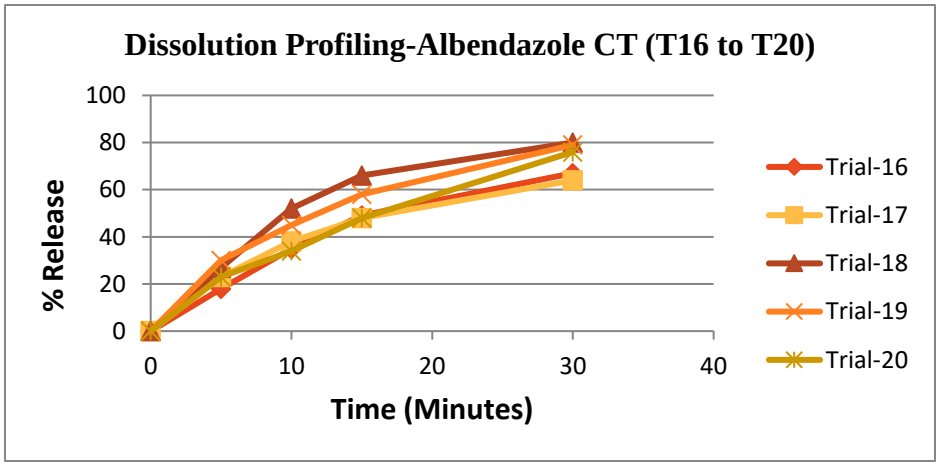


Figure 4.31: Dissolution curve of Albendazole CT (T16 to T20)

Raw Materials	**T-21**	**T-22**	**T-23**	**T-24**	**T-25**
KEY POINTS	Mannitol in place of Lactose, MCC in EG, M. Starch increase	Alb (33.33% in slurry)	Crospovidone is used	Maize Starch increase, MCC decrease	Total Lactose in dry mix, 40 mesh used
IG PART					
Albendazole	400	250	400	400	400
Lactose	-	-	-	-	200
Mannitol	180	180	180	180	60
Maize Starch	100	100	100	150	50
MCC 101	-	-	-	-	110
CCS	80	80	-	80	80
Crospovidone	-	-	80	-	-

Aerosil-200	50	50	50	50	50
BINDER SOLN					
Albendazole	-	150	-	-	-
Lactose	-	20	-	-	-
Mannitol	20	-	20	20	-
SLS	10	10	10	10	10
Povidone K-30	10	10	10	10	10
Aerosil-200	-	-	-	-	-
Sod Saccharin	5	5	5	5	5
PW (at 45°C)	100%	100%	100%	100%	100%
EG PART					
MCC 102	150	150	150	100	30
Orange Fla	10	10	10	10	10
Mg Stearate	10	10	10	10	10
TOTAL	1025	1025	1025	1025	1025
KEY OBSERVATION	initial disso good, 30 min less	initial disso less	Disso at 30 min & Infinite are less. Crospovidone didn't help	In visual inspection, increase qty. of M.Starch help in better segregation	No impact of Lactose soln (compare to T-19)
DT (minutes)	6:47-7:19	5:30 – 6:20	1:23-1:25	4:32-6:22	7:44-7:46
% Dissolution					
5 min	31	20	35	19	26
10 min	53	40	46	47	49
15 min	62	49	52	62	67
30 min	**72**	**57**	**61**	**74**	**81**

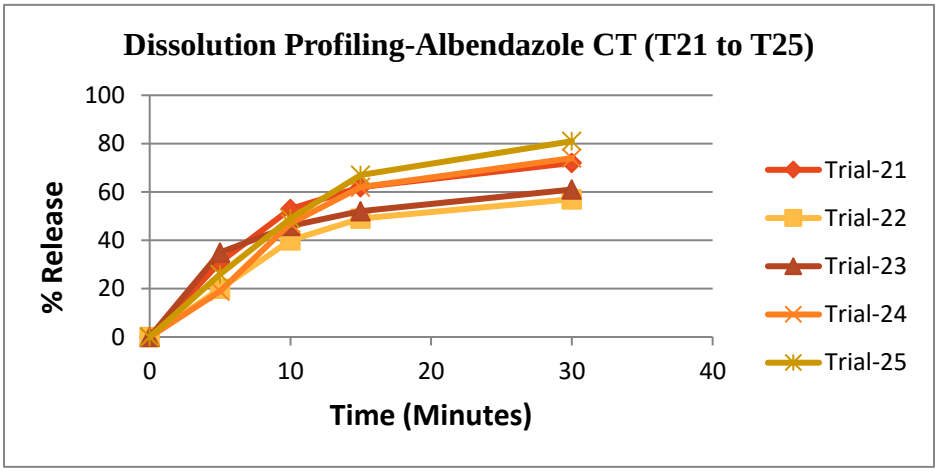


Figure 4.32: Dissolution curve of Albendazole CT (T21 to T25)

Raw Materials	T-26	T-27	T-28	T-29	T-30
KEY POINTS	Dry granl, Lactose based	50% CCS in soln along with SLS, PVP in dry mix, Total Mannitol in dry mix	50% ALB along with SLS (10 mg/tab), PVP, 25% CCS in slurry	50% ALB along with SLS (4 mg/tab), PVP, 25% CCS in slurry	IPA granl, SLS 0.5%
IG PART					
Albendazole	400	400	275	275	400
Lactose	200	-	-	-	-
Mannitol	-	200	200	206	200
Maize Starch	100	100	100	100	150
CCS	80	40	40	40	30
Aerosil-200	50	50	50	50	50
Povidone K-30	10	-	-	-	-
SLS	10	-	-	-	5
Sod Saccharin	5	-	-	-	5
Mg Stearate	7.5	-	-	-	-
BINDER SOLN					
Albendazole	-	-	125	125	-
SLS	-	10	10	4	-
Povidone K-30	-	10	10	10	20
Sod Saccharin	-	5	5	5	-
CCS		40	40	40	-
PW (at 45°C)	-	100%	100%	100%	-
IPA	-	-	-	-	100%
EG PART					
MCC 102	150	150	150	150	145
Orange Fla	10	10	10	10	10
Mg Stearate	2.5	10	10	10	10
TOTAL	1025	1025	1025	1025	1025
KEY OBSERVATION	Initial disso too high	Disso at 30 min is less though initially good	Disso at 30 min is less though initially good	Disso good in less qty. of SLS	Disso at each time point is very good, more than innovator
DT (minutes)	0:30-1:00	5:30-6:30	6:00-9:25	2:23-4:59	2:00-2:15
% Dissolution					
5 min	45	33	40	51	47
10 min	62	52	56	65	66
15 min	68	58	60	68	72
30 min	**77**	**66**	**67**	**76**	**81**

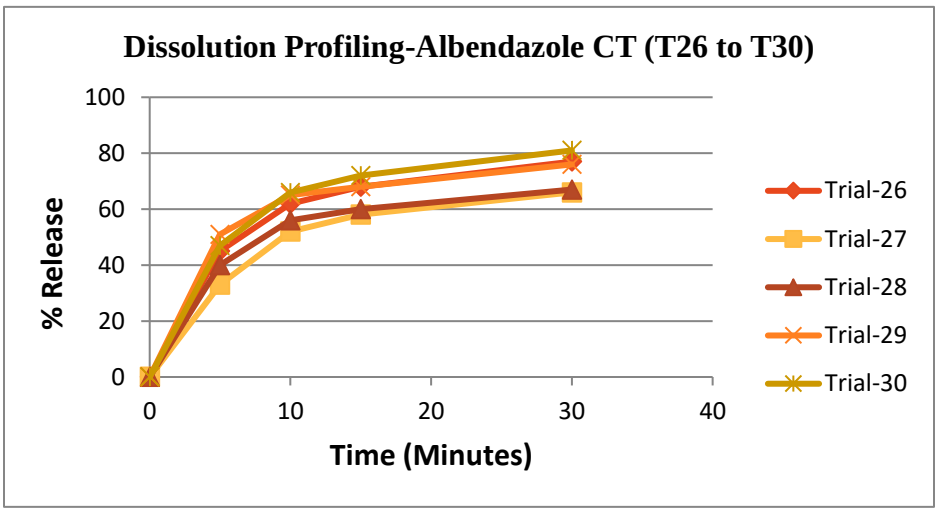


Figure 4.33: Dissolution curve of Albendazole CT (T26 to T30)

Raw Materials	T-31	T-32	T-33	T-34	T-35
KEY POINTS	IPA granl, ALB in slurry along with PVP, SLS 0.5%	Water granl by using spray nozzle	70:30 granl, spray nozzle used	70:30 grnl using spray nozzle	Using Syloid (5%) in place of aerosil
IG PART					
Albendazole	-	400	400	400	400
Lactose	-	-	200	250	250
Mannitol	200	180	-	-	-
Maize Starch	150	150	150	120	100
CCS	30	30	30	20	80
Aerosil-200	50	50	10	10	-
SLS	5	-	-	-	-
Sod Saccharin	5	-	-	-	-
Syloid 244 FP					50
BINDER SOLN					
Albendazole	400	-	-	-	-
Mannitol	-	20	-	-	-
SLS	-	10	10	-	10
Povidone K-30	20	20	20	20	10
Sod Saccharin	-	5	5	5	5
PW (at 45°C)	-	100%	70%	70%	100%
IPA	100%	-	30%	30%	-

EG PART		**L-1**	**L-2**		**L-1**	**L-2**	
MCC 102	145	140	-	180	150	150	100
MCC 105	-	-	140	-	-	-	-
CCS	-	-	-	-	20	-	-
SLS	-	-	-	-	10	10	-
Orange Fla	10	10	10	10	10	10	10
Mg Stearate	10	10	10	10	10	10	10
TOTAL	1025	1025	1025	1025	1025		1025
KEY OBSERVATION	At terminal point disso is less	Though the DT is good, but disso at terminal point falls	Though the DT is good, but disso at terminal point falls	Granulation by spray nozzle didn't help in respect to disso	Though DT less, but disso at terminal point is not satisfactory, Maybe due to extra-granular SLS. EG CCS didn't help.		Syloid didn't help, Aerosil is better
DT (minutes)	3:46-5:22	2:37-4:00	2:35-3:10	4:09 – 5:35	1:53 - 2:27	2:31 - 3:03	5:45 - 6:33
% Dissolution							
5 min	40	25	29	24	39	32	19
10 min	52	46	48	42	51	46	44
15 min	59	56	57	52	54	50	56
30 min	**69**	**65**	**68**	**64**	**65**	**66**	**67**

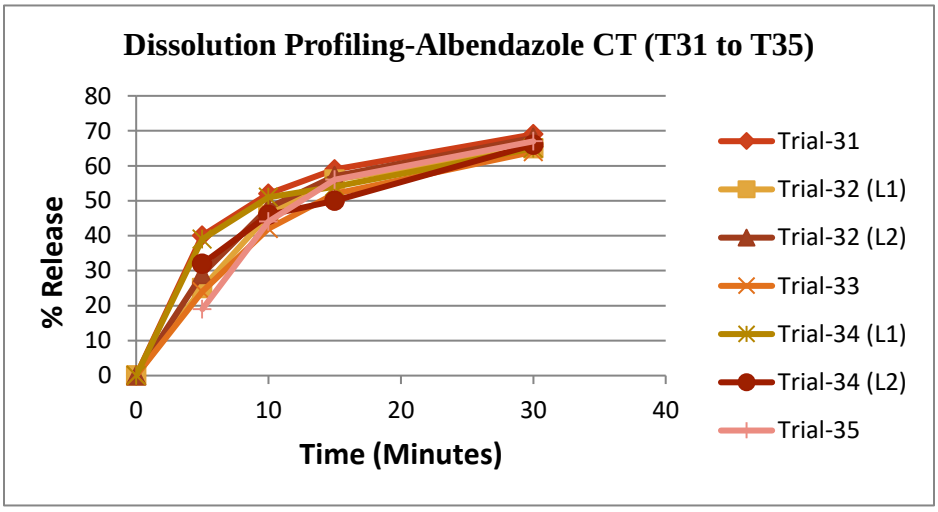


Figure 4.34: Dissolution curve of Albendazole CT (T31 to T35)

Raw Materials	**T-36**	**T-37**	**T-38**	**T-39**	**T-40**
KEY POINTS	Using Syloid (1%) in place of aerosil	Using Lasa Labs Albendazole (Stability formula)	Using Lasa Labs Albendazole (Unsatisfactory formula-Trial-5)	Replacing total Maize Starch by Mannitol	Following stability formula (PVP increased to 2%), optimizing granulation process-less granulation (+60---30%)
IG PART					
Albendazole	400	400	400	400	400
Lactose	250	250	230	250	240
Mannitol	-	-	-	100	-
Maize Starch	120	100	150	-	100
MCC 101	-	-	150	-	-
CCS	80	80	30	80	80
Aerosil-200	-	50	10	10	50
SLS	-	-	10	-	-
Sod Saccharin	-	-	5	-	-
Syloid 244 FP	10	-	-	-	-
BINDER SOLN					
SLS	10	10	-	10	10
Povidone K-30	10	10	20	10	20
Sod Saccharin	5	5	-	5	5
PW (at 45°C)	100%	100%	100%	100%	100%
EG PART					
MCC 102	120	100	-	140	100
Orange Fla	10	10	10	10	10
Mg Stearate	10	10	10	10	10
TOTAL	1025	1025	1025	1025	1025
KEY OBSERVATION	Syloid didn't help, Aerosil is better	Good	Not-comparable	There should be some Maize Starch in the formulation	Less granulation didn't help
DT (minutes)	5:14 - 5:48	3:08 - 4:16	5:41 - 6:23	5:37 - 6:07	4:46 - 5:29
% Dissolution					
5 min	16	35	32	16	24
10 min	32	51	44	35	44
15 min	42	59	54	51	54
30 min	**53**	**72**	**68**	**68**	**65**

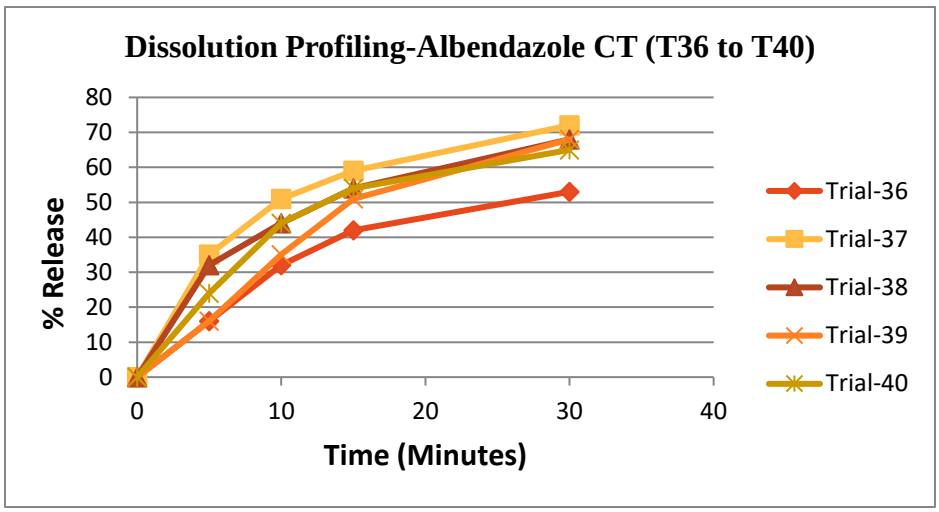


Figure 4.35: Dissolution curve of Albendazole CT (T36 to T40)

Raw Materials	**T-41**			**T-42**		**T-43**	**T-44**	**T-45**	
KEY POINTS	Repeatation of stability formula (optimum grnl-+60=75%)			Water grnl, Under granulation (+60=42%)		Water grnl, Using Granulac 230 in place of lactose	Water grnl, Using Pharmatose 350M in place of lactose	IPA grnl, Lactose in place of Mannitol	
IG PART									
Albendazole	400			400		400	400	400	
Lactose	250			250		-	-	200	
Granulac 230	-			-		250	-	-	
Phamatose 350M	-			-		-	250	-	
Maize Starch	100			100		100	100	150	
CCS	80			80		80	80	30	
Aerosil-200	50			50		50	50	50	
SLS	-			-		-	-	5	
Sod Saccharin	-			-		-	-	5	
BINDER SOLN									
SLS	10			10		10	10	-	
Povidone K-30	10			10		10	10	20	
Sod Saccharin	5			5		5	5	-	
PW (at 45°C)	100%			100%		100%	100%	-	
IPA	-			-		-	-	100%	
EG PART	**L-1 (DG 24 mesh)**	**L-2 (DG 40 mesh)**	**L-3 (DG 24 mesh, 0.5%**	**L-1**	**L-2 (0.5% Aerosil added)**			**L-1**	**L-2 (0.5% Aerosil added)**

			Aerosil added)						
MCC 102	100	100	100	100	100	100	100	145	145
Aerosil-200	-	-	5	-	5	-	-	-	5
Orange Fla	10	10	10	10	10	10	10	10	10
Mg Stearate	10	10	10	10	10	10	10	10	10
TOTAL	1025			1025		1025	1025	1025	
KEY OBSERVATION	Though the stability result is good, Trial-41 result is not that good. May be due to over granulation. DG passed through 40 mesh (L-2) is not helping			Result is ok. May be we have to do under granulation for better result. 0.5% extra-granular Aerosil is helping, so we will use it in future batches		Granulac is not that much helping, we will do one best batch with granulac if we want extra good result	Pharmatose is not helping	Very good result. Mannitol & Lactose give similar result	
DT (minutes)	3:15-3:29	3:25-5:08	3:24-4:12	4:03-6:09	3:21-4:35	3:21-4:03	3:22-4:48	1:39-2:59	1:45-4:45
% Dissolution									
5 min	28	25	30	27	38	36	29	50	
10 min	54	47	50	46	56	53	47	65	
15 min	64	56	57	58	66	60	57	73	
30 min	64	65	68	70	75	70	65	82	

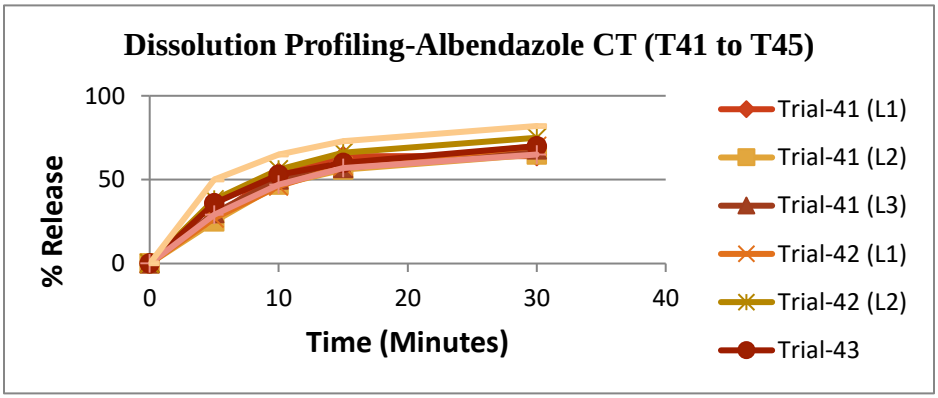


Figure 4.36: Dissolution curve of Albendazole CT (T41 to T45)

Raw Materials	**T-46**		**T-47**	**T-48**	**T-49**	**T-50**	**T-51**	**T-52**
KEY POINTS	70:30 grnl, Lactose in place of Mannitol		90:10 grnl	100% water granulation	90:10 grnl, sifting through 24 mesh	90:10 grnl with 1% Aerosil & 3% CCS	70:30 grnl, sifting through 24 mesh	70:30 grnl with 1% Aerosil & 3% CCS
IG PART								
Albendazole	400		400	400	400	400	400	400
Lactose	200		200	200	200	235	200	235
Maize Starch	150		150	150	150	150	150	150
CCS	30		30	30	30	30	30	30
Aerosil-200	50		50	50	50	10	50	10
SLS	5		5	5	5	5	5	5
Sod Saccharin	5		5	5	5	5	5	5
BINDER SOLN								
Povidone K-30	20		20	20	20	20	20	20
PW (at 45°C)	70%		90%	100%	90%	90%	70%	70%
IPA	30%		10%	-	10%	10%	30%	30%
EG PART	**L-1**	**L-2 (0.5% Aerosil added)**						
MCC 102	145	145	140	140	140	145	140	145
Aerosil-200	-	5	5	5	5	5	5	5
Orange Fla	10	10	10	10	10	10	10	10
Mg Stearate	10	10	10	10	10	10	10	10
TOTAL	1025		1025	1025	1025	1025	1025	1025
KEY OBSERVATION	Very good result.		Very good result	As compare to Water:IPA grnl, it is not that much good	Though initial disso is good but infinite disso is less	Aerosil should be 5% in IG because- 1. It helps to maintain DT less 2. Disso at every time point falls, especially 30 mins & Infinite	The result can be compared with T-46 where 60 mesh was used. The result is quite similar, so no impact of 60 mesh.	Decrease amount of aerosil is responsible for less disso (10%)
DT (minutes)	2:03-3:31	2:05-2:17	2:05-2:45	2:48-3:30	2:20-3:02	3:13-4:09	1:47-1:56	2:28-2:48
% Dissolution								
5 min	51	53	53	36	41	34	48	34
10 min	64	65	63	54	60	54	67	53
15 min	70	72	70	61	68	62	74	61

30 min	**88**	**89**	**85**	**70**	**81**	**68**	**95**	**72**

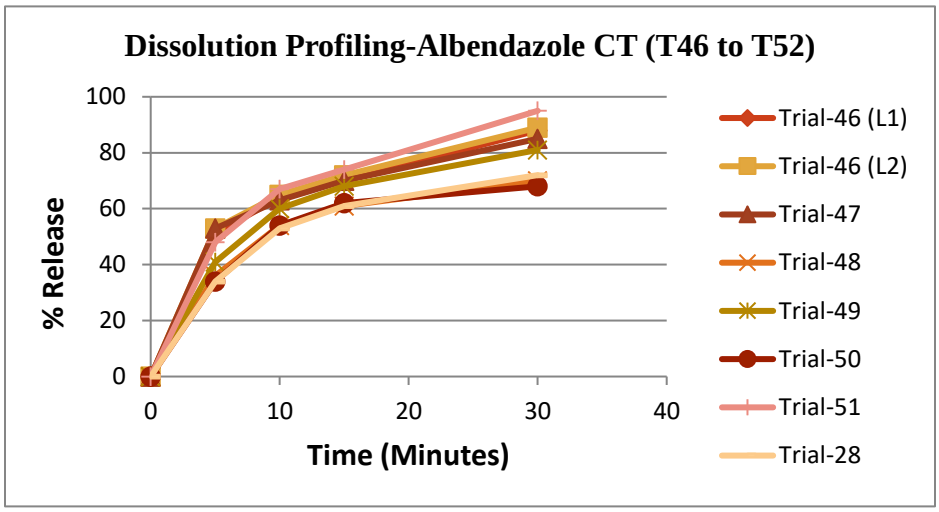


Figure 4.37: Dissolution curve of Albendazole CT (T46 to T52)

Levofloxacin Tablets

Ingredients	**Trial-1**	**Trial-2**	**Trial-3**	**Trial-4**	**Trial-5**
Intragranular Part	HPMC based	HPC based	Copovidone in place of Crospovidone	Combination of Crospovidone & Copovidone	Silica in intra & extra
Levofloxacin Hemihydrate	76.5	76.5	76.5	76.5	76.5
Microcrystalline Cellulose	6	6	6	6	5.8
Crospovidone	4	4	-	2	4
Colloidal Anhydrous Silica	-	-	-	-	0.6
Copovidone	-	-	4	2	2.5
Binder Solution					

HPMC 5 cps	2.5	-	2.5	2.5	-
HPC	-	2.5	-	-	-
Extragranular Part					
Microcrystalline Cellulose	4	4	4	4	**4**
Crospovidone	4	4	-	2	4
Copovidone	-	-	4	2	
Talc	1	1	1	1	1
Colloidal Anhydrous Silica	1	1	1	1	0.6
Magnesium Stearate	1	1	1	1	1
Total	**100**	**100**	**100**	**100**	**100**
Findings					
DT (min)	2:30 – 3:40	3:10 – 3:50	3:20 – 4:10	2:05 – 3:50	1:50 – 2:30
Dissolution (%)					
10 min	45	41	51	55	58
15 min	51	55	62	67	81
30 min	58	61	71	78	85
45 min	68	65	75	91	97

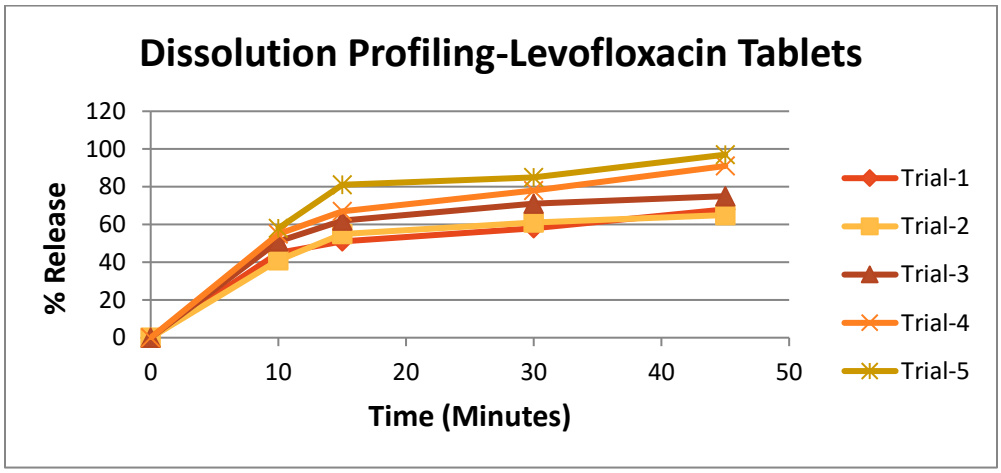


Figure 4.38: Dissolution curve of Levofloxacin Tablets

Pregabalin Capsules

Some trial batches were made by changing the percentage of Talc. The fill weight was adjusted with the quantity of Pregelatinized Starch. Given below are the composition of the trials and the results.

Composition of Pregabalin Capsules			
Ingredients	**Quantity in %**		
	Trial-1	**Trial-2**	**Trial-3**
Pregabalin	75	75	75
Pregelatinised Starch	20	17	15
Talc	5	8	10
Findings			
Bulk Density	0.57	0.55	0.51
Tapped Density	0.71	0.69	0.78
Angle of Repose	37.85	33.10	31.90
Hausner Ratio	1.25	1.25	1.15
Disintegration Time (min)	2:10	2:15	2:40
Dissolution (%)			
10 min	87	91	80
15 min	95	96	90
30 min	99	99	97
45 min	99	100	97

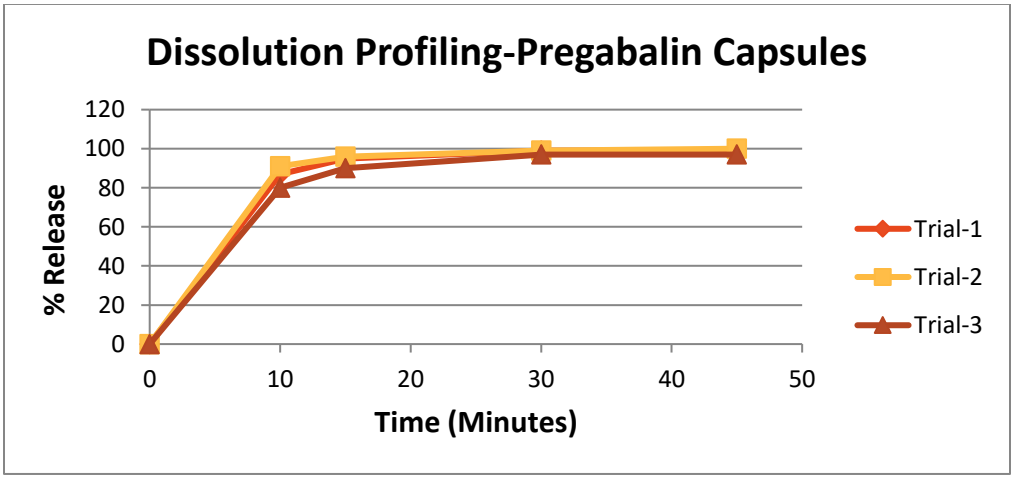


Figure 4.39: Dissolution curve of Pregablin Capsules

5.1 Discussion

This work was proposed to assess the compatibility of Actives viz. Albendazole, Levofloxacin and Pregabalin with different functional excipients like fillers/diluents, disintegrants, binders and lubricants which are commonly used in solid dosage formulation. Samples were made by mixing active and excipients in different ratio and put in stability chamber at different stability conditions. Samples were withdrawn at different time intervals and tested accordingly. Assay, Impurity and IR spectrum were chosen as testing parameter to determine the compatibility of actives with particular excipient. Results were given as tabulated manner and also graphical representation was shown under the section of 4.1 and 4.2.

IR spectrum was also illustrated for standards, 1 month stability samples of pure API and mixture of API with various excipients. For Albendazole, IR was done for Albendazole WS, 1 month stability samples of pure Albendazole, separate mixture of Albendazole with Microcrystalline Cellulose/Lactose/Maize Starch/Mannitol/Povidone/Crospovidone/Sodium Starch Glycolate/Croscarmellose Sodium/Magnesium Stearate/Sodium Lauryl Sulfate/Colloidal Anhydrous Silica/Purified Talc/Saccharin Sodium/Orange Powder Flavor/Vanilla Powder Flavor/Passionfruit Powder Flavor. For Levofloxacin, IR was done for Levofloxacin WS, 1 month stability samples of pure Levofloxacin, separate mixture of Levofloxacin with Microcrystalline Cellulose/Lactose/Maize Starch/Hypromellose/Hydroxypropyl Cellulose/Povidone/Crospovidone/Sodium Starch Glycolate/Croscarmellose Sodium/Magnesium Stearate/Sodium Lauryl Sulfate/Colloidal Anhydrous Silica/Purified Talc. For Pregabalin, IR was done for Pregabalin WS, 1 month stability samples of pure Pregabalin, separate mixture of Pregabalin with Pregelatinized Starch/Maize Starch/Purified Talc/Colloidal Anhydrous Silica. Absorbance for particular samples were given in section 4.3.

This research work has demonstrated the relationship between active and excipients and their compatibility in dosage form formulation. Tentative formula of the dosage forms viz. Albendazole Chewable Tablets, Levofloxacin Film Coated Tablets and Pregabalin Capsules were also established and evaluated.

From the data and representation, the following demonstration can be illustrated.

Albendazole

- IR results showed that there is an interaction occurred when Albendazole was mixed with Sodium Lauryl Sulfate, Colloidal Anhydrous Silica and Purified Talc.
- Assay results showed Albendazole is compatible with mostly excipients studied such as Microcrystalline Cellulose, Lactose, Maize Starch, Mannitol, Crospovidone, Sodium Starch Glycolate, Croscarmellose Sodium, Sodium Lauryl Sulfate, Purified Talc, Saccharin Sodium, Colloidal Anhydrous Silica, Orange Powder Flavor, Mango Powder Flavor and Passionfruit Powder Flavor. Study showed that Albendazole may be less compatible with Magnesium Stearate and Povidone (K 30) at a ratio of 1:0.5. But at a ratio of 1:0.02 (actual usage), it is compatible.
- Total impurity which was generated during the coarse of time was found within the specified limit.

Levofloxacin

- IR results showed that Levofloxacin is compatible with all the excipients studied except some physical interaction observed when it mixed with Hypromellose 5 cps.
- Study showed that Levofloxacin is compatible with all the excipients under this study such as Microcrystalline Cellulose, Lactose, Maize Starch, Hypromellose, Hydroxypropyl Cellulose, Sodium Starch Glycolate, Croscarmellose Sodium, Sodium Lauryl Sulfate, Colloidal Anhydrous Silica, Purified Talc and Magnesium Stearate. Levofloxacin may be less compatible with Povidne and Crospovidone at a ratio of 1:0.5. But at a ratio of 1:0.1 (actual usage), it is compatible.
- Total impurity which was generated during the coarse of time was found within the specified limit.

Pregabalin

- Pregabalin is compatible with Pregelatinized Starch, Maize Starch and Purified Talc. But it may not be compatible with Colloidal Anhydrous Silica.
- Impurity was generated when Pregabalin was mixed with Colloidal Anhydrous Silica.

Based on all the experiments the following formulation of the selected dosage forms was established which showed better result in physical and analytical evaluation.

Formulation of Albendazole Chewable Tablets 400 mg

Ingredients	**Quantity in mg**
Intragranular Part	
Albendazole	400
Lactose	200
Maize Starch	150
Croscarmellose Sodium	30
Colloidal Anhydrous Slica	50
Sodium Lauryl Sulfate	5
Saccharin Sodium	5
Binder Solution	
Povidone (K 30)	20
IPA	100%
Extragranular Part	
Microcrystalline Cellulose 102	145
Orange Powder Flavor	10
Magnesium Stearate	10
Total	**1025**

Formulation of Levofloxacin Tablets

Ingredients	**Quantity in %**
Intragranular Part	
Levofloxacin Hemihydrate	76.5
Microcrystalline Cellulose	5.8
Crospovidone	4
Colloidal Anhydrous Silica	0.6
Copovidone	2.5
Binder Solution	
Purified Water	100%

Extragranular Part	
Microcrystalline Cellulose	4
Crospovidone	4
Talc	1
Colloidal Anhydrous Silica	0.6
Magnesium Stearate	1
Total	**100**

Formulation of Pregabalin Capsules

Ingredients	**Quantity in %**
Pregabalin	75
Pregelatinised Starch	17
Talc	8
Total	**100**

5.2 Conclusion

Compatibility study is the first consideration of any bioequivalent formulation development. It is a complete characterization and understanding of physicochemical interactions of an active pharmaceutical ingredient (API) in the dosage forms. It is an integral part of preformulation stage of new dosage form development as it is most desirable for consistent efficacy, safety and stability of a drug product.

Careful selection of the excipients is required for a robust and effective formulation of dosage forms that make administration easier, improve patient compliance, promote release and bioavailability of the drug and increase its shelf life.

In this research work three actives from different section was chosen to see the impact when it mixed with the excipients intended to incorporate in their subsequent formulation. This research work was proposed to assess the compatibility of Albendazole, Levofloxacin and Pregabalin with different functional excipients like fillers/diluents, disintegrants, binders and lubricants

which are commonly used in solid dosage formulation. Samples were made by mixing active and excipients in different ratio and put in stability chamber at different stability conditions. Samples were withdrawn at different time intervals and tested accordingly. Assay, Impurity and IR spectrum were chosen as testing parameter to determine the compatibility of actives with particular excipient.

This research work has demonstrated the relationship between active and excipients and their compatibility in dosage form formulation. Tentative formula of the dosage forms viz. Albendazole Chewable Tablets, Levofloxacin Film Coated Tablets and Pregabalin Capsules were also established and evaluated.

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