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Formulation and Characterization of Orlistat Fast Dissolving Tablets

N. Krishna Veni*

Department of Pharmaceutics, Sri Venkateswara College of Pharmacy, Andhra Pradesh, India

***Corresponding author:** N. Krishna Veni, Department of Pharmaceutics, Sri Venkateswara College of Pharmacy, Andhra Pradesh, India; E-mail: krishnaveniuka 49@gmail.com*

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ABSTRACT

The present study was aimed at the formulation of immediate release Orlistat. The therapy with these drugs offers a good quality of life for patients who are suffering from obesity. The key advantage of this drug is its specificity of action, high safety and excellent efficacy.

***Aim of the study:** The oral drug delivery has been famous for many years because the most generally utilized route of administration among all the routes that are explored for the general delivery of drugs via varied pharmaceutical product of various indefinite quantity forms. The reasons that the oral route achieved such quality could also be partially attributed to its simple administration likewise because the ancient belief that by oral administration the drug is as well absorbed as the foodstuffs that are ingested daily. Pharmaceutical product designed for oral delivery and presently on the market on the prescription and over the counter markets are principally the immediate-release kind, which are designed for immediate release of drug for rapid absorption. These systems guarantee complete solubilisation of the pill through surface erosion resulting in elimination of lag time for disintegration thereby offering faster absorption and rapid onset of action.*

Despite increasing interest in controlled–release drug delivery systems, the most common tablets are those intended to be swallowed whole and to disintegrate and release their medicaments rapidly in the gastro intestinal tract. In more recent years, increasing attention has been paid to formulate immediate release dosage forms.

***Objective of study:** The main objective of this work is to design and development of Orlistat fast dissolving tablets by direct compression technique.*

It is the best method to decrease the wetting and disintegration time and to increase the patient compliance.

Immediate breaking of the tablet takes place when it is placed into the mouth. Thus immediate release formulation shows the good results.

Keywords: Orlistat, Fast disintegration tablets, Direct compression technique, Self-administration

INTRODUCTION

Another way to define a drug is as an associate degree agent intended to be utilized in the diagnosis, treatment, mitigation, cure, or interference of disease in humans or animals. The way that medications work and affect the body is one of their most remarkable features. Because of this characteristic, they can be used selectively to treat a variety of common and uncommon illnesses that affect almost every organ, tissue and cell in the body.

Seldom are drugs given in their unadulterated original form. When they are transformed into a suitable formulation, they are given in a variety of dosage forms. Each dosage form combines the medication with various non-pharmacological substances known as "additives." To administer precise dosages in a safe and convenient manner, a medicine is transformed into several dosage forms [1].

To create the required form during production, the medication is combined with additional chemicals. The following categories are used to group drug dose forms based on their chemical makeup and physical state:

- Solid dosage form
- Liquid dosage form
- Semi solid dosage form

Solid dosage forms

The majority of solid dosage forms come in unit dosage forms, which are made up of doses that are taken in numerical order. Examples of these include tablets, capsules, pills, cachets and powders. Solid dose forms of medications are readily accessible; in fact, the majority of drugs are offered in both liquid and solid form. When determining if a solid dosage form is the best option for a patient, several aspects need to be considered. There are various ways to administer solid drugs, including topically, vaginally, rectally and orally. Compared to other types of medication, solid drugs have a number of benefits and drawbacks. Synthetic effects are most commonly administered orally because of its simplicity of consumption, pain, avoidance, variety and-above all-patient compliance. Additionally, solid oral administration devices are less expensive to manufacture because they do not require sterile conditions or an area unit. Tablets are the preferred solid dose form because to its high precision dosing, patient compliance and production efficiency [2].

Advantages:

- It is easier for patients to self-administer solid drugs.
- Generally speaking, solid drugs last longer before going bad.
- It is simpler to manufacture, distribute, ship and keep solid pharmaceuticals.
- The dosing is more accurate with solid dosage forms, since the medication is already in a distinctive unit/measure.
- Solid dosage forms have been created to release the medication over a longer period of time in the patient's body extended release medications. This allows the patient to take fewer doses, while still getting the same desired effects.

Disadvantages:

- Large tablets or capsules may be difficult for certain people to swallow.
- Patients using nasal/mouth breathing tubes for ventilation or those who are unconscious should not take solid drugs.
- It takes longer for the body to absorb, process and distribute solid drugs. Before the drug takes effect, it must be metabolized in the stomach.
- Solid drugs do not work quickly enough for treatments that take effect right away. Liquids or injectable drugs are better options when treatments need to be administered right away.
- Tablets are the most practical dose form when medications are to be taken orally in a dry state. They work well and patients have no trouble administering, handling or identifying them.

Tablets

A solid unit dosage form of medication that contains one or more active components and appropriate pharmaceutical excipients is called a tablet. Tablets are solid drugs that have been shaped into tiny shapes. The majority of the time, tablets are administered orally. Tablets are made up of various parts. Together, these elements guarantee that the tablet is easily swallowed, provides flavorings or sweeteners for taste and regulates the drug's scheduled release to produce the intended effect. The term "inactive" or "inert" refers to all of the components other than the active medication.

Types and classes of tablets

Oral tablets for ingestion

- Compressed tablets
- Multiple compressed tablets
- Repeat-action tablets
- Delayed-release tablets
- Sugar coated tablets
- Film coated tablets
- Chewable tablets
- Rapidly dissolving tablets

Tablets used in the oral activity:

- Buccal tablets
- Sublingual tablets
- Troches and lozenges
- Dental cones

Tablets administered by other routes:

- Implantation tablets
- Vaginal tablets

Tablets used to prepare solution:

- Dispensing tablets
- Hypodermic tablets
- Effervescent tablets
- Tablet triturate

Compressed tablets: The outside of compressed tablets is coated with enteric, film, or sugar. Sugar coating or fill coating can be used to cover up unpleasant-smelling or noxious-tasking medications, give the tablet some color, or shield the medication from the humidity of the air.
Film coating: In order to make the tablet more robust and simpler to swallow, film coating also gives it a hard shell. Powdered, crystalline, or granular materials are compressed using a die punch to create compressed tablets.
Enteric–coated: The coating on oral tablets shields the tablet from stomach acid and prevents the medication from irritating the gastrointestinal tract's lining. Another method for creating sustained-release tablets is enteric coating.
Chewable tablets: Chewable pills are tablets that can be chewed rather than swallowed; chewing rather than swallowing is necessary for the desired effects of chewable tablets. The majority of pediatric drugs are chewable tablets since little children have trouble swallowing tablets. In order to cover up the unpleasant taste and make the prescription simpler to take, chewable pills are also known to contain flavorings and sweeteners. Adult drugs like aspirin and antacids can also be chewed [3].

Advantages:

- Tablets are widely used and have a sophisticated look.
- They are commonly administered in a solid unit dose form that makes administration simple.
- Compared to liquid dose forms, they exhibit greater chemical and physical stability.
- They offer precise, reliable dosage information.
- Of all the solid oral dosage forms, they are the least expensive.
- There are two types of medication release from tablets: Prolonged release and rapid release.
- Tablets make portability simple.
- Tablets are simple to dispense and take up less storage space.
- Tablets will be packaged in lightweight, cost-effective containers.
- Simple product identification is made possible by an adorned or branded punch used for pill compression.

Disadvantages:

- The beginning of action of tablets is slower than that of parent dosage forms.
- Medication that tastes harsh, has an unpleasant smell, or is sensitive to environmental factors should not be used in pill form.
- It can be difficult to compress amorphous, absorbent and Tenuity medications into tablets.
- Drugs with weak physical characteristics or water solubility cause problems while being tableted.
- Patients who are comatose or unconscious cannot receive tablets.
- Children and patients who are really ill find it difficult to handle tablets.
- Once the medication has passed metabolism, the new drug delivery method is preferred over tablets.

Ideal properties of tablets:

- The pills were designed to be consistent in size, weight and appearance.
- It should be strong enough and resistant to shocks, fractures and erosion that may occur during production, transit and use.
- Throughout its duration, the pill aimed to maintain its chemical and physical stability.
- The pill was designed to be inexpensive in size and shape so that the patient could administer it easily.
- The active medication or medications should be evenly dispersed throughout the tablet. The medication aimed to be incompatible-free.
- A controlled and repeatable rate of drug unharnessing from pills was the goal.
- It must be free of any capping or lamination-causing flaws.
- The pill was intended to be free of any pollutants, excipients, or dangerous microbes.
- The pill aimed to change affordable and straightforward production [4].

Oral drug delivery

Because of its many benefits, such as simplicity of consumption, pain avoidance, versatility and-above all-patient compliance, the oral route of administration remains the most popular among the numerous routes of administration. Tablets and capsules are among the several dosage forms. Due to their ease of production, compact size and self-administration convenience, tablets are the most commonly used dose form.
Because of its systemic effects, oral medication delivery is the most favored and preferable way to provide therapeutic medicines. Additionally, due of patient acceptance, ease of administration and value-effective production methods, oral medication is typically regarded as the first avenue studied in the research and development of new pharmacological entities and pharmaceutical formulations. Typical immediate unharness formulations for numerous pharmacological substances provide clinically effective medical care while preserving the appropriate level of patient safety and the ideal balance of pharmacokinetic and pharmacodynamics characteristics. There are three types of Oral Drug Delivery Systems (ODDS): There are three types of preparations: Targeted release, controlled release and Immediate Release (IR) (Figure 1) [5].

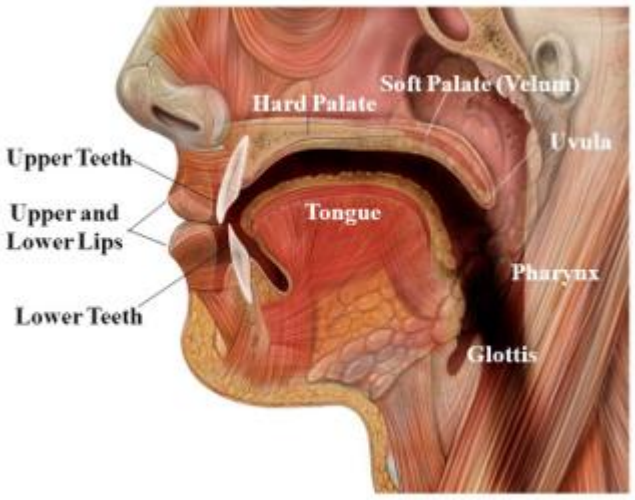

Figure 1: The anatomy of oral cavity.

Sublingual glands

Prior to the sub-mandibular glands, these glands are located beneath the mouth's foundation membrane. They open into the ground of the mouth by a variety of small channels [6].

Structure of salivary glands

There is a fibrous capsule that encloses each gland. They are composed of several lobules bordered by structural cells and composed of tiny acini. Larger ducts that lead into the mouth are formed when the secretions are pumped into ductless (Figure 2).

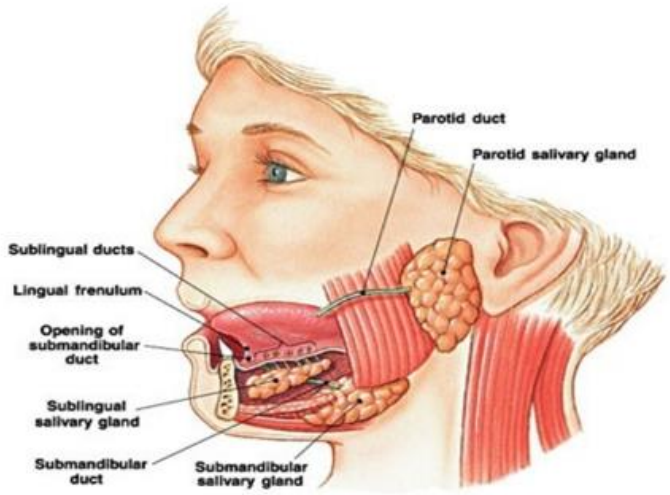

Figure 2: Parts of oral cavity.

Composition of saliva

The joint secretion of the salivary glands and the tiny mucus-secreting glands of the oral cavity lining is called saliva. Saliva production is approximately 1.5 liters per day and is composed of

- Water
- Mineral salt
- The salivary amylase enzyme
- Lysozyme
- Immunoglobulins
- Blood-clotting components

Function of saliva

Chemical digestion of polysaccharides: The amylase enzyme found in saliva starts the process of breaking down complicated carbohydrates into the disaccharide maltose. Salivary amylase functions best at a pH of 6.8, which is somewhat acidic. Protein action continues while swallowing until it is stopped by the strongly acidic pH (1.5 to 1.8) of the stomachic acids, which breaks down the enzyme. The pH of saliva varies from 5.8 to 7.4 based on the rate of flow; the faster the rate of flow, the higher the pH [7].

Introduction to fast dissolving tablets

Because it is described as "rapid dissolving tablets are meant to disintegrate and unleash their medications without unique rate dominant options like special coatings and totally different processes," the fast dissolving drug delivery system is also a typical form of drug delivery system.

Advantages and significance

- Immediately release the medication.
- Greater adaptability in changing the dosage
- It frequently has the bare minimum of medication.
- No dosage merchandising drawbacks exist.
- The immediate unleash medicine delivery mechanism is used at the beginning and end of the illness.
- The drug is not present in the system at the site of action.

Challenges to develop FDDDS

- It should quickly dissolve or disintegrate in the stomach.
- Be transportable without worrying about fragility.
- Having a comfortable mouthfeel
- After oral administration, there should be little to no residue left in the mouth.
- It should be less sensitive to external factors like temperature and humidity.
- Be produced at a minimal cost utilizing standard processing and packaging equipment.
- Quick medication absorption and dissolution, which could result in a quick start of action.

Formulation aspects in developing IRDDS

- The traditional methods for making fast-dissolving tablets are listed below.
- The method of tablet molding
- The method of direct compression
- The wet granulation method
- Dry granulation
- The mass extrusion method

Tablet molding

Water-soluble chemicals are utilized in this technology to make tablets dissolve and disintegrate quickly. A hydroalcoholic solvent is utilized to hydrate the powder blend, which is then molded into tablets with a compression pressure that is lower than that of traditional tablets.
After that, the solvent is eliminated by air drying. The porous nature of molded tablets promotes dissolving. Poor style masking features and unit mechanical strength are two problems that are frequently encountered. Using binding agents like polyvinylpyrrolidone, acacia, or sucrose can improve the tablet us mechanical strength. Van Scoik used a drug with distinct particles to get around the bad style masking feature. These particles were created by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium bicarbonate, lecithin, polythene glycol and the active ingredient into a pill triturate type that was primarily based on milk sugar [8].

Direct compression method

Without any prior processing, tablets are crushed using this approach straight from the medication and excipient mixture. Pretreatment and wet granulation are necessary because the mixture to be crushed needs to have sufficient flow characteristics and cohesiveness under pressure. Unnecessary. A small number of drugs are frequently compressed straight into respectable-quality tablets. The kind of disintegrant and how much of it is used are crucial. Other considerations include pill hardness, water absorption capacity, contact angle, pore size distribution and area unit particle size distribution. The disintegration is determined by each of these parameters. At the industrial level, the disintegration addition technology is simple to use and reasonably priced.

Wet granulation method

One technique for using a liquid binder to gradually agglomerate the powder mixture is wet granulation. The fluid content must be carefully regulated since too much moisture will make the granules too hard and too little moisture would make them too soft and friable. Although aqueous solutions are safer to handle than solvent-based systems, they might not be suitable for medications that undergo chemical degradation.

Procedure
Step 1: Weigh and combine the excipients and active substance.
Step 2: The liquid binder-adhesive is added to the powder mixture and well mixed to create the wet granulate. Aqueous cornstarch preparations, natural gums like acacia and cellulose derivatives like methyl cellulose, gelatin and povidone are a few examples of binders and adhesives.
Step 3: The moist mass is screened through a net to create granules or pellets.
Step 4: Drying the granulation: The most popular methods are a fluid-bed dryer or a traditional tray-dryer.
Step 5: To produce granules of consistent size, the dried granules are run through a screen that is smaller than the one used for the wet mass.

Low shear wet granulation methods might take a long time to reach a uniformly mixed state and require very basic mixing equipment. The manufacturing process is accelerated by the high shear wet granulation technique, which uses machinery that rapidly mixes the powder and liquid. In order to pre-heat, granulate and dry the powders, fluid bed granulation is a multi-step wet granulation procedure carried out in the same vessel. Because it enables precise control over the granulation process, it is utilized [9-11].

Dry granulation

Slugging may be utilized to create granules when the tablet ingredients have adequate intrinsic binding or cohesive qualities and are either moisture-sensitive or cannot withstand high temperatures during the dying process. This method is called pre-compression dry granulation. Because small powders are more likely to flow into large cavities, slugging is employed to turn large tablets into slugs.
After the granulation is gently combined with lubricants, the compressed slugs are ground through the appropriate mesh screen by hand or in large quantities using Fitzpatrick or other comminuting mills to form tablets. The alternative is to use a machine like a chilsonator to pre-compress the powder using pressure rolls [12].

Steps in dry granulation
- Drug and excipient milling
- Blending ground powders
- Slugs are created by compressing them into big, hard tablets.
- Checking for slugs
- Blending with disintegrant and lubricant.
- Compression of tablets.

Two main dry granulation processes

Slugging procedure: Slugging is the process of compressing dry tablet formulation powder using a tablet press that has a die cavity big enough to fill rapidly. The slug's condition or accuracy is not very significant. Use only enough pressure to crush the powder into uniform slugs. After slugs are created, they are screened and milled to the proper granule size for subsequent compression.
Roller compaction: A device known as a Chilsonator can also be used to compaction powder using a pressure roll. The chilsonator produces a compressed material in a continuous, steady flow, in contrast to a tablet machine. The hopper, which has a spiral auger to deliver the powder into the compaction zone, feeds the powder down between the rollers. The agreegates are filtered or ground into granules for manufacture, just like slugs.

Mass-extrusion

With this process, the active mix is softened using a solvent mixture of fuel and soluble polythene glycol. The softened mass is then expelled through a syringe or extruder to cause the product to split into even segments using a hot blade to create tablets. To provide pleasant masking, the dried cylinder can also be employed to coat bitter medicine pellets.

Introduction to tablet disintegration and binders

Disintegrants, an essential component of the pill formulation, are continuously added to the pill to cause the pill to break up once it comes into contact with a binary compound fluid. This process of integrating the constituent particles prior to the drug dissolving is known as the disintegration method and excipients that use it are referred to as disintegrants [13].

Mechanism of tablet disintegrant

The tablet breaks to primary particles by one or more of the mechanisms listed below.

By use of capillary action

The pill splits into fine particles when it is placed in the proper binary compound medium because the medium penetrates the pill and replaces the air adsorbate on the particles, weakening the building block binding.

Through edema

Due to insufficient swelling force, very porous tablets disintegrate poorly. On the other hand, the pill with limited porosity exerts spare swelling force. It is important to remember that a very high packing percentage makes it difficult for fluid to enter the tablet and slows down breakdown.

As a result of soaking heat (air expansion)

Tablet disintegration is aided by the localized stress created by capillary air expansion when exothermic disintegrants are wetted.

As a result of particle disintegration and repair forces

Water is necessary for the disintegration process, which is caused by the electric repulsive interactions between particles [14].

Super disintegrants

Pharmacists must create disintegrants or super disintegrants, that are more effective intragranulary, have a higher disintegration efficiency and work well at low concentrations. Additionally, these super disintegrants work by swelling and when swelling pressure is applied in a radial or outward direction, it can cause tablets to burst or speed up the absorption of water, which increases the volume of granules significantly and aids in disintegration [15].

LITERATURE REVIEW

The literature was carefully examined and comprehended from a variety of textbooks, pharmacopoeias, journals and the Internet. The following abstracts of the earlier reports would provide an overview of the investigation that has been conducted and the references that were determined to be pertinent to the current investigation have been properly cited (Table 1) (Figure 3).

Table 1: Literature review of collected data.

S.NO	Drug	Polymer	Method	Purpose
1	Telmisartan	sodium starch glycolate, β - cyclodextrin, microcrystalline cellulose, magnesium stearate	Direct compression techinque	immediate release tablets
2	Sildenafil	croscarmellose sodium, Avicel pH 101, pregelatinized starch,microcrystalline cellulose, magnesium st	Direct compression techinque	immediate release tablets
3	Metoclopramide HCl	Ac-Di-Sol, Polyplasdone XL and Explotab, agar (AG),gellan gum (GG)	direct compression method	immediate release tablets
4	Antibiotics	croscarmellose sodium, microcrystalline cellulose, magnesium stearate	direct compression method	immediate release tablets
5	orlistat	sodium starch glycolate, croscarmellose sodium, microcrystalline cellulose, magnesium stearate, talc	direct compression method	orodispersable tablets
6	orlistat	β - cyclodextrin, span 60	reverse phase evaporation technique	niosomes from proniosomes
7	orlistat	Eudragit RL 100, cellulose acetate and ethyl cellulose	solvent diffusion evaporation technique	floating microspheres
8	orlistat	crospovidone (CP), Croscaramellose sodium (CCS), Sodium starch glycolate (SSG), PEG 6000	direct compression technique melt granulation method	orodispersable tablets

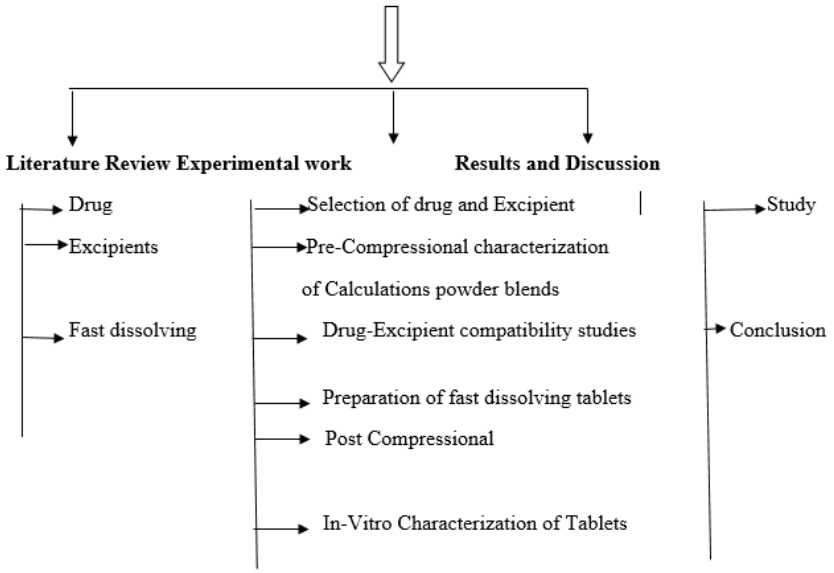

Figure 3: Plan of work.

Drug profile

Orlistat

Function: To treat obesity
Class: 2
Chemical formula: C_{29} H_{53} NO_5
Synonym: Tetrahydrolipstatin
Mol Wt: 495.735g/mol
Route of administration: Oral (Capsules, Tablets)
Half-life: 1-2hrs
Bioavailability: Negligible
Protein binding: less than 99%
Metabolism: In the GIT
Absorption: systemic absorption is minimum
Excretion: Fecal (Figure 4)

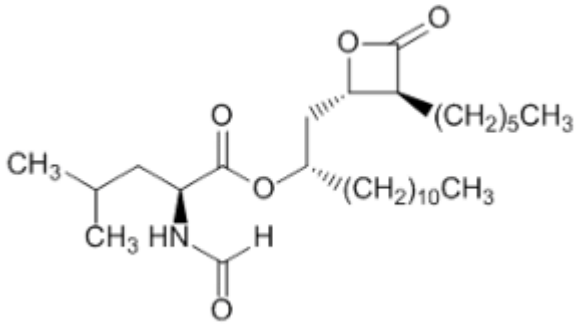

Figure 4: Structural representation of oralistat.

Medical uses

Orlistat is used for the treatment of obesity. The amount of weight loss achieved with orlistat varies. In one-year clinical trials, between 35.5% and 54.8% of subjects achieved a 5% or greater decrease in body mass, although not all of this mass was necessarily fat. Between 16.4% and 24.8% achieved at least a 10% decrease in body fat. After orlistat was stopped, a significant number of subjects regained weight-up to 35% of the weight they had lost. It reduces the incidence of diabetes type II in people who are obese around the same amount that lifestyle changes do. Long-term use of orlistat also leads to a very modest reduction in blood pressure (mean reductions of 2.5 and 1.9 mmHg in systolic and diastolic blood pressure respectively) [16].

Contraindications

Orlistat is contraindicated in:

- Malabsorption.
- Hypersensitivity to orlistat.
- Reduced gallbladder function (e.g. after cholecystectomy)
- Pregnancy and breast feeding.
- Anorexia and Bulimia.
- Use caution with: obstructed bile duct, impaired liver function, pancreatic disease.

Mechanism of action

Orlistat works by inhibiting gastric and pancreatic lipases, the enzymes that break down triglycerides in the intestine. When lipase activity is blocked, triglycerides from the diet are not hydrolyzed into absorbable free fatty acids and instead are excreted unchanged. Only trace amounts of orlistat are absorbed systemically; the primary effect is local lipase inhibition within the GI tract after an oral dose. The primary route of elimination is through the feces.
At the standard prescription dose of 120 mg three times daily before meals, orlistat prevents approximately 30% of dietary fat from being absorbed. Higher doses do not produce more potent effects [17].

Adverse effects

Common side effects of Orlistat include:

- Oily spotting on underwear

Other side effects of Orlistat include:

- Gas (flatulence) with discharge, Fatty/oily stools, Increased defecation, Fecal incontinence/inability to control bowel movements, Clay- colored stools, Diarrhea, Rectal Pain, Reduced absorption of fat soluble vitamins and beta-carotene, Dark urine, Oxalate nephropathy, Leukocytocrastic vasculitis, Stomach pain, Headache, Skin rash.

Interactions

All drugs interact differently for person to person. You should check all the possible interactions with your doctor before starting any medicine.

- Interaction with Alcohol:
- Description- Interaction with alcohol is unknown. It is advisable to consult your doctor before consumption.
- Instructions- Interaction with alcohol is unknown. It is advisable to consult your doctor before consumption.

Interactions with medicine

- Warfarin
- Antidiabetic medicines
- Cyclosporine

Disease interactions

Malabsorption: Orlistat may worsen the condition in patients with malabsorption due to the decrease in the absorption of vitamins, minerals and fats. Therefore, not recommends to the patients with digestive system disorder and cholestasis.
Diabetes: Orlistat should be used with caution in patients with diabetes due to increase in the risk of low blood glucose levels. The dose of antidiabetic medicines should be reduced based on the clinical condition.
Food interactions: Take with meals, or upto 1hr after a meal of patient misses a meal, or has a fat- free meal, he/she may skip the corresponding dose.
Toxicity: The results of a massive overdose of Xenical are unknown, although the drug seems relatively harmless [18].

Excipient profile

Croscarmellose sodium:

- Nonproprietary Name: USP-NF : Croscarmellose sodium.
- Synonyms: Ac-Di-Sol, cross-linked carboxymethyl cellulose sodium,
- Chemical Name: Cellulose, carboxymethyl ether, sodium salt, crosslinked.
- CAS RegestryNumber :74811-65-7.
- Molecular Weight: 90000-700000.
- Functional Category: Tablet and capsule disintegrant.
- Description: Croscarmellose sodium occurs as an odorless, white or grayish white powder.
- Structural formula: pH: 5.0-7.0 in aqueous dispersion.
- Specific Surface Area: 0.81 m^2 /g-0.83 m^2 /g.

Sodium starch glycolate:

- Nonproprietary Name: BP: Sodium starch glycolate.
- PhEur: Carboxymethylamylumnatricum.
- USPNF: Sodium starch glycolate.
- Synonyms: Carboxymethyl starch, Sodium salt, Explotab, Primojel.
- Chemical Name: Sodium carboxymethyl starch.
- CAS RegestryNumber: 9063-38^{-1}.
- Molecular Weight: $5 \times 105^{-1} \times 10^{6}$
- Functional Category: Tablet and capsule disintegrant.
- Description: Sodium starch glycolate is a free-flowing, white to off-white powder with no taste or odor. It is made up of spherical or oval granules that range in diameter from 30 to 100 µm.
- Structural Formula: pH: 3.0-5.0.
- Melting Point: Does not melt, but chars at approximately 200°C.
- Specific Surface Area: 0.24 m^2 /g.

Mannitol:

- Nonproprietary Name: BP: Mannitol.
- PhEur: Mannitolum.
- USP: Mannitol.
- Synonyms: Cordycepic acid, manna sugar, pearlitol.
- Chemical Name: D-Mannitol.
- CAS Registry Number: 69-65-8.
- Empirical Formula: C6H14O6.
- Molecular Weight :182.17.
- Functional Category: Diluent, diluent for lyophilized preparations, sweetening agent, tablet and capsule diluent.
- Description: Mannitol can be found as free-flowing granules or as a white, odorless crystalline powder. It gives the mouth a cooling feeling and tastes sweet, about half as sweet as sucrose and as sweet as glucose.
- Melting Point: 166-168^{0}C.
- Specific Surface Area: 0.37-0.39 m^2 /g [19].

Talc

- Nonproprietary Name:
- BP: Purified talc.
- PhEur: Talcum.
- USP: Talc.
- Synonyms: Altalc, magnesium calcium silicate, powdered talc, magsil star.
- Chemical Name: Talc.
- CAS Registry Number: 14807-96-6.
- Empirical Formula: Mg6(SiO_5)4 (OH)4.
- Functional Category: Glidant, tablet and capsule lubricant, diluent and anti-caking agent. Talc is a crystalline powder that is impalpable, odorless, white to grayish white and extremely fine. It is pleasant to the touch, grittiness-free and easily adheres to the skin..
- pH: 7-10 for a 20% w/v aqueous dispersion.
- Moisture Content: At 250C and relative humidity levels up to roughly 90%, talc absorbs negligible amounts of water.
- Specific Surface Area: 2.41-2.42 m^2/g.
- Specific Gravity :2.7-2.8.
- Solubility: Practically insoluble in acids and alkalis, organic solvents and water.

Magnesium sterate:

- Chemical name: Octadecanoic acid magnesium salt
- Synonym: Magnesium octadecanoate, octadecanoic acid, magnesium salt, stearic acid, magnesium salt.
- Description: A extremely fine, light white, precipitated or milled powder with a low bulk density, magnesium stearate19 has a distinct flavor and a slight stearic acid odor. The powder sticks to the skin easily and feels oily to the touch.
- Solubility: Slightly soluble in warm benzene and warm ethanol (95%), but practically insoluble in ethanol, ether and water [20].
- Bulk density: 0.159 g/cm^3
- Specific surface area: 1.6-14.8 m^2/g.
- Tapped density: 0.286 g/cm^3
- Melting range: 117ºC-150ºC

Microcrystalline cellulose:

- Nonproprietary Names:
- BP: Microcrystalline cellulose
- JP: Microcrystalline cellulose
- PhEur: Cellulosummicrocristallium
- USPNF: Microcrystalline cellulose
- Synonyms:
- Avicel PH; Celex; Cellulose gel; Celphere; Ceolus KG; Crystallinecellulose E460;
- Emcocel; Ethispheres; Fibrocel; Pharmacel; Abulose; Vivapur.
- Chemical name and CAS Registry Number: Cellulose (9004-34-6)
- Empirical Formula and Molecular Weight: $(C_6H_{10}O_5)n$
- Functional category: Adsorbent; suspending agent; tablet and capsule diluents; tablet disintegrant.

Uses of microcrystalline cellulose

Moisture content: Generally, less than 5%w/w, though water content can vary throughout grades. Cellulose in microcrystalline form is hygroscopic.
Stability and Storage Requirements: Although hygroscopic, microcrystalline cellulose is a stable substance. The bulk material needs to be kept dry and cool in a well-sealed container.
Incompatibilities: Strong oxidizing agents cannot be used with microcrystalline cellulose (Table 2).

Table 2: Composition of excipients.

Uses	Concentration (%)
Adsorbent	20-90
Anti-adherent	May-20
Capsule binder/ diluents	20-90
Tablet disintegrate	May-15
Tablet binder/ diluents	20-90

MATERIALS AND METHODS

The materials and other equipment's were used in the experiment are mentioned below (Tables 3 and 4).

Table 3: List of drugs and materials.

S.No	Ingredients	Use
1	Orlistat	API
2	Mannitol	Diluent
4	Plasdone	Super disintegrant
5	SSG	Super disintegrant
6	CCS	Super disintegrant
7	MCC	Binder
8	Sodium saccharine	Sweetening agent
9	Magnesium stearate	Lubricant
10	Talc	Glidant

Table 4: List of equipment.

S.No	Equipment	Manufactured by
1	Electronic balance	Elite
2	PH meter	Elite
3	Laboratory sieves	Elite
4	UV-Visible spectrophotometer	Elico SL 150 double beam spectrophotometer
5	Tablet compression machine	Elite
6	Monsanto hardness tester	Elite
7	Vernier calliper	Elite
8	Roche friability tester	M/s. Elite Scientific and Equipments
9	Dissolution test apparatus	M/s Lab India (Model-DS 8000)

Preformulation studies

In order to create stable, secure and efficient dosage forms, preformulation can also be defined as a step in the analysis and development process where someone describes the mechanical, chemical and physical characteristics of the novel pharmacological compounds. Preformulation should ideally start early in the discovery process so that the most recent chemical entities entering the development process can be chosen with the help of appropriate physical and chemical knowledge. The current study additionally takes into account potential interactions with different inert substances that are meant to be used in the final dosage form throughout this evaluation. The information below needs to be taken into account.

Organoleptic properties
Colour: A tiny amount of orlistat powder was placed on butter paper and examined in a bright area.

Taste and odour: With the use of the tongue, a very small amount of orlistat was used to obtain taste and the odor was detected by scent.

Physical characteristics
- Solubility tests
- Micromeritic characteristics
- Drug compatibility studies
- PH

Solubility

The descriptive phrases in the preceding table showed the approximate solubilities of the compounds. For the solubility tests, solvents including methanol, alcohol, water and isopropyl alcohol were employed.
Solubility studies of orlistat: Ten milliliters of various solutions were mixed with an excess amount of orlistat that had been taken separately. For a few minutes, these liquids were vigorously shaken. The solubility was then noted (Table 5).

Table 5: Solubility studies.

Descriptive term	Parts of solvent required for 1 part of solute
Very soluble	Less than 1
Freely soluble	From 1to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1,000
Very slightly soluble	From 1,000 to 10,000
Practically insoluble or Insoluble	Greater than or equal to 10,000

By creating compatibility mixes with the medicine at various ratios of various excipients based on a rough average weight, a compatibility research was carried out. These mixtures were kept in accelerated storage at 40ºC and 75% relative humidity. At 40ºC, control samples were kept. Depending on the intended application, the medication to excipient ratio can range from 1:1 to 1:10. The samples were stored in double-lined plastic bags. These samples were compared to a controlled sample that was kept at 40ºC for 15 days in order to assess any changes in their physical properties. The potassium bromide disc (pellet) method was used in this investigation. IR spectroscopy was used to confirm chemical stability.

PH of the solution: Orlistat was dissolved in the appropriate solvents for the PH experiments and a PH potentiometer was used to measure the PH.

Preparation of calibration curve

Standard curve of Orlistat: The curve in 100 milliliters of methanol is in accordance with Beer's lambert law.

Calibration curve for Orlistat in methanol at 203 nm

Orlistat's standard curve was measured at 203 nm; the results are displayed in the table below, which demonstrates that the values adhere to Beer's law (Table 6) [21].

Table 6: Graphical values of Orlistat's standard curve.

Concentration	Absorbance (203nm)
0	0
2	0.1195
4	0.2143
6	0.329
8	0.4111
10	0.4905

Plotting the Orlistat standard curve involves using the X-axis for concentration and the Y-axis for absorbance (Figure 5).

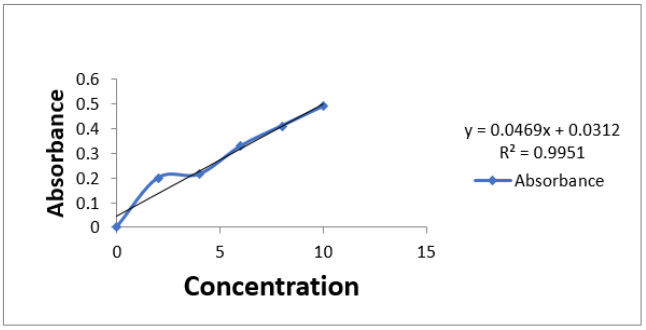

Figure 5: Calibration cure of Orlistat.

Pre- compression characterization of API

Critical information provided during pre-formulation can enhance the rapid and roaring introduction of the newest medicine entities for humans. Pre-formulation activities can range from supporting the discovery of new active agents to characterizing physical properties necessary for the design of dosage forms. Pre-formulation testing examines a pharmacological substance's chemical and physical characteristics. Pre-formulation testing's main goal is to produce data that will be helpful in creating a stable, bioavailable formulation. Additionally, using pre-formulation parameters increases the likelihood that a product will be formulated that is acceptable, safe, effective and stable. The physiochemical characteristics of the bulk drug, such as its physical appearance, solubility, bulk density, tapped density, compressibility, melting temperature, molecular weight, sieve analysis and angle of repose, must be studied before any medicinal ingredients are formulated into a dosage form.

Angle of repose: The greatest angle that can exist between the powder pile's surface and the horizontal plane is known as the angle of repose21. On a piece of paper that is held horizontally, the granule should be permitted to flow out of the funnel hole (Table 7). Granules are piled up on the paper as a result.

Where,

h=height of the pile

r= radius of the pile

tanθ= h/r

Table 7: Limits of angle of repose according to I.P.

S.No	Angle of repose (O)	Property
1	<25	Excellent
2	25-30	Good
3	30-40	Fair -Passable
4	>40	Very Poor

Bulk density:

It is the mass of powder divided by the volume of bulk.

Bulk density is equal to the powder's bulk divided by its total weight.

After transferring a specific amount of the powder to the measuring cylinder, it is mechanically tapped-either by hand or with a device-until a constant volume is achieved.

This volume, which is known as bulk volume(v), comprises the actual volume of the powder as well as the vacuum space between its particles.

Tapped density:

Tapped density24 is defined as the ratio between weight of sample powder taken and the tapped volume.

Tapped density (t) =M/Vf

Where M= weight of sample powder taken

Vf = tapped volume

Hausners ratio:

By using the following formula the Hausners ratio25 can be calculated. Hausners ratio26 = tapped density/Bulk density (Table 8).

Table 8: The limits of Hausners ratio.

S.No.	Hausners ratio	Property
1	1.00-1.11	Excellent
2	1.12-1.18	Good
3	1.19-1.24	Fair
4	1.25-1.34	Passable
5	1.35-1.45	Poor
6	1.46-1.54	Very poor
7	>1.55	Very very poor

Compressibility index: It is a crucial measurement that may be derived from both tapped and bulk density (Table 9).

Carr's Index= bulk density-tapped density/Tapped density

Table 9: The limits of Carr's ratio.

S.No.	Carr's ratio	Property
1	05-Dec	Excellent
2	Dec-18	Good
3	18-21	Fair
4	21-25	Passable
5	26-31	Poor
6	32-37	Very poor
7	>38	Very very poor

Compatibility studies

The compatibility of various excipients with active ingredients was assessed as part of the item development process. These excipients were combined with the medicine in varying ratios based on the functional category and they were kept in airtight containers for three months at 30 ± 2°C/65% RH ±5% RH. FTIR spectroscopy (Fourier transform infrared spectrometer Perkin-Elmer) was used to examine the drug's compatibility with all other excipients as well as the drug by itself. Prior to being examined using FT-IR, compatibility studies are also examined using a UV-Vis-Spectrophotometer [22].

Preparation of calibration curve

λ_{max}: A 10µg/ml solution of Orlistat was made and the sample was scanned for λ max (maximum absorbance peak) between 200 and 400 nm.

Calibration curve: To create the stock solution (1 mg/ml), 100 mg of orlistat was dissolved in 10 ml of methanol and then added to 100 ml of water. Ten milliliters of the stock solution were pipetted into a volumetric flask and 100 milliliters of water were added to make 100 micrograms per milliliter. To get 100 µg/ml, 10 ml was pipetted out of this and added to a volumetric flask. After that, solutions containing 2, 4, 6 and 8 µg/ml were made and the absorbance at 203 nm was measured. Solutions containing 1, 2, 4, 6 and 8 µg/ml are produced and measured at 203 nm if linearity is not detected and Beer-Lambert's law is not followed (Table 10).

Table 10: Composition of Orlistat fast dissolving tablets

S.No	Ingredients(mg)	S1	S2	S3	S4	S5	S6	S7	S8	S9
1	Orlistat	10	10	10	10	10	10	10	10	10
2	Mannitol	100	100	100	100	100	100	100	100	100
4	Plasdone	4	6	8	_	_	_	_	_	_
5	SSG	_	_	_	4	6	8	_	_	_
6	CCS	_	_	_	_	_	_	4	6	8
7	MCC	80	80	80	80	80	80	80	80	80
8	Sodium saccharine	2	2	2	2	2	2	2	2	2
9	Magnesium stearate	2	2	2	2	2	2	2	2	2
10	Talc	2	2	2	2	2	2	2	2	2

Preparation of Orlistat immediate release tablets

Selection of drug and excipients for preparation of orally disintegrating tablets (ODTs):

- In order to prepare ODT, orlistat was chosen as a model medication.
- Super disintegrants are needed for quick disintegration when preparing ODT with orlistat. Among the many kinds of super disintegrants, we used varied amounts of CCS (cross caramellose sodium), SSG (sodium starch glycolate) and plasdone.• Microcrystalline cellulose and mannitol are employed as diluents. Their characters are directly compressible.
- Talc and magnesium stearate are utilized as glidants and lubricants.
- You can use sodium saccharin as a sweetener.

Preparation of ODTs containing super disintegrants by direct compression method:

- very component listed above has been precisely weighed and taken.
- Using a motar and pestle, 10 mg of orlistat was combined with mannitol, microcrystalline cellulose and super disintegrants in varying amounts based on table no.
- After completely mixing the aforementioned combination with the addition of magnesium sterate, sodium saccharin and talc, the tablets were compressed.

Post compression characterization of Orodispersable orlistat tablets

A variety of physical attributes, including crushing strength, friability, thickness, diameter, disintegration and wetting times, weight variation, drug content and evaluation of Orlistat immediate release tablets, were applied to all of the produced tablets.

Physical appearance

For tablets to be accepted by consumers, their overall elegance and visual identity are crucial. The measurement of several characteristics, including tablet size, shape, color, taste, surface texture and consistency of any identifying marks, is necessary to manage the overall appearance of the tablet.

Tablet size and thickness

Controlling the tablets' physical attributes, like as thickness and size, is crucial for both consumer adoption and tablet consistency. The die and punches used to make the tablets determine the tablet us diameter and punch size. Vernier calipers are used to measure tablet thickness. The tablet us thickness can be employed as an initial control parameter and is correlated with its hardness. Tablet thickness should be regulated within a range of +/- 5%. Controlling thickness is also necessary to make packaging easier.

Weight variation of tablets

20 tablets are chosen at random, precisely weighed and their average weight is determined.
Average weight= weight of 20 tablets/20
The standard deviation is calculated for each tablet. The limits allowed is upto 7.5%.

Tablet friability

A Roche friabilator (M/s. Elite Scientific & Equipments) was used to measure the tablets' friability. A sample of 20 tablets or tablets with a known weight (WO) are dedusted in a drum for a predetermined amount of time (100 revolutions) and then weighed once more (w). The weight loss was used to calculate the percentage friability, as shown in the equation below. The weight loss should not more than 1%. Determination was made in triplicate. %Friability = 100(WO–W)/WO [23].

Tablet hardness

The force needed to shatter a tablet in a diametric compression force is known as the tablet hardness. The Monsanto hardness tester, which uses an integrated spring to apply force on the tablet diametrically, was the one employed in the study.

Drug content analysis

10 tablets in all were weighed and ground into powder. A little amount of methanol was used to dissolve the powder that was comparable to orlistat and then distilled water was added to make up the necessary volume. Following serial dilution, an aliquot of the sample was spectrophotometrically examined at 203 nm using an Elite UV-150 double beam spectrophotometer.

Wetting time

In the wetting time investigation, a sheet of tissue paper that had been folded twice was put inside a petridish that held five milliliters of distilled water. The petridish's internal diameter was 6.5 cm. A tablet was set on the paper and the number of seconds it took for the tablet to completely wet was recorded.

***In-vitro* disintegration time**

The tablets were taken and placed in each tube of the disintegration equipment for the disintegration time research. The tablet rack of the disintegration apparatus was then placed into a 1-liter beaker filled with 900 milliliters of distilled water and the disintegration time was recorded at 37±2.℃.

***In- Vitro* dissolution studies**

M/s Lab India (model: DS 8000) type 2 (paddle) was the USP dissolution test apparatus used for the in-vitro dissolution investigation. After placing 900 milliliters of the dissolution medium (6.8 phosphate buffer) in a basket, 3% SLS was added. A constant temperature of 37±0.5°C was maintained. The paddle was configured to run at 50 rpm. Five milliliters of the dissolving medium were taken out and replaced with an equivalent volume of new medium. Before being analyzed in the UV Spectrophotometer (Elite UV-150 double beam spectrophotometer) at 203 nm, the extracted sample was filtered and diluted with 6.8 phosphate buffer.

Higuchi release model:

To study the Higuchi release Kinetics, the release rate data were fitted to the following equation,
$F = K.t_{1/2}$
Where,
F is the amount of drug release
K is the release rate constant and
t is the release time.
Plotting the cumulative drug release against the square root of time results in a straight line, suggesting that the medication was released by a diffusion mechanism. K is equal to the slope.
Korsmeyer and Peppas release model:
The release rate data were fitted to the following equation
$M_t/M_\infty = K.t_n$
Where,

M_t/M_∞ is the fraction of drug release
K is the release rate constant
T is the release time.

The drug release's diffusion exponent, n, is influenced by the matrix dosage form's shape. Plotting the data as log percentage of drug released versus log time results in a straight line with a slope of n and the Y-intercept can be used to get the K. Fickian (case 1) diffusion has n = 0.5 and zero order release, whereas non-Fickian release has n values between 0.5 and 1.0. (I transport case) n=1.0

Zero order release rate kinetics:

The following equation is fitted to the release rate data in order to investigate the zero-order release kinetics.

F = K.t

Where,

F is fraction of drug release
K is release rate constant and
T is the release time.

If the cumulative percent drug release data is plotted against time and the curve is linear, then the data follows zero-order release kinetics, with a slope of Ko.

Stability studies

The stability of the active ingredient must be a key factor in deciding whether a medicine is accepted or rejected in any logical drug design or dosage form review. A medicine is said to be stable if, after the formulation's manufacturing date and packaging, its chemical or biological activity does not fall below a predetermined level of stated potency and its physical properties have not altered noticeably or negatively.

Objective of the study

The goal of stability testing is to demonstrate how a drug substance's or drug product's standard changes over time under the influence of various environmental factors like temperature, humidity and light. This allows for suggested storage conditions, retest times and shelf lives.

The stability test requirements for drug registration for applications in the US, Japan and the EU are outlined in the Stability Testing of New Drug Substance and Products (QIA) guidelines published by the International Conference on Harmonization (ICH). The duration of the investigation and storage conditions are specified by ICH (Table 11) [24].

Table 11: Storage conditions.

Study	Storage conditions	Minimum time period covered by data at submission
Long term	25ºC ± 2ºC/ 60% RH ± 5% RH	12 months
Intermediate	30ºC ± 2ºC/ 65% RH ± 5% RH	6 months
Accelerated	40ºC ± 2ºC/ 75% RH ± 5% RH	6 months

For a month, stability tests were conducted for the chosen formulation at 40ºC ± 2ºC and 75% RH ± 5% RH.

RESULTS

Pre formulation studies

Pre formulation results of Orlistat were included below (Table 12).

Table 12: Physical characters of Orlistat.

S.no.	Character	Inference
1	Nature	Amorphous powder
2	Color	White
3	Odour	Odoured
4	Melting point	Less than 44^{O}c
5	**Solubility** In 6.8PH Phosphate buffer In 1N HCl In 0.1N HCl In methanol In chloroform	Soluble Slightly Soluble Slightly Soluble Soluble Soluble

Drug- excipients compatibility ratio

FT-IR studies

The Figure shows the infrared spectra of the medications, the excipient mixture and their tablets, which were manufactured using the direct compression method. The KBr disk approach was used to scan all of the samples over the wave number area 4000 cm^{-1}-400 cm^{-1} at a resolution of 4 cm^{-1}. The medication and KBr were taken in a 1:100 ratio to create these KBr disks. After that, the mixture was evenly distributed, sandwiched between the pellets and compressed for one minute at 20,000 psi using a KBr pellet press. After releasing the pressure, the pellet was put into the pellet container and scanned in the infrared spectrum (Figures 6-22) (Table 13).

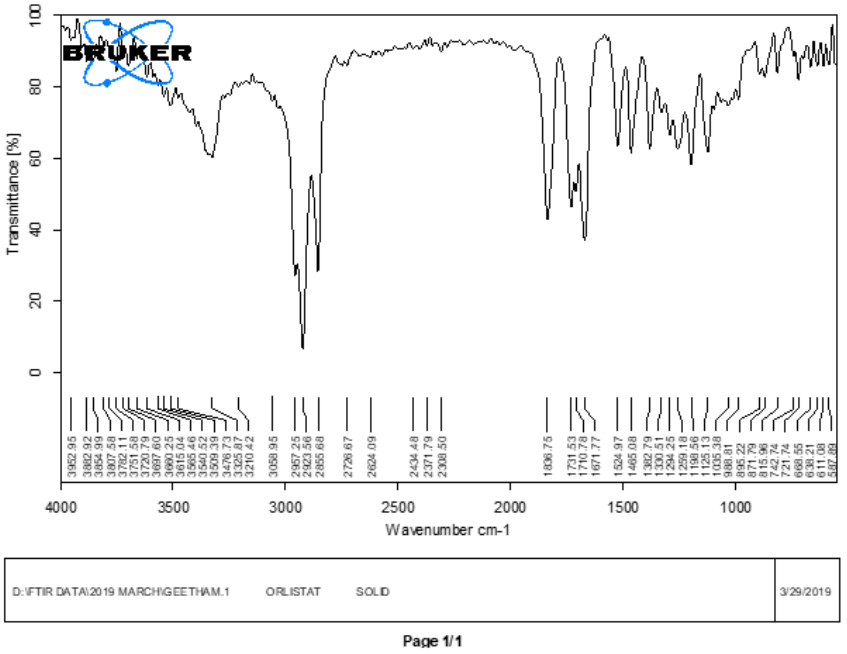

Figure 6: Infrared spectra (Trail 1).

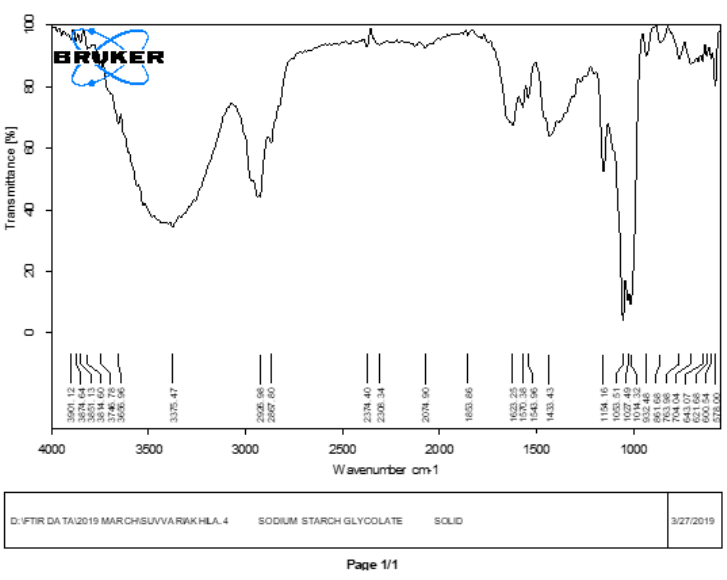

Figure 7: Infrared spectra (Trail 2).

Table 13: Chemical used for formulation.

Test for chemical groups	Successive extracts
	Phytochemical compounds presence in juice
Alkaloids	+
Amino acids	+

Carbohydrates	+
Fats and oils	-
Flavonoids	+
Glycosides	+
Gums	-
Lignin	+
Mucilage	-
Proteins	+
Steroid	-
Saponin	+
Tannins and Phenolic compounds	+
Triterpene	+

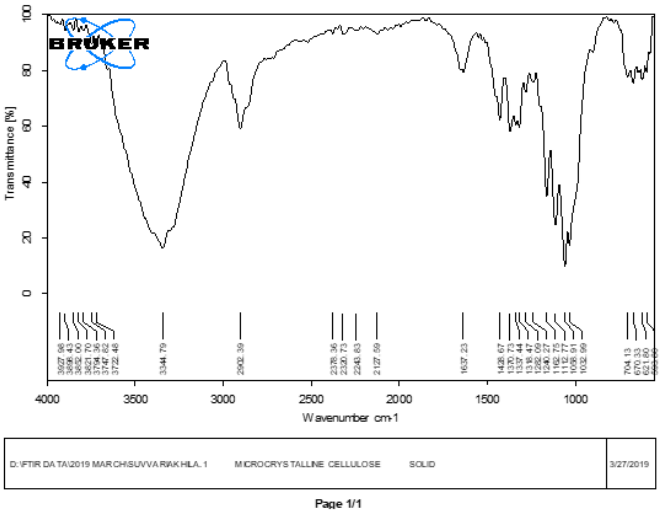

Figure 8: Infrared spectra (Trail 3).

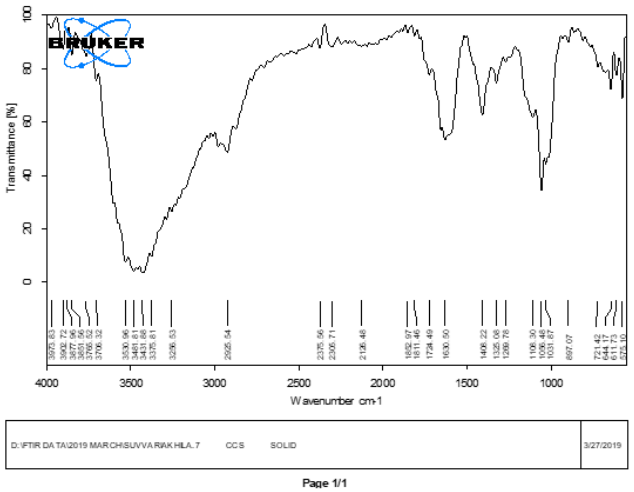

Figure 9: Infrared spectra (Trail 4).

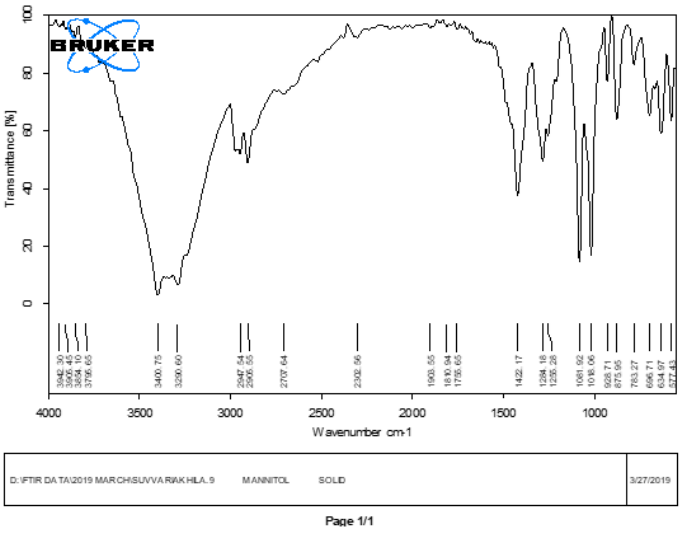

Figure 10: Infrared spectra (Trail 5).

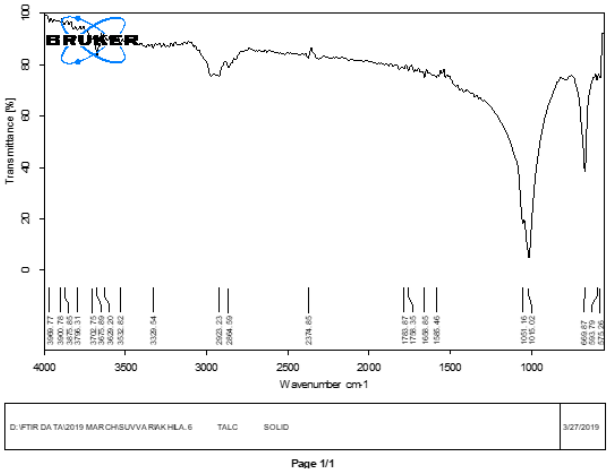

Figure 11: Infrared spectra (Trail 6).

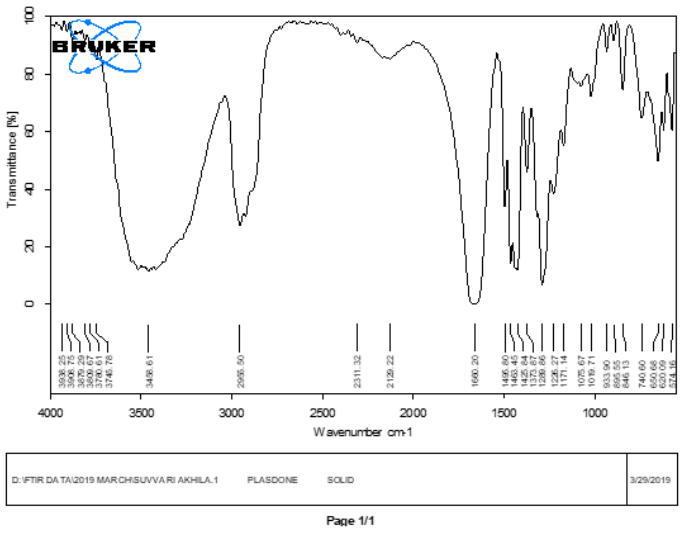

Figure 12: Infrared spectra (Trail 7).

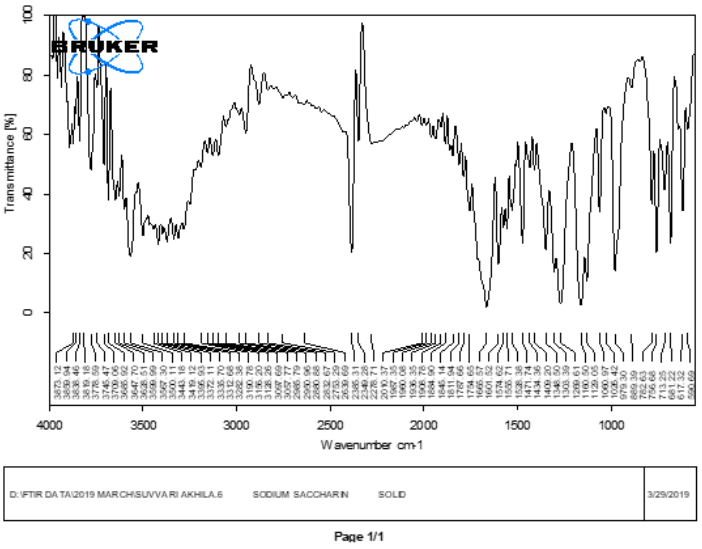

Figure 13: Infrared spectra (Trail 8).

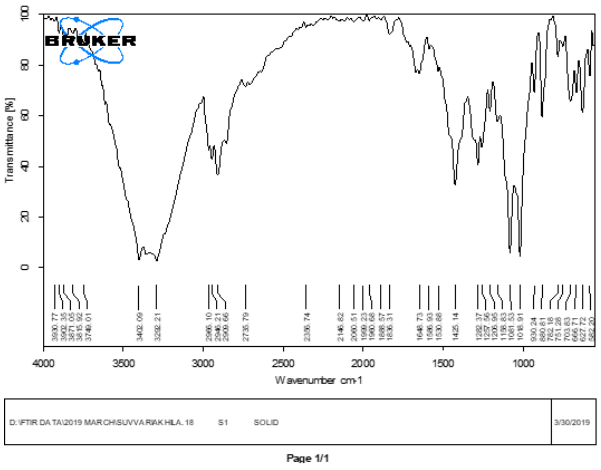

Figure 14: Infrared spectra (Trail 9).

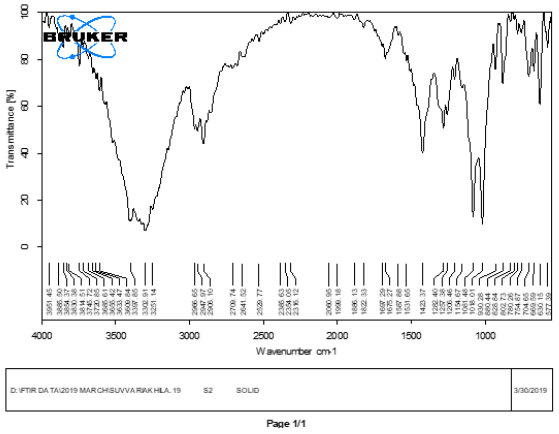

Figure 15: Infrared spectra (Trail 10).

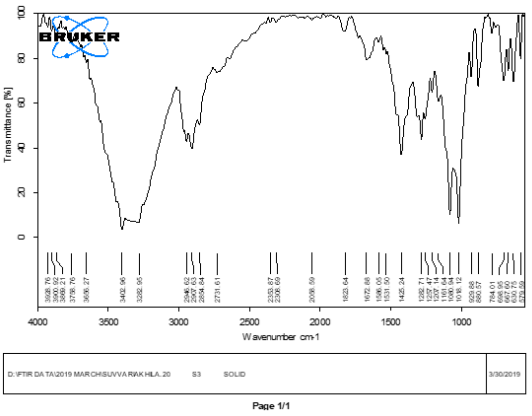

Figure 16: Infrared spectra (Trail 11).

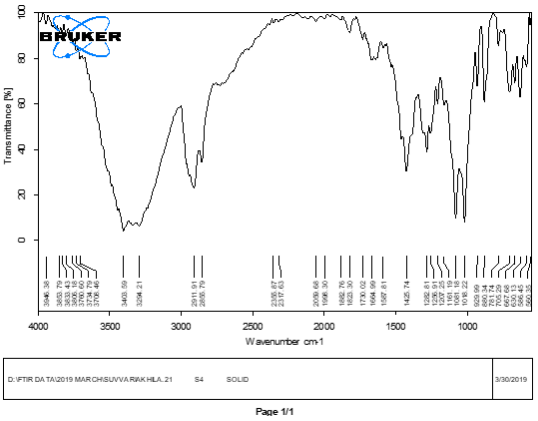

Figure 17: Infrared spectra (Trail 12).

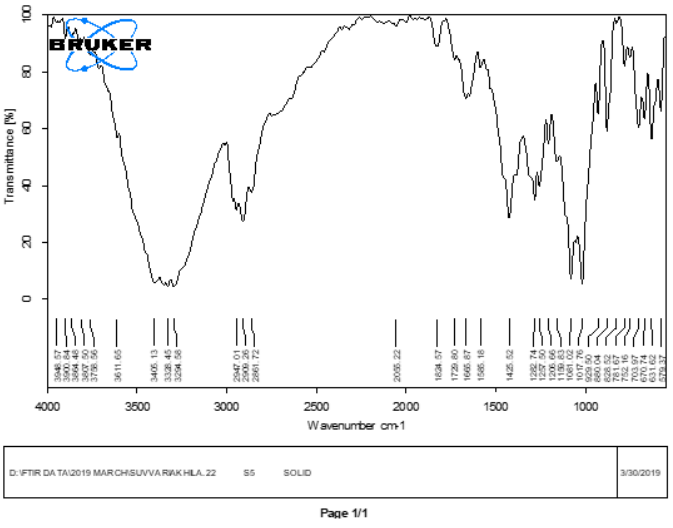

Figure 18: Infrared spectra (Trail 13).

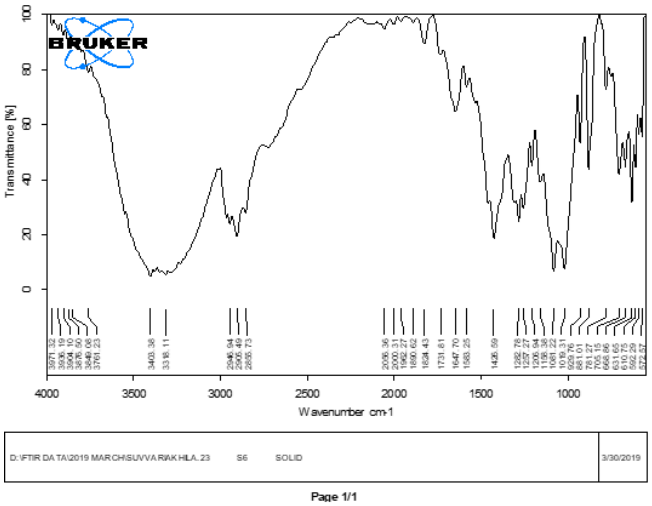

Figure 19: Infrared spectra (Trail 14).

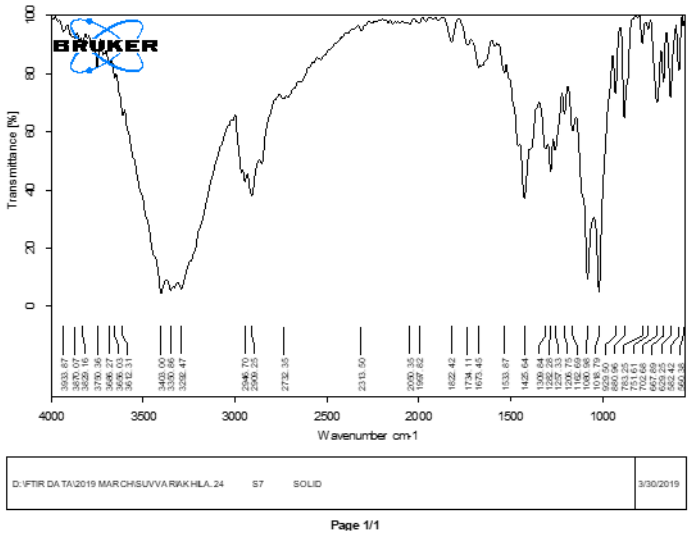

Figure 20: Infrared spectra (Trail 15).

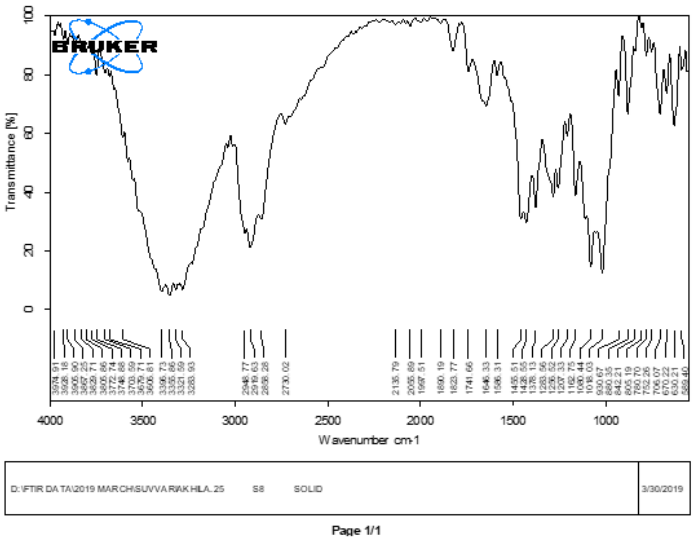

Figure 21: Infrared spectra (Trail 16).

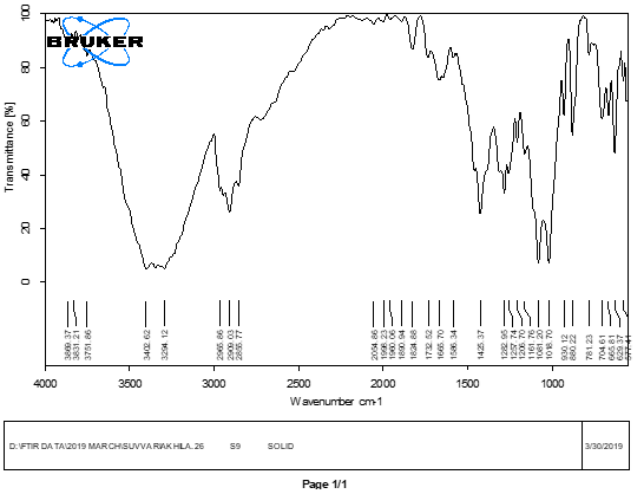

Figure 22: Infrared spectra (Trail 17).

Formulation and evaluation

Based on the inference from the excipient compatibility studies, the compatible excipients were used for formulation development of fast dissolving tablets which were further evaluated for various parameters (Table 14).

Table 14: Evaluation of granules of Orlistat

Formulation code	Bulk density (g/ml)	Tapped density	Angle of repose (º)	carr's index(%)	Hausners ratio
S1	0.52	0.61	32.1	20.2	1.25
S2	0.55	0.64	32.2	26.21	1.21
S3	0.48	0.57	32.5	1404	1.12
S4	0.49	0.55	31.8	12.72	1.24
S5	0.53	0.58	32.4	13.79	1.51
S6	0.51	0.55	33.5	13.11	1.16
S7	0.53	0.66	32.2	18.62	1.14
S8	0.51	0.62	31.5	10.90	1.24
S9	0.50	0.59	29.82	12.72	1.16

Observation: The angle of repose for Orlistat powder mixes was found to be between 29 and 82 degrees. Hausner's ratio is less than 1.18 and Carr's index is less than 15.5. The findings show that the powder blends have good flow characteristics (Table 15).

Table 15: parameters of Orlistat fast dissolving tablets

S.no	Parameters	S1	S2	S3	S4	S5	S6	S7	S8	S9
1	Weight variation (mg)	198.1 ± 1.21	199.2 ± 1.04	198.6 ± 1.32	201.3 ± 1.25	197.8 ± 1.29	199.1 ± 1.36	202.9 ± 1.39	198.7 ± 1.28	200 ± 1.9
2	Thickness (mm)	2.1 ± 0.20	2 ± 0.25	2.1 ± 0.21	2 ± 0.32	2.2 ± 0.41	1.9 ± 0.73	2.1 ± 0.52	2.1 ± 0.45	2.2 ± 0.46
3	Hardness (kg/cm2)	2.5 ± 0.23	2.3 ± 0.41	2.6 ± 0.32	2.1 ± 0.27	2.5 ± 0.70	1.9 ± 0.35	2.5 ± 0.41	2.2 ± 0.45	2.4 ± 0.51

4	Disintegration time (sec)	42 ± 0.37	300 ± 0.42	45 ± 0.36	35 ± 0.66	320 ± 0.47	49 ± 0.54	48 ± 0.37	58 ± 0.26	16 ± 0.34
5	Wetting time(sec)	94 ± 0.33	82 ± 0.31	102 ± 0.32	83 ± 0.52	68 ± 0.61	90 ± 0.72	70 ± 0.36	68 ± 0.32	60 ± 0.62

Observation: Wetting time was determined to be between 60 and 102 seconds and the average weight of orlistat fast dissolving tablets was between 198 and 200 mg, the thickness was between 1.9 and 2.2 mm and the hardness was between 1.9 and 2.5 kg/cm^2 (Table 16) (Figures 23-29).

In- vitro release studies

Table 16: *In vitro* release study of fast dissolving tablets.

		Cumulative % drug release								
S.No	**Time (mins)**	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**
1.	0	0	0	0	0	0	0	0	0	0
2.	5	34.92	43.63	51.25	31.27	37.26	47.60	39.76	42.77	51.04
3.	10	48.93	50.27	56.49	42.88	49.54	51.48	43.86	55.11	56.20
4.	15	67.81	68.89	73.09	62.05	55.26	67.73	60.75	64.72	68.06
5.	30	76.45	81.53	86.87	77.77	72.59	77.96	81.67	87.94	88.54
6.	45	87.31	89.90	93.08	81.75	83.39	87.94	89.28	91.76	95.04

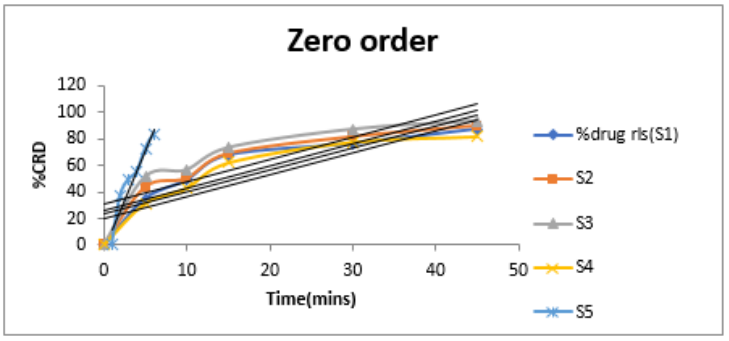

Figure 23: Zero order kinetics (Trail 1).

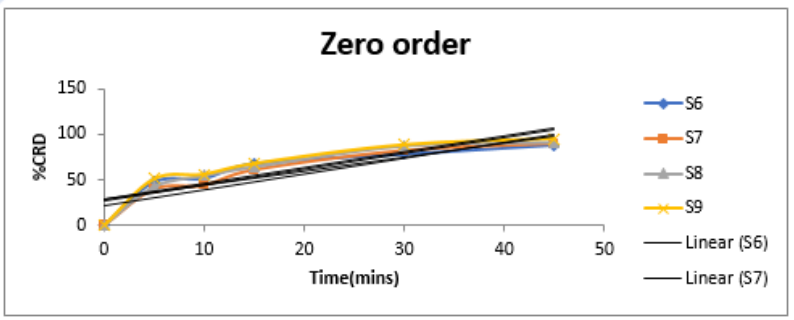

Figure 24: Zero order kinetics (Trail 2).

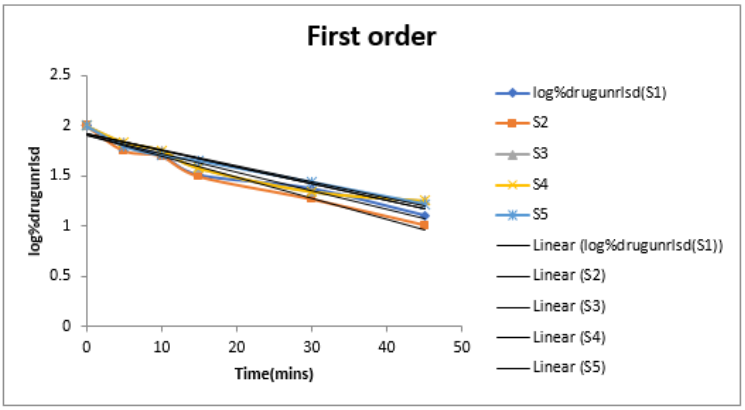

Figure 25: Zero order kinetics (Trail 3).

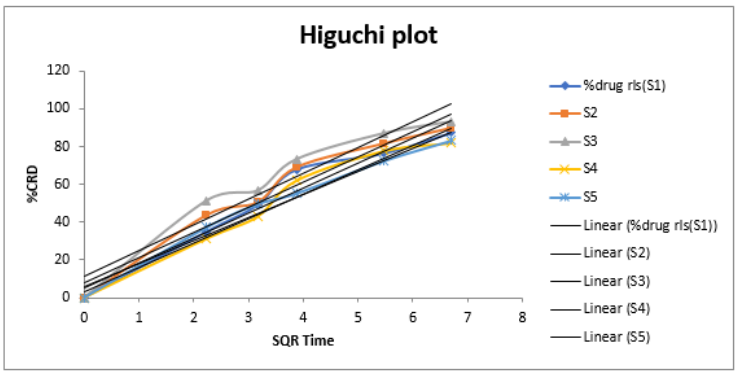

Figure 26: Graphical representation of Higuchi plot (Trail 1).

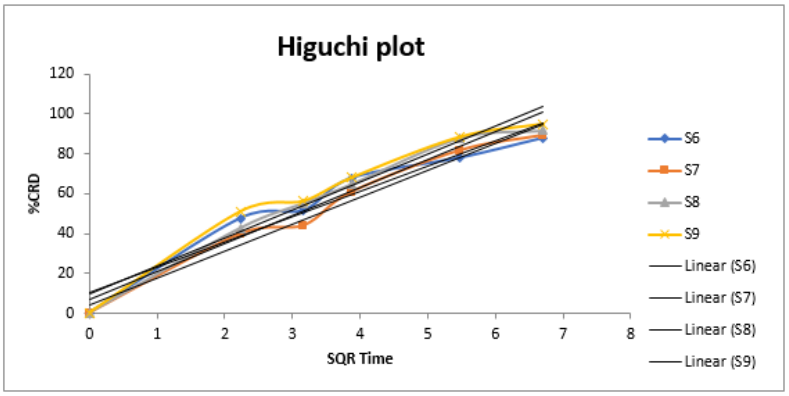

Figure 27: Graphical representation of Higuchi plot (Trail 2).

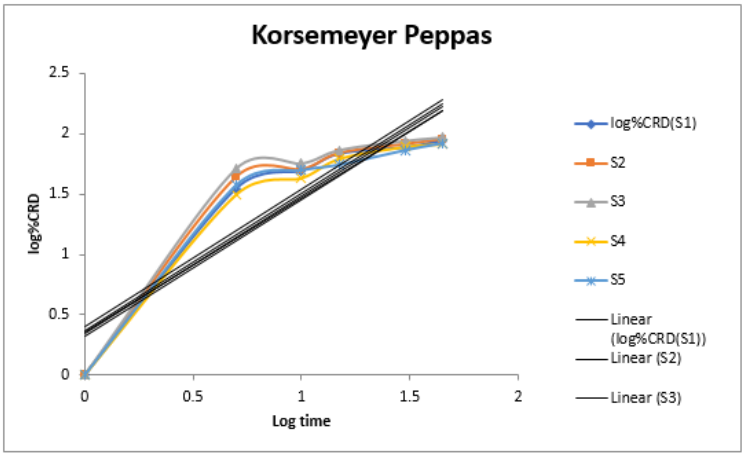

Figure 28: Graphical representation of Korsemeyer Peppas (Trail 1).

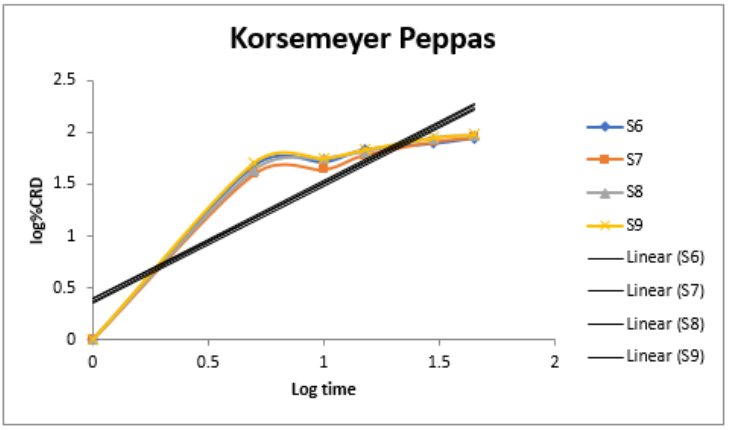

Figure 29: Graphical representation of Korsemeyer Peppas (Trail 2).

Kinetic study: Water penetration in the matrix, hydration and swelling of the polymer (with its expansion), diffusion of the dissolved drug and erosion of the gelatinous polymer layer are some of the hypothesized mechanisms for drug release from hydrophilic matrices. According to Fick's law, drug release from a matrix is regulated by diffusion across the polymeric matrix. The drug release mechanism is reliant on the PH, the drug and its own polymeric support. The following mathematical models were used to assess the release data of particular formulations in order to look into the release model from tablets.

Zero order equation……Q = K0t

First order equation……In (100-Q) = InQ-K1t

Korsmeyer and Peppas equation……Q= Kρtn

where K0 and Kt are the equations' constants and Q is the percentage of drug release at time t. Kρ is the constant that incorporates the release device's structural and geometric characteristics; KS is the constant that incorporates the surface volume relation; and n is the release indicator that indicates the release mechanism. The dissolution data were analyzed using Higuchi, Korsmeyer-Peppas, zero order and first order models (Table 17).

Table 17: Kinetic models of optimized batch.

Release kinetics	Correlation coefficient (R2)
Zero order equation	0.8247
First order equation	0.9427
Higuchi (diffusion) coefficient	0.9779
Korsmeyer Peppas equation	0.8338

Stability study of optimized formulation

Studies on the optimized batch's stability were carried out (S9). For three months, the stability research was conducted at 40ºC ± 2ºC and 75% RH ± 5% RH. After ninety days, the tablets were examined for hardness, drug content and *in vitro* drug release. The collected findings are displayed in the table. Hardness, drug content (assay) and *in vitro* drug release (dissolution) all exhibited consistency in the formulation. Overall, the results demonstrated the formulation's stability throughout time under the aforementioned storage conditions (Table 18).

Table 18: Stability studies of Orlistat for 3 months.

		Dissolution	Assay
Storage conditions	**Description**	**Orlistat-1**	**Orlistat-2**
Label claim	-	200 mg/tab	200 mg/tab
Initial	Complies	97.68%	97.78%
1st month	Complies	97.52%	97.72%
2nd month	Complies	97.58%	97.79%
3rd month	Complies	97.62%	97.82%

Observation: The current study set out to create an ideal recipe for an orlistat-containing fast-dissolving tablet. Orlistat is used to assist people lose weight or lower their chance of gaining it back. This medication must be taken in conjunction with a diet low in calories. It was determined to create fast-dissolving tablets using the direct compression approach following pre-formulation research. were employed as super disintegrants in the sodium starch glycolate formulation. The granules were assessed for Hausner's ratio, compressibility index, bulk density, tapped density and angle of repose before compression. Weight variation, hardness, friability, drug content, disintegration time and *in vitro* drug release were also assessed for the compressed fast-dissolving tablets. The S9 formulation produced encouraging results in the aforementioned studies. FTIR study, which demonstrated that S9 had no interaction with excipients, provided additional support for it. For 30 days, stability tests were conducted on the optimized batch S9 and the findings were satisfactory. Thus, the S9 formulation was thought to be the best one.

CONCLUSION

The suggested study project is innovative and can be effectively used for the formulation of orally disintegrating tablets, according to the results of the disintegration time and dissolution rate.
When compared to all other methods, this one is more effective. This study also found that the orodispersible tablets' unique excipients, known as super disintegrants, are crucial in their ability to dissolve when they come into touch with a solvent.

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CONFLICTS OF INTEREST

Authors declare no conflicts of interest.

ETHICAL APPROVAL

Not applicable.

CONSENT TO PARTICIPATE

Not applicable.

CONSENT TO PUBLICATION

Not applicable.

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