



FORMULATION AND EVALUATION OF LINEZOLID FILM COATED TABLETS

Surbhi Sirswal^{1*} and Aman Mittal²

^{1*} Assistant Professor, Smt. Tarawati Institute of Biomedical & Allied Sciences, Roorkee, UK.

² Associate Professor, Global Institute Pharmaceutical Education & Research, Kashipur, UK.

***Corresponding Author: Surbhi Sirswal**

Assistant Professor, Smt. Tarawati Institute of Biomedical & Allied Sciences, Roorkee, UK.

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ABSTRACT

The present investigation is undertaken with an aim to formulate and evaluate Film coated tablet of linezolid. The drug powders were subjected for preformulation studies. The Preformulation characteristics are within the Pharmacopoeial specifications. The drugs and excipients compatibility were carried out by FT-IR studies. The spectra showed that there was no interaction between them. The dissolution profile were carried out in Dissolution apparatus and then in UV spectrophotometer. For Linezolid-600 mg tablets, the main purpose of this study is to improve the hardness and dissolution profile of the core tablet and to minimize the defects occurs during coating of tablet. Optimization was done and it was found that dissolution release profile and hardness were found to be best and after coating, the tablet was found without any coating defect by non-aqueous coating i.e. IPA. Film coating of TiO₂ and IPA coating of 2 % w/w was done on Linezolid tablets as to avoid spores which occurs during the aqueous coating. Five formulations were prepared by the name of SAD01-SAD-05. For coating, two different types of coating material were used (aqueous coating and non-aqueous coating). The granules were evaluated for angle of repose, bulk density, compressibility index and drug content etc. The tablets were also subjected for thickness, hardness, friability and in vitro release studies. Evaluation parameters like weight variation, hardness, thickness, friability and disintegration test were performed. Results found that release profile of batch no. SAD-05 shows better hardness and dissolution profile of core tablet and good coating appearance after non-aqueous coating. This formulation is taken as an ideal or optimized formulation.

KEYWORDS: Linezolid; Preformulation; Film Coating; Hardness; Dissolution study etc.

INTRODUCTION

Oral drug delivery (OOD) is the most preferred and convenient route of drug administration due to high patient compliance, cost-effectiveness and ease of production.^[1] It is the most common and advantageous route of administration, if it is compared to all other route of administration. Of all those medicaments that are administered orally, solid oral dosage form is the one which represents the preferred class of products. Solid oral dosage form such as pills, tablets, capsules, and powders are commonly used in today era.^[2,3]

TABLETS

According to the IP, tablet are solid flat or biconvex in shape which is manufactured by compressing a single medicament or a mixture of drug with or without excipient either by dry granulation, wet granulation process or by direct compression.^[4] The compressed tablet is the most popular dosage form in today use. About two-thirds of all drugs currently prescribed are in solid form and many of these are compressed tablets.^[5]

ADVANTAGES

1. Tablets are elegant in appearance and convenient to use.
2. The tablets dosage form is simple, economical in manufacturing, most stable and most convenient in packaging, shipping and for any transportation.
3. Tablets is formulated to contain maybe more than one therapeutic ingredients showing a combination thus reducing multiple tablets use.^[6]
4. Provide protection of medicaments from environmental conditions like air, humidity and light.
5. Provide prolonged stability to medicaments.
6. It has Low manufacturing cost as compare to all other solid dosage form.
7. Administration of small quantity of drug in accurate amount.
8. Unpleasant order taste can be masked by sugar coating of tablet.
9. Easy to divide into halves and quarters whenever fraction dose is required as scored tablets are also manufactured.
10. Packaging and production is cheap and does not require more space for storage of tablet.^[7]

DISADVANTAGES

1. Its manufacturing involve several process thus at each step there is loss of ingredients of tablets.^[6]
2. Drugs which are hygroscopic in nature are not suitable for compressed tablets.
3. Drugs those have low or poor water solubility, slow dissolution and high absorbance in GI tract is difficult to formulate.
4. The cost of production is increased because of coating material.
5. It is Difficult to formulate liquid or tiny droplets into tablet and swallowing of tablet is difficult for children and for the patients who are unconscious.^[7]

ADDITIVES USED IN FORMULATION OF TABLETS

EXCIPIENTS

Excipients are the additives which are chemically inert substances, non-toxic and inactive in nature and do not show any therapeutic action. It doesn't even interact with any active ingredient and other excipients. The good choice of excipients is necessary during the manufacturing process. If the excipients are not compatible with the API it shows some chemical reactions which may change the property of the drug.

DILUENTS

Diluents are the fillers which are used to produce the bulkiness and volume of the tablet when the tablet itself is not able to produce the appropriate quantity for the manufacturing of tablet. Diluents selection should be made carefully as physicochemical changes might render the product quality and may cause problems in the manufacturing process.

Examples: MCC, DCP, starch, lactose, sucrose, lactose anhydrous and all other cellulose derivatives.

BINDERS

Binders are those binding agents which help to make the bond between the particles and help to increase the strength of the powder during compression. For the formation of granules. Binder is added in both dry and wet forms.

Binders are categorized into two forms

Powder Binders: Methyl cellulose, Poly Vinyl Pyrolidone, PEG.

Natural Binders: Xanthan gum, Gaur gum, Agar.

Solution Binders: Gelatin, PVPK 30, HPMC, PEG, Sucrose, Starch.

DISINTEGRANTS

Disintegrants are those excipients which are used for the breakdown of tablet when it comes in contact with water in the oral cavity or into the gastrointestinal tract. If the disintegrant is used in a proper amount the dissolution release profile will improve.

Example: SLS, Crosscarmellose sodium, cellulose derivatives, crospovidone and alginates.

LUBRICANTS

Lubricants are the agents used during manufacturing operation of tablet which is used to diminish the friction between die wall and tablet. It helps to prevent clinginess of the tablet to dies and punches by the use of lubricant, the tablet is easily ejected from the die cavity.

Lubricants are classified into two categories

1. **Insoluble lubricants-** Stearic acid, magnesium stearate, talc, calcium stearate.
2. **Soluble lubricants-** Sodium lauryl sulfate, sodium benzoate, PEG 400, 600 and 8000.

GLIDANTS

Glidants are the additives which help to improve the flow of powder. a tablet machine with high speed requires smooth flow of powder to die cavity. For this, glidants are used which improve the flow property of granules from hopper to die cavity and the tablet can be easily ejected from the cavity. Glidants are used to diminish the friction between the particles during the manufacturing operation of the tablet.^[8, 9, 10]

COLORING AGENTS

Approved drug and cosmetic dyes or mixture, water-soluble food or their corresponding lakes are used colouring agent. In tablet color is mainly serves as a mean of identification and for good appearance. Colouring agents also increase the stability of light-sensitive drugs during coating of tablet. Tablet color dye increases the aesthetic appearance of the tablet. Mostly food dyes are used during tablet coating whereas organic dyes that are synthetic dyes may interact with the human body may lead to health potential especially when it is taking in excessive amount.^[11]

TYPES OF TABLET

Tablets are classified into tow broad categories:

1. Compressed tablets &
2. Molded tablets

These two tablet types are further classifiable on purpose, use, and mode of administration as:

1. Compressed tablets

- a) Chewable tablets
- b) Buccal or sub-lingual tablets
- c) Lozenges
- d) Effervescent tablets
- e) Enteric coated tablets
- f) Sustained release tablets
- g) Vaginal tablets
- h) Sugar-coated tablets
- i) Film-coated tablets
- j) Layered tablets
- k) Implants
- l) Soluble tablets.

m) Pressed coated tablets.

2. Molded tablets

a) Hypodermic tablets

b) Dispensing tablets

The main difference is that the compressed tablets are made on large scale while molded ones are made in very short scale for experimentation or for rare use.

❖ **Based on surface Coating of tablets**

a) Film coated tablets

❖ **Based on drug release profile**

a) Fast release tablets.

b) Regular release tablets.

c) Delayed release tablets.^[12]

MANUFACTURING PROCESS OF TABLETS



DISPENSING (Weighing of ingredients)

Dispensing is the first step for any pharmaceutical manufacturing process. It is the most important and critical step of dispensing.^[13] In this the weight of each and every ingredient is determined according to the dose and according to the requirements of the batch which is manufactured. In most pharmaceutical companies dispensing is done through analytical balance. A balance is defined as an instrument used to determine the relative weight of the drug.^[14] The dispensing process technology can enhance the speed and accuracy of the dispensing operation. Pharmacy material is dispensed by analytical balance under the dispensing booth to prevent contamination during dispensing of material and the

material is dispensed by stainless steel hand-scoops and pumping and pouring liquids.^[15] Weighing should be performed on calibrated weighing balance. Each raw material must be weighed by one operator and should be checked by the second operator.^[16]

SIFTING AND SIZING

Sifting i.e., sieving and sizing i.e., milling or screening of powder or mass of mixture is important before compression of the tablet. Those ingredients which are in solid form or in hard lumps form convert into granules by the screening of it. This provides higher uniformity dose in sized granules and mixing of lubricants become easy for its proper functioning.^[18]

The sizing (size reduction, milling, crushing, grinding, pulverization) is an important step (unit operation) involved in the tablet manufacturing. In manufacturing of compressed tablet, the mixing or blending of several solid ingredients of pharmaceuticals is easier and more uniform if the ingredients are approximately of same size. This provides a greater uniformity of dose.

A fine particle size is essential in case of lubricant mixing with granules for its proper function.

Advantages associated with size reduction in tablet manufacture are as follows.

- It increases surface area, which may enhance an active ingredient's dissolution rate and hence bioavailability.
- Improved the tablet-to-tablet content uniformity by virtue of the increased number of particles per unit weight.
- Improved flow properties of raw materials.
- Improved color and/or active ingredient dispersion in tablet excipients.
- Uniformly sized wet granulation to promote uniform drying.

There are also certain disadvantages associated with this unit operation if not controlled properly. They are as follows.

- A possible change in polymorphic form of the active ingredient, rendering it less or totally inactive, or unstable.
- A decrease in bulk density of active compound and/or excipients, which may cause flow problem and segregation in the mix.
- An increase in surface area from size reduction may promote the adsorption of air, which may inhibit wettability of the drug to the extent that it becomes the limiting factor in dissolution rate.^[13]

GRANULATION

Granulation is a process of collection of particles or the mixture of powder together to form bonds between them which are formed by compression and by using appropriate binding agents. In the process of granulation one or more powder form combines and the granules are formed. that will produce quality tablet within required tablet press speed range. If the process of granulation is uniform it improves granulation flow, compression parameters, the content of uniformity and increases productivity.^[19] If granulation is proper according to the requirement, it will provide better hardness and variability, disintegration time as well as dissolution rate.^[20]

DRYING

In a pharmaceutical organization, many technologies are used for drying. It is important to keep the product free from moisture which prevents the powder from sticking during compression of tablets as if the Powder will not be properly dried and moisture is present in it then it may cause tablet effect during compression and during

coating of tablets. Drying ensure the Powder have free-flowing properties.

FINAL BLENDING

Blending of powders is a critical step during manufacturing as the homogeneous blending of powder is necessary for uniform mixing of API and other excipients especially lubricants before the compression process in the final dosage form.

If the Powder is not uniformly mixed for an evenly distributed composition of powder made to cause heart problem so to minimize every problem which may occur during compression because of uneven distribution of powder and no uniform blending homogenous blending needed to determine the homogenous blending of powder pre-compression parameters are analyzed of blended powder.^[22]

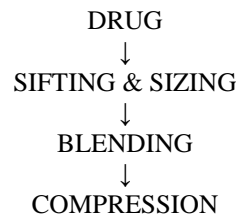
TABLET COMPRESSION

After the pre-compression analysis of blend powder and preparation of granules, it proceeds for the next process i.e., for the formation of core tablet. The manufacturing of tablet is categorized into three different types of methods which are as follows.

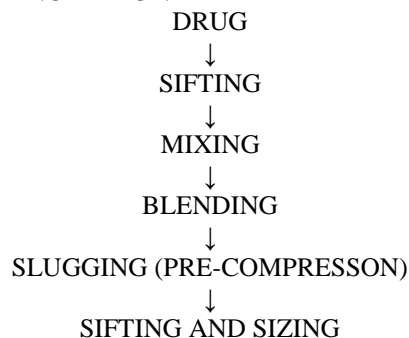
1. Direct compression
2. Dry granulation
3. Wet granulation techniques

Compression of the tablet is a critical step in the process of tablet manufacturing through which a tablet is formed. The tablet should be compressed according to their size and shape so it is necessary to set the required shape and size of punches. It is necessary to identify all the official and unofficial parameters during compression of the tablet which started in a sequence like weight variation of the tablet, hardness, thickness, disintegration time friability and dissolution release rate.^[23]

DIRECT GRANULATION/COMPRESSION



DRY GRANULATION



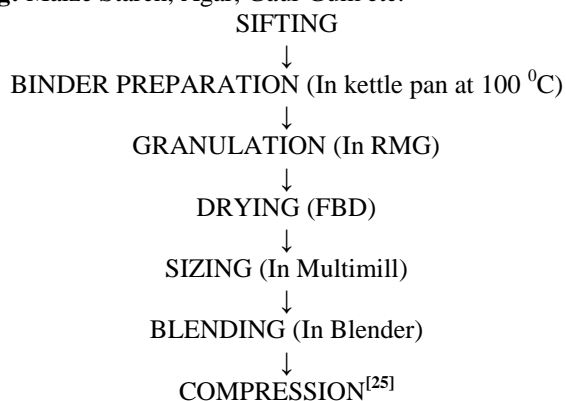


WET GRANULATION

Wet granulation is process in which binder is added to the mixture of blend powder and the components are massed to a predetermined end point at given mechanical speed.

The binder used during wet granulation may be aqueous or solvent based. Choice of binder is depend upon the properties of the powder. If only water is used for binding, it may form bonds between powder particles but after drying the water get dries, bonds will break and powder may fall apart from each other. in such cases, a binding agent is requires that should be stable enough after drying too.

Eg: Maize Starch, Agar, Gaur Gum etc.^[19,26]



1.7 WORKING PRINCIPLE OF COMPRESSION

The compression machine works on the principle of hydraulic pressure and pneumatic pressure. Hydraulic pressure play a key role in the formation of a tablet in which the upper punch and lower punch is compressed in the die cavity (hole) by which the tablet is formed. If the hydraulic pressure will be increased (maximum 4 ton) of the compression machine, the force will increase which affect the hardness of tablet. The tablet becomes too hard which may lead to the problem during disintegration time and dissolution time of tablet.

Tablet process divided into four main stages.

1. Filling
2. Metering
3. Compression
4. Ejection from die.^[24]

COMPRESSED TABLET CHARACTERISTICS

1. **General appearance:** The general appearance of the tablet include overall appearance of the tablet like size, colour, surface, consistency for control of

uniformity in tablet lot and for monitoring trouble free manufacturing.

2. **Tablet thickness:** Tablet thickness is determined by using vernier calliper which may be digital or manual. The tablet thickness is depend on the pressure applied on the compression machine. The standard limit of thickness varies in $\pm 5\%$. Of the tablet thickness.

3. **Tablet hardness:** Hardness of the tablet is defines as the force required for breaking of tablet. Appropriate pressure is given during tablet compression as if the tablet become too hard it will not disintegrate at the given time and if tablet become too soft it will washout. The hardness of conventional tablet should be 2.5 to 5kg/cm² and for extended release tablet, the hardness should be between 5 to 7.5kg/cm². Various types of harness tester is used for the determination of hardness of tablet.

- Strong cobb hardness tester
- Pfizer hardness tester
- Schleuniger hardness tester.

4. **Tablet friability:** The friability of the tablet is determine to know the mechanical strength of the tablet during transportation but according to the scientific reason friability is determine to check its mechanical strength during coating of the tablet. The process is done for 4 minute i.e., 25 rotations per minute.

5. **Weight variation:** The weight should be checked at every 30 minutes during compression of tablet. It is the most important parameter of the tablet manufacturing. For the tablets that contain more than 90% of the drug then weight variation test can be used as drug content uniformity of the tablet. Specified number of tablets is taken at random manner and average weight was determined. The average weight of tablets should not deviate from the maximum percentage deviation allowed.

According to the IP, the standard limit of the tablets should is categorized according to their weight.

Table 1.1: Weight Variation Limit of Tablet According to IP & BP.

Weight of tablet (mg)	Standard limit (%)
Less than 80 mg	Deviation upto 10%
80mg to 250mg	Deviation upto 7.5%
Above 250mg	Deviation upto 5%

6. **Content uniformity:** It is the intended amount of drug substance contained by every tablet with little variation among tablets within a batch. A fundamental quality attribute for all pharmaceutical preparation is the requirement for a constant dose of drug between individual tablets. Specified numbers

of tablets are individually assayed for their content and requirements for content uniformity are met if the amount of active ingredient in each dosage unit lies within the range specified in the monograph.

- 7. Disintegration:** The disintegration of tablet is define as the breaking up or disintegration of tablet at a given temperature and a given time in the liquid medium. This test is not applicable for sustained release tablets. Disintegration time of the following types of tablets are as follows.
- Uncoated tablet: NMT 15 minutes
 - Film coated tablet: NMT 30 minutes
 - Enteric coated tablet: 2 hours in 0.1N HCL, 1 hour in 6.8Ph Phosphate buffer.
 - Sugar coated tablet: NMT 1 hour
 - Dispersible tablet: NMT 3 minutes
- 8. Dissolution:** Dissolution is defined as, how much time a tablet is taken to dissolve its active ingredient into the medium under specified condition as in vitro test.

Six tablets are taken and place one tablet into each tube of the basket, add the disc to each individual tube and operate the apparatus with using water by maintain its temperature at 35⁰C to 39⁰C.

The temperature of medium should be:

1. Basket type apparatus.
2. Paddle type apparatus.^[26]

1.9 COMMON DEFECTS DURING COMPRESSION OF TABLET

1. Sticking And Picking

Sticking and picking is the common defect during the manufacturing of the tablet. Sticking refers to the tablet material adhering to the die wall.

It occur when the powder is not completely dried or too much of binders are used during granulation which cause sticking of powder in the face of the punches picking occur when small amount of material is stick out or being remove off from the tablet surface by the punch faces. Mostly picking occur in embossed tablets.

2. CAPPING

Capping occur when upper and lower part (segment) of the tablet separate out horizontally from the main body of the tablet in CAP form. Capping occur due to improper binding of granules of tablets or by using too much lubricants.

3. BLACK SPOTS

Small spots occur by the oil used in compression machine. It is usually occur during the first 10 rounds of the machine or when the oil or Grease is used.

4. CHIPPING

Chipping occurs when the tablet started breaking up from the edge.

5. BINDING

When the tablet is adhere, tear or seize in the die cavity the powder started to chock the cavity and a film is formed in the die due to which ejection of die is hinder.

6. DOUBLE IMPRESSION

Double impressing occurs mostly in the embossed tablets i.e, those punches have monographer other engraving on them.^[27-33]

TABLET COATING

Tablet coating is perhaps one of the oldest Pharmaceutical process still in existence. Any introduction to tablet coating must be prefaced by an important question- "Why coat tablets???"-since many instances, the coating is being applied to a dosage form that already is functionally complete.^[34]

Coating can be applied to several kinds of solid dosage forms like tablets, pellets, pills, drug crystals, etc.^[35]

Tablet coating is a pharmaceutical technique of applying a thin polymer-based film to a tablet or a granule containing active pharmaceutical ingredients (APIs).

The amount of coating on the surface of a tablet is critical to the effectiveness of the oral dosage form. Tablets are usually coated in horizontal rotating pans with the coating solution sprayed onto the free surface of the tablet bed.^[36]

The coating can be specially formulated to regulate how fast the tablet dissolves and where the active drugs are to be absorbed into the body after ingestion.^[37]

After making a tablet you must coat it. The coating can have several functions,^[38] the most important of which is controlling the release profiles, produce an elegant product^[36, 39], to mask unpleasant taste and odor^[40,41,42], enhance stability against light and moisture.^[40,43,44] Coating also provide identity to product and creating smooth covering to promote and improve swallow ability.^[45,46,47]

There are three primary process involved in tablet coating

- i. Properties of tablet coating
- ii. Coating process
 - a) Coating equipment
 - b) Parameters of the coating process
- iii. Coating composition^[48]

Properties of coating tablet

1. It also helps to control and increase the bioavailability of the drug and impart a functional

purpose such as the modification of drug release profile.^[44,49]

2. Improves product appearance and product identity.
3. Helps to mask the bitter taste and oral tablets.
4. Tablet coat also allow higher packaging speed by reducing friction as well as reducing dust generation from tablet.
5. Helps maintain the shape of the tablet.^[47-49]

Coating equipment: The coating system consists of the.

- a. Coating pan
- b. Spraying system
- c. Peristaltic pumps
- d. Fans & Filters
- e. Inlet and outlet heating pipes
- f. Air handling unit
- g. Dust collector
- h. Controls^[50]

Coating pan is consist of stainless steel 316 in the shape of drum with the cabinet which allow to control the air flow, air temperature and controlled solution application. Coating pans are used to for an aqueous or organic film around any type of pellets and tablets. RPM of the pan is variable. In this film coating is done by appropriate air handling system & spraying equipment.

Spraying system consists of spray gun, a peristaltic pump, silicon tube and air lines.

Spray gun used to distribute the coating solution uniformly through peristaltic pump which works in the principle of active diffusion. Spray gun is connected to peristaltic pump through silicon tube which is made up of food grade and is non-reactive with solution. Uniform solution distribution is depend on the RPM of peristaltic pump. If the solution is distributed properly then it may cause many coating defects like bridging, mottling, peeling, spores formation, twinning etc.

Some of the critical parameters which should be monitored during coating is given below

1. Spray rate
2. Inlet and exhaust temperature
3. Bed to gun distance
4. Atomized air pressure
5. RPM of coating pan and peristaltic pump
6. Bed temperature
7. Environmental condition of coating room

Advantages of Tablet Coating

1. Tablet coatings must be stable and strong enough to survive the handling of the tablet, must not make tablets stick together during the coating process, and must follow the fine contours of embossed characters or logos on tablets.
2. Coatings can also facilitate printing on tablets, if required. Coatings are necessary for tablets that have an unpleasant taste, and a smoother finish makes large tablets easier to swallow.

Disadvantages of Tablet Coating

1. Disadvantages of coating such as relatively high cost, long coating time and high bulk have led to the use of other coating materials.
2. This process is tedious and time-consuming and it requires the expertise of highly skilled technician.^[55-56]

TYPES OF COATING

1. ENTERIC COATING

An enteric coat is designed to resist the low pH of gastric fluids in which the tablet breaks into the stomach but release and dissolves its content into the small intestine into the high pH place in Duodenum. The reasons for enteric coating are as follows.

1. To protect acid-labile drugs from the gastric fluid.
2. To prevent gastric distress due to irritation from a drug.
3. To deliver drugs intended for local action in the intestines.
4. To deliver drugs that are optimally absorbed in the small intestines to their primary absorption site in their most typical concentrated form.
5. To provide a delayed- release component for repeat action of the tablet.

❖ **Phthalate derivative**

- i) HPMC
- ii) ACETONE
- iii) Acrylcoat L-100

❖ **Surfactant**

❖ **Plasticizer**

❖ **Solvent/vehicles**

❖ **Colorant**

❖ **Flavors and sweeteners**

❖ **Antioxidants**

❖ **Antimicrobials/ preservatives**

2. SUGAR COATING

Sugar coating serves the various purposes of masking the bitter taste and odor so the drug which are not able to take without coating can be administered easily. These are the compressed tablets and have a multistep process. Tablets intended to be coated are manufactured to be thin edged and highly convex to allow the coatings to form rounded rather than angular edges. The process can be divided into six main stages.

1. Sealing
2. Sub-coating
3. Smoothing
4. Colour coating
5. Polishing
6. Printing

SEALING: It is applied directly into the core tablet to separate out the water constituent to assure the stability of the product as if the water is present in the tablet for long duration it may change the characteristics of the

product which may directly cause the stability of the drug.

Composition of seal coat: Alcoholic solution of resins such as shellac, zein or cellulose derivatives (10 to 30% of solids).

SUBCOATING: It is achieved by gum-based solution to the sealed tablet cores. Once this solution has been distributed uniformly throughout the tablet mass, it is followed by a liberal dusting of powder, which serves to diminish facilitate tablet building up. A sub coating suspension containing both the binder and the insoluble powder is sprayed intermittently on the tablet bed. The product at the end of the sub coating will be too rough to continue with color coating.

SMOOTHING AND FINAL ROUNDING: After the tablets are sub coated, 5 to 10 additional coatings of thick syrup are applied to complete the rounding and smooth the coatings. This syrup is sucrose based, with or without additional components such as starch and calcium carbonate.

FINISHING AND COLORING: To attain final smoothness and the appropriate color to the tablets, several coats of thin syrup containing the desired colorants are applied in the usual manner. This step is performed in a clean pan, free from previous coating materials.

POLISHING: After the coloring process the tablet loss its appearance which requires some separate polishing step to give them the high degree of shining associated with sugar coated tablets. Application of an organic solvent/ suspension of waxes e.g beeswax or carnauba is generally used.

3. FILM COATING

Purpose of film coating includes increasing product shelf-life, aesthetic enhancement, mask the bitter taste and enhance release profile.

Film coating involves the deposition of solution by forming an outer polymer based thin covering into the tablet by spray method in which the solution is sprayed uniformly into a rotating bed inside the CC pan. Coating solution containing a polymer which was mixed into the suitable medium with other ingredients. The drying is accomplished by hot air into the tablet by which the solvent or moisture will easily remove and formed a thin film surrounding into each core tablet.

- It provide functional production barrier to the outer surface of the core tablet.
- It is less time consuming as compared to sugar and enteric coating.
- Film coating facilitate product identification.
- Improve product organoleptic properties.
- Increase process efficiency and output
- Increase flexibility in formulation.

- Improve resistance to the chipping of the coating
- Film coating can protect the tablet from light, temperature and moisture, mask undesirable taste or odor, improve the appearance, provide tablet identity, facilitate swallowing and control or modify the release of the drug. There should be no abrasion of tablet.

Polymer can be applied as

- Organic-solvent-based solution (typically reversed for modified release applications today)
- Aqueous solution (immediate release film coating)
- Aqueous dispersion (modified release applications)

Film coating is categorized into two parts

1. Aqueous coating- Water
2. Solvent-based coating- Acetone, IPA.^[61-64]

FILM FORMER

A film former should be capable of producing smooth, thin films reproducible under conventional coating condition and applicable to a variety of tablet shapes. It should maintain the film strength and minimizes film cracking during handling or subsequent storage. The thickness of such coating is usually between 20-100 µm. under close inspection the film structure can be seen to be structure and quite distinct in appearance, from a film forming, from casting a polymer solution on a flat surface.

Film coating formulation usually contains the following components:

- Polymer
- Plasticizer
- Colorants / Opacifiers
- Solvent/Vehicles

1. POLYMERS

Amongst the vast majority of the polymers used in film coating are cellulose derivatives or acrylic polymer & copolymers.

- Non-enteric polymers
- Hypermellose
- Hydroxyethyl cellulose
- Hydroxyethylmethyl cellulose
- Polyethylene glycol
- Ethylcellulose

EntericPolymers: some example of enteric polymers are:

- Hypermellose Phthalate
- Polyvinyl Acetate Phthalate
- Cellulose Acetate Phthalate
- Polymethacrylates
- Shellac

A) Immediate Release Coating Polymers

a) Cellulose Derivates: The most widely used of cellulosic polymers is HPMC (Hydroxypropyl Methyl

Cellulose). It is readily soluble in aqueous media, forms film with good mechanical properties (strength, flexibility and adhesion to the tablet core).

Other examples: MC (Methyl Cellulose) & HPC (Hydroxypropyl Cellulose),

- ❖ **Hydroxyl Propyl Methyl Cellulose:** The polymer is prepared by reacting alkali treated cellulose first with methyl chloride to introduce methoxy groups and then with propylene oxide to introduce propylene glycol ether group. Hydroxy Propyl methyl cellulose closely approaches the desired attributes of an ideal polymer for film coating.
- ❖ **Methyl Hydroxy Ethyl Cellulose:** This polymer is prepared by reacting alkali treated cellulose first with methyl chloride and then with ethylene oxide. A wide variety of viscosity grades are available. It is structurally similar to Hydroxyl Propyl Methyl Cellulose. It is soluble in fewer organic solvents.
- ❖ **Ethylcellulose:** Ethylcellulose is manufactured by the reaction of ethyl chloride or ethyl sulfate with cellulose dissolved in sodium hydroxide. This material is completely soluble in water & gastrointestinal fluids, and thus cannot be used alone for tablet coating. It is usually combined with other water soluble polymers to prepare films with reduced water soluble properties.
- ❖ **Hydroxypropyl cellulose:** Hydroxypropyl cellulose is manufactured by treatment of cellulose with sodium hydroxide, followed by a reaction with propylene oxide at an elevated temperature and pressure. It is soluble in water below 40° C, gastrointestinal fluids and many polar organic solvents.
- ❖ **Sodium Carboxy Methyl Cellulose:** Sodium Carboxy Methyl Cellulose is sodium salt of carboxy methyl cellulose and is manufactured by the reaction of soda cellulose with the sodium salt of monochloro acetic acid. It is available in low, medium, high and extra high viscosity grades. It is easily dispersed in water to form colloidal solution but insoluble in most organic solvents.

b) Vinyl Derivatives

The most widely used vinyl polymer derivative is PVP. It has a limited use in film coating because of its inherent tackiness. A copolymer of PVP and vinyl acetate forms better films. Povidone: Povidone is a synthetic polymer consisting of linear 1-vinyl-2-pyrrolidinone groups. Povidone is available in various grades. The most common uses of Povidone in pharmaceuticals is as a tablet binder and tablet coating material.

c) Poly Ethylene Glycols

Polyethylene glycols are manufactured by the reaction of ethylene glycol with ethylene oxide in the presence of sodium hydroxide at elevated temperature and under pressure. The materials with low molecular weights (200-600) are liquids at room temperature and are used as plasticizer for coating solution films.

Acrylate Polymer

Acrylate polymers are available only as organic solution and solid materials. These polymers produce films for the delayed action preparation similar to ethyl cellulose formulation.

B) Modified Release Coating Polymers

a) Extended Release Coating Polymers They are dissolved in organic solvent or dispersed in aqueous medium. Cellulose derivatives also often used. Cellulose derivatives are highly substituted cellulosic ether, thus rendering the polymer water-insoluble. **Example:** Ethylcellulose.

b) Enteric Coating Polymers

An enteric coat is designed to resist the low pH of gastric fluids but to disrupt or dissolve when the tablet enters the higher pH of the duodenum. The important reasons for enteric coating are as follows.

- To protect acid-labile drugs from the gastric fluid.
- To prevent gastric distress or nausea due to irritation from a drug.
- To deliver drugs intended for local action in the intestines.
- To deliver drugs that are optimally absorbed in the small intestines to their primary absorption site in their most concentrated form.
- To provide a delayed-release component for repeat action tablet.

i) Phthalate Derivative

❖ **Cellulose Acetate Phthalate (CAP):** It has been widely used in the industry. It is also hygroscopic and relatively permeable to moisture and gastric fluids in comparison with some other enteric polymers. It dissolves only above pH 6.0 CAP films are brittle and usually formulated with hydrophobic film forming materials or adjuvants to achieve a better enteric film.

❖ **Hydroxypropyl Methylcellulose Phthalate:** They are derived from hydroxy propyl methylcellulose by esterification with phthalic anhydride. These polymers dissolve at a low pH (at 5 to 5.5) than CAP or acrylic co polymers, and this solubility characteristic may result in higher bioavailability of some specific drugs.

❖ **Polyvinyl Acetate Phthalate (PVAP):** Polyvinyl acetate phthalate is manufactured by the esterification of a partially hydrolyzed polyvinyl acetate with phthalic anhydride. This polymer is similar to Hydroxypropyl methylcellulose phthalate in stability and pH dependent solubility.

ii) Acrylate Derivative

❖ **Acrylate Polymers:** Two forms of commercially available enteric acrylic resins are Eudragit L and Eudragit S. Both resins produce films that are resistant to gastric fluid and are soluble in the intestinal fluids at pH at 6 and 7 respectively.

2) SURFACTANTS

Surfactants because of their chemical structure have tendency to accumulate at the boundary between two phases. They lower the interfacial tension between oil and water phases and also enhance the spreadability of the film during application. **Eg:** Spans, Tweens.

3) PLASTICIZERS

Affords flexibility and elasticity to the coat and thus provide durability. Plasticizers are simply relatively low molecular weight materials which have the capacity to alter the physical properties of the polymer to render it more useful in performing its function as a film coating material. It is generally considered to be mechanism of plasticizer molecules to interpose themselves between individual polymer strands thus breaking down polymer-polymer interactions. Thus polymer is converted in to more pliable materials.

Plasticizers are classifying in three groups. Polyols types contain glycerol, propylene glycol, PEG (Polyethylene glycol). Organic esters contain phthalate esters, dibutylsebacate, citrate esters, triacetin. Oils/ Glycerides contain castor oil, acetylated, monoglycerides, and fractionated coconut oil.

4) SOLVENTS/VEHICLES

The key function of a solvent system is to dissolve or disperse the polymers and other additives. Volatile organic solvents may be used to allow good spread ability of the coat components over the tablet and allowing rapid evaporation, but they are expensive and show environmental hazards and solvent residue in the formulation must be investigated (certain limit). Aqueous vehicles are safer, but they show slower evaporation and may affect drug stability. All major manufactures of polymers for coating give basic physicochemical data on their polymers. These data are usually helpful to a formulator.

The major classes of solvents being used are:

- a. Water
- b. Chlorinated hydrocarbons

5) COLORANTS/OPACQUANTS

It provides an elegant appearance. **Eg.:** Iron, oxide, pigment, Titanium dioxide and Aluminium lakes. Identification of the product by the manufacturer and therefore act as an aid for existing GMP procedures.

- ❖ Reinforcement of brand imaging and reduction in product counterfeiting.
- ❖ Identification of the product by patients by using colorants.

Colorants for film coating are having, in more or less amount, property of opacifier. So they would give protection to active ingredients in presence of light. Colorants are mainly classified in to three parts. Sunset yellow, tartrazine, erythrosine are examples of Organic

dyes and their lakes. Iron oxide yellow, red and black, titanium dioxide, talc are the examples of Inorganic colours. Anthocyanins, riboflavin and carmine are the examples of natural colours.

6) FLAVORS AND SWEETENERS are added to mask unpleasant odours or to develop the desired taste. For example, aspartame, various fruit spirits (organic solvent), water soluble pineapple flavour (aqueous solvent) etc.

7) ANTIOXIDANTS are incorporated to stabilize a dye system to oxidation and colour change. For example oximes, phenols etc.

8) ANTIMICROBIALS/PRESERVATIVES are added to put off microbial growth in the coating composition. Some aqueous cellulosic coating solutions are mainly prone to microbial growth, and long-lasting storage of the coating composition should be avoided. For example alkylisothiazolinone, carbamates, benzothiazoles etc.^[65-74]

PREFORMULATION STUDIES DESCRIPTION

Table No. 7.1: Description of Linezolid.

Sr. No.	Tests	Results
1.	Color	White
2.	Odor	Unpleasant
3.	Nature	Powder
4.	Taste	Bitter

Discussion

The color, odor, nature and taste of the API were evaluated. It was found to be as per the monograph.

MELTING POINT

Melting point of linezolid was determined using open capillary method. The melting point was found out to be 324°C which is in range.

7.1.1 SOLUBILITY

Table 7.2: Solubility of drug in different solvent

Description term	Solubility
Freely soluble	0.1 M NaOH
Sparingly	Water & Methanol
Slightly	0.1 mol/L HCL & ethanol

Discussion

The results revealed that the drug was soluble in water, methanol and ethanol.

7.1.2 DRUG - EXCIPIENT COMPATIBILITY STUDY

Table 7.3: Excipient Compatibility Study.

Sr. No.	Composition	Description		
		Initial Period	2 nd Week	4 th Week
1.	Linezolid + Magnesium stearate	White powder	NCC	NCC
2.	Linezolid + Starch	White to off white powder	NCC	NCC
3.	Linezolid + Microcrystalline Cellulose	White to off white powder	NCC	NCC
4.	Linezolid + Colloidal anhydrous silica	White powder	NCC	NCC
5.	Linezolid + Cross carmellose sodium	White powder	NCC	NCC
6.	Linezolid + Sodium Lauryl Sulphate	White powder	NCC	NCC

Note: NCC – No Characteristic Change

Discussion

From the drug excipients compatibility study, it was observed that there was no change between drug and excipients. Thus it was concluded that the excipients selected for the formulation were compatible with Linezolid.

spectrometer in the wavelength region of 4000-400 cm^{-1} . The procedure consisted of dispersing a sample (drug alone) in KBr & compressing into discs by applying a pressure of 5 tons for 5 minutes in a hydraulic pressure. The pellet was placed in the light path & the spectrum was obtained.

FTIR

Identification of drug purity through FTIR

Infrared spectra were taken by using KBr pellets technique using a Perkin Elmer IR (spectrum Two TM)

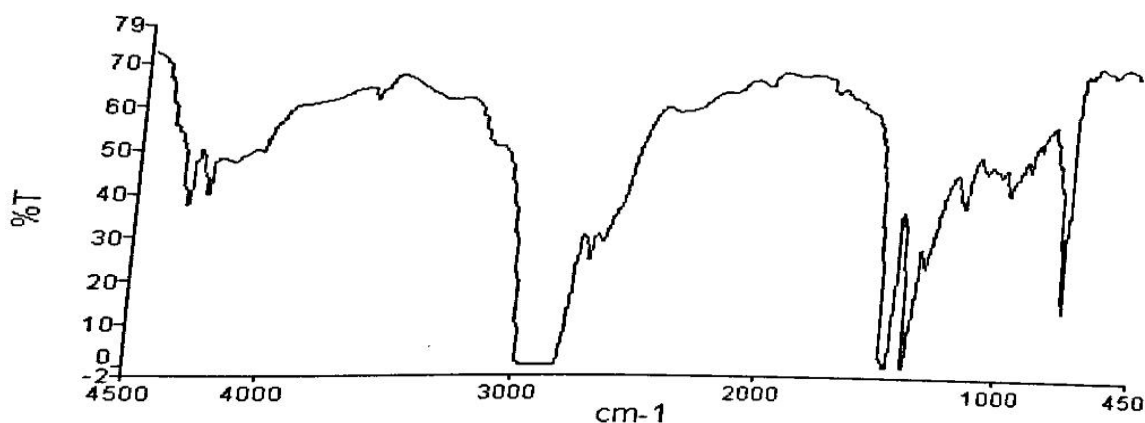


Figure 7.1: FTIR of pure drug (Linezolid) Reference standard IP 2018.

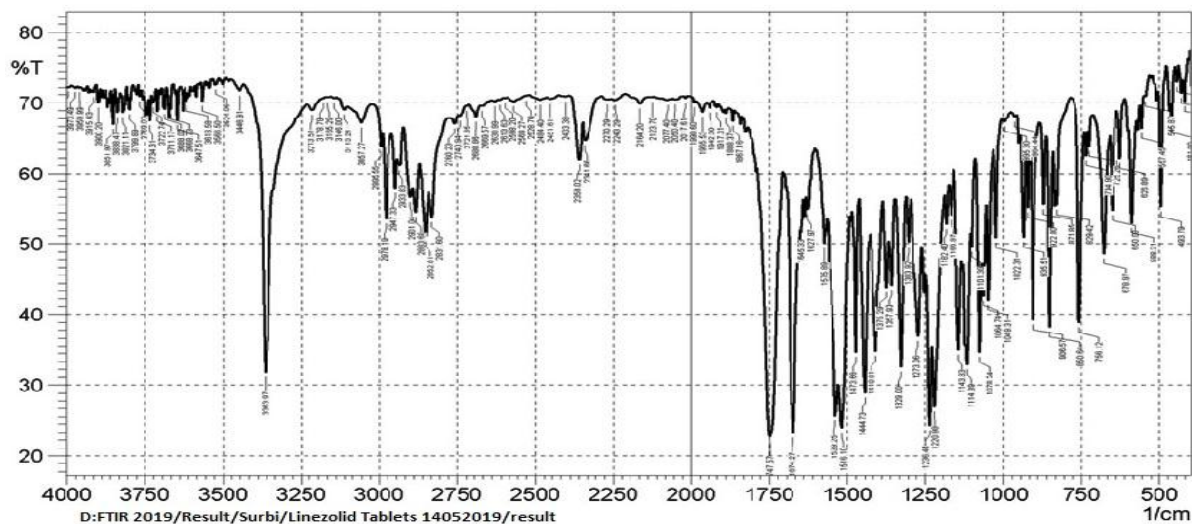


Figure 7.2: FTIR spectra of Linezolid.

Table 7.4: Characteristic IR peaks of Linezolid.

Sr. No.	Reference peaks (cm ⁻¹)	Obtained peaks (cm ⁻¹)	Functional group
1.	3100-3400	3363	N-H stretching
2.	2820-3000	2818	C-H stretching
3.	1760-1820	1335	C=O bending
4.	1550-1640	1452	N-H stretching

7.1.3 PREPARATION OF STANDARD CURVE OF LINEZOLID

The standard curve of linezolid was prepared using methanol. The data of absorbance values for all the dilution in different solvent. The UV scan the standard solution between 200-400 nm with absorption maxima at

250 nm. The graph was plotted between concentration and absorbance taking points that seemed to be coincide within the linear line and it was found that it follows the beer's law in a concentration range of 7-9ug/ml in a methanol.

Table 7.5: Drug absorbance data for standard graph in different media.

Concentration (µg/ml)	Mean absorbance (at λ _{max} 250 nm) In Methanol
0	0
1.0	0.048
2.0	0.055
3.0	0.078
4.0	0.101
5.0	0.133
6.0	0.150
7.0	0.172
8.0	0.191
9.0	0.207
10.0	0.224

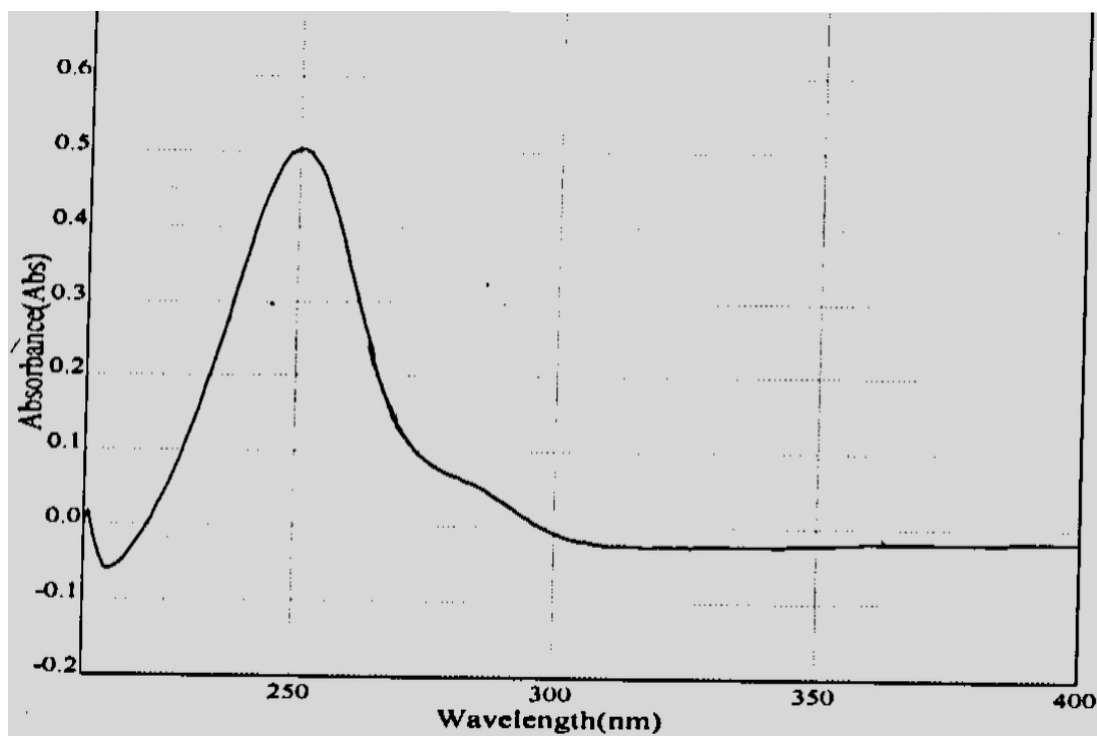


Figure 7.3: Calibration curve at 250nm.

Standard curve

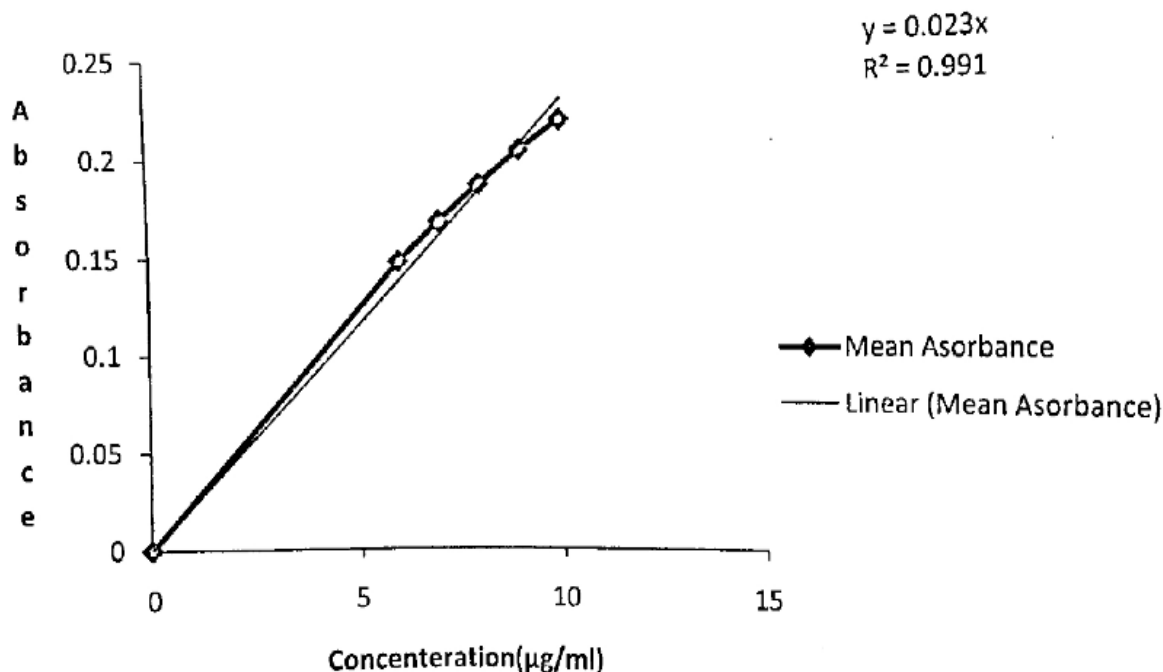


Figure 7.4: Calibration graph of Linezolid in Methanol.

Line of equation: $Y = Mx + C$

Where, Y is absorbance

M is the slope

X is the concentration of linezolid in mcg/ml

$y = 0.0235x + 0.256$

Beer's range: 0-10 $\mu\text{g/ml}$

R2 value: 0.9917

λ_{max} : 250 nm

7.2 EVALUATION OF PRECOMPRESSION PARAMETERS

Table 7.6: Pre-compression Parameters of Linezolid Powder.

Formulation Code	Bulk Density (g/ml)	Tapped Density (g/ml)	Compressibility index (%)	Hausner's ratio
SAD-01	0.54	0.51	7.27±0.2	1.07±0.3
SAD-02	0.50	0.47	6.00±0.3	1.06±0.4
SAD-03	0.51	0.48	5.88±0.6	1.06±0.2
SAD-04	0.50	0.47	6.00±0.4	1.06±0.1
SAD-05	0.51	0.48	5.88±0.4	1.06±0.2

7.2.1 Bulk density of Linezolid Powder

Table 7.7: Bulk density of Linezolid Powder

FormulationCode	BulkDensity(g/ml)
SAD-01	0.54
SAD-02	0.50
SAD-03	0.51
SAD-04	0.50
SAD-05	0.51

Discussion

• The bulk density of all formulations was measured by using bulk density apparatus. The bulk density was in the range of 0.50±0.2 to 0.55±0.1 g/ml.

7.2.2 Tapped density of Linezolid Powder

Table 7.8: Tapped density of Linezolid Powder

FormulationCode	TappedDensity(g/ml)
SAD-01	0.51
SAD-02	0.47
SAD-03	0.48
SAD-04	0.47
SAD-05	0.48

Discussion

• The tapped density of all formulations was measured by using tapped density apparatus. The tapped density was found in the range of 0.47±0.2 to 0.51±0.3 g/ml.

7.2.3 Compressibility of Linezolid Powder

Table 7.9: Compressibility of Linezolid Powder

FormulationCode	Compressibility index (%)
SAD-01	7.27±0.2
SAD-02	6.00±0.3
SAD-03	5.88±0.6
SAD-04	6.00±0.4
SAD-05	5.88±0.4

Discussion

- The compressibility index was in the range of 5.88±0.4 to 7.27±0.2 %. It proved that the flow behaviors and compressibility of the granules are good.

Hausner's ratio of Linezolid Powder

Table 7.10: Hausner's ratio of Linezolid Powder

FormulationCode	Hausner's ratio
SAD-01	1.07±0.3
SAD-02	1.06±0.4
SAD-03	1.06±0.2
SAD-04	1.06±0.1
SAD-05	1.06±0.2

Discussion

- The hausner's ratio lies in the range of 1.06±0.1 to 1.07±0.3. Hence the flow properties of all formulations were good.

7.3. EVALUATION OF POST COMPRESSION PARAMETERS

Table 7.11: Evaluation of Linezolid-600 mg Uncoated Tablets.

Formulation Code	Thickness (mm)	Hardness (kg/cm ²)	Weight Variation (%)	Friability (%)	Assay (%)
SAD-01	5.90± 0.014	5.00	872±0.19	0.23	95.5
SAD-02	6.00± 0.010	3.20	868±1.20	0.57	103.16
SAD-03	5.90± 0.026	5.00	870±2.30	0.40	100.00
SAD-04	5.90 ± 0.022	2.50	879±0.40	0.86	101.35
SAD-05	5.93 ± 0.010	6.45	873±0.20	0.32	104.00

Discussion

General Appearance

The formulated tablets were evaluated for their organoleptic characters. The tablets were caplet in shape and white in color and having break line at one side. All the tablets showed elegance in appearance.

Thickness

Thickness of the tablets was found to be in the range of 5.90± 0.014 mm to 6.00± 0.010 mm. The results showed that the thickness of all formulated tablets was found to be uniform.

Hardness

The hardness of the tablets was measured by Monsanto hardness tester. The hardness of all the formulations was found to be in the range of 2.50 to 6.45 kg/cm². The hardness of formulation SAD-02 & SAD-04 were not under acceptance criteria.

Table 7.12: Hardness of tablet of formulation SAD-01 to SAD-05.

FORMULATION	HARDNESS (kg/cm ²)
SAD-01	5.00
SAD-02	3.20
SAD-03	5.00
SAD-04	2.50
SAD-05	6.45

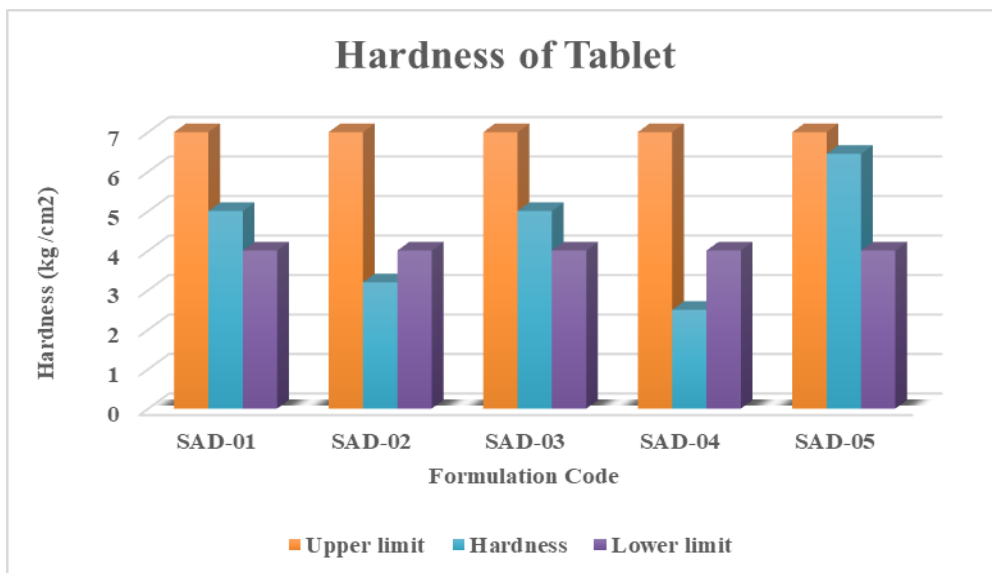


Figure 7.5: Graphical representation for Hardness of linezolid tablet of all formulation (SAD-01 to SAD-05).

To improve the hardness of the tablet, procedure of granulation was changed for 5th trial. Quantity of starch for paste and mixing were same as SAD-04 but inlet and outlet temperature of FBD was increased (70 and 60^o C respectively). Due to more heat of FBD, granules become harder as compared to other formulations which was determined by the end point method of drying.

Weight variation

Twenty tablets of each formulation were selected for weight variation test. The accepted percentage deviation was ±5.0 % for 875 mg weight tablets. The results showed that weight variation was ranging from 868±1.20 to 879±0.40 mg. It was within the I.P. limit and all the tablets passed the weight variation test.

Friability test

Friability test was carried out by Roche friabilator. The maximum weight loss should be not more than 1%. The maximum and minimum friability values among 5 formulations were found to be in the range of 0.23 to 0.86% respectively. Hence the friability of formulation SAD-04 was passed but not uniform as compared to other formulations.

Table 7.13: Data for Friability of tablet.

Formulation Code	Friability (%)
SAD-01	0.23
SAD-02	0.57
SAD-03	0.40
SAD-04	0.91
SAD-05	0.32

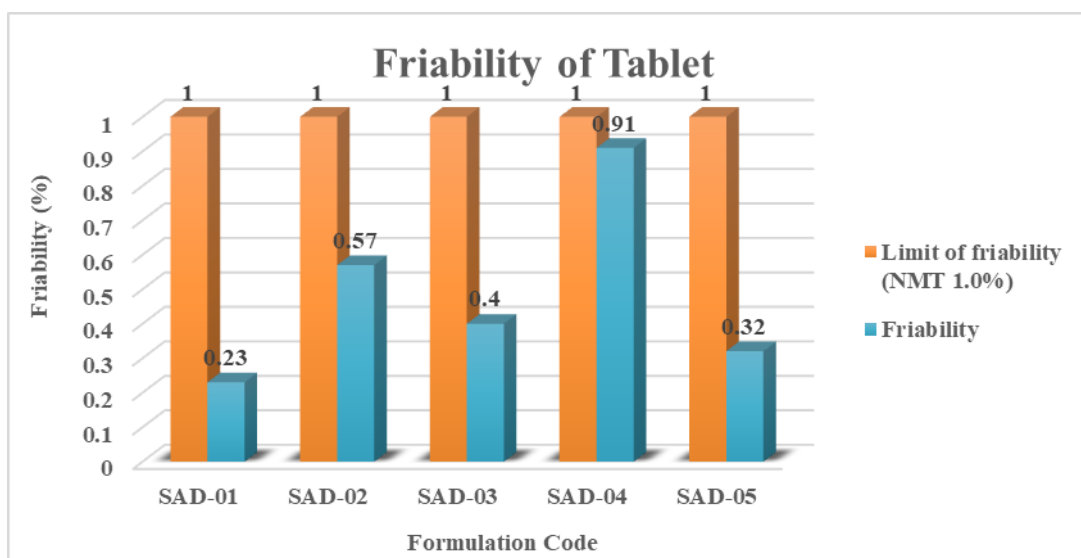


Figure 7.6: Graphical representation for Friability of linezolid tablet of all formulation (SAD-01 to SAD-05)

To improve the friability of tablets, formulation SAD-05 was prepared in which some internal parameters of FBD

for drying and quantity of SLS during mixing in RMG and blending were changed.

Drug content

The assay of Linezolid-600 mg film coated tablets were found in the range between 95.5 and 104.000%. The acceptable limit of Linezolid-600 mg content as per I.P. is 90 to 110%. The results revealed that the assay of Linezolid-600 mg was within the acceptable limit.

Table 7.14: Data for Assay of Linezolid Tablet.

FORMULATION	Assay (%)
SAD-01	95.5
SAD-02	103.16
SAD-03	100.00
SAD-04	101.35
SAD-05	104.00

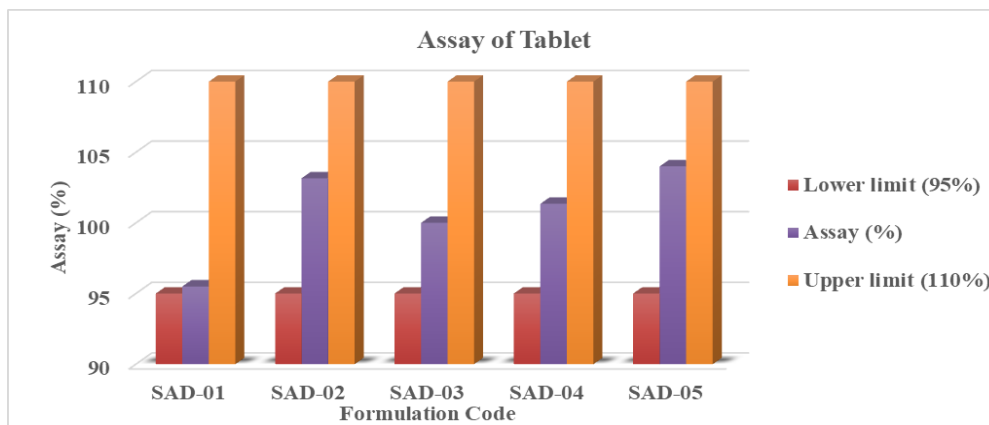
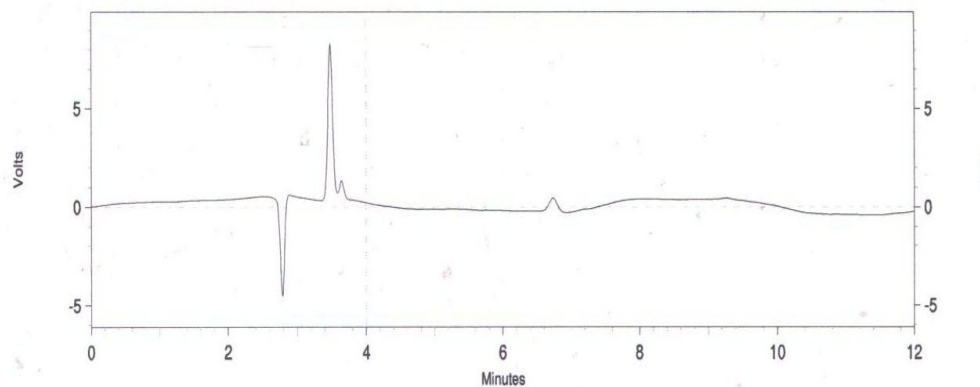


Figure 7.7: Graphical Representation for Assay (%) of Linezolid tablet.

GRAPH REPRESENTATION FOR ASSAY OF LINEZOLID FORMULATIONS (SAD-01-SAD-05)

Sample Name: Linezolid Blank Solution
 Data File: D:\HPLC 2019\Result\Surbi\Linezolid Tablet 14052019.rsl\Linezolid Blank Solution
 Method: D:\HPLC 2019\Method\linezolid Tab Assay.met
 Run Time: 5/14/2019 7:25:14 PM (GMT +05:30)

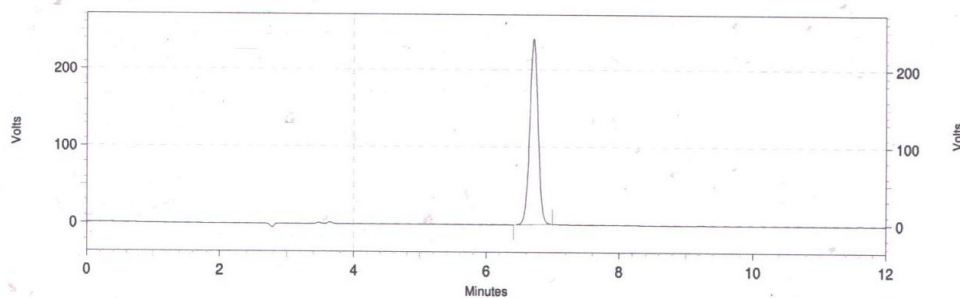


VWD: Signal
 A, 250 nm
 Results

Name	Retention Time	Area	Area %	Height	Height %
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Table 7.8: Graphical Representation for Blank Solution.

Sample Name: Linezolid Std
 Data File: D:\HPLC 2019\Result\Surbi\Linezolid Tablet 14052019.rslt\Linezolid Std
 Method: D:\HPLC 2019\Method\linezolid Tab Assay.met
 Run Time: 5/14/2019 7:38:15 PM (GMT +05:30)



VWD: Signal
 A, 250 nm
 Results

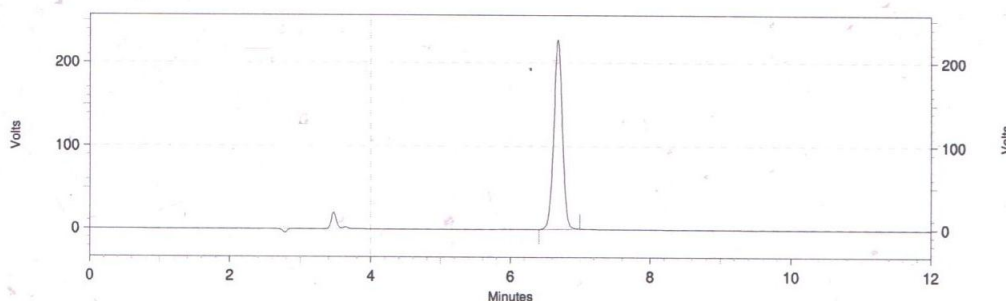
Name	Retention Time	Area	Area %	Height	Height %
	6.713	35759747	100.00	4040901	100.00
Totals		35759747	100.00	4040901	100.00

Table 7.9: Graphical Representation for Standard Solution.

Formulation SAD-01, during this formulation starch was used 3 % for paste formation and 2% was used for mixing whereas SLS was used 50-50% during mixing in RMG and for blending respectively.

After the granulation process, blend powder was proceed for compression of tablet in which all the in-process parameters were under acceptance criteria but dissolution of the tablet was less i.e 95.50% according to the acceptable data.

Sample Name: Linezolid Tabs Test Solution (F-140519001)
 Data File: D:\HPLC 2019\Result\Surbi\Linezolid Tablet 14052019.rslt\Linezolid Test Solution
 Method: D:\HPLC 2019\Method\linezolid Tab Assay.met
 Run Time: 5/14/2019 7:51:13 PM (GMT +05:30)



VWD: Signal
 A, 250 nm
 Results

Name	Retention Time	Area	Area %	Height	Height %
	6.683	33510765	100.00	3814560	100.00
Totals		33510765	100.00	3814560	100.00

Figure 7.10: Assay of Formulation No 1 (Sad-01)

Then it was proceed for coating, in which the tablet was coated from aqueous based solvent that is water where

many problems were occurred during water coating such spore formation, twinning of tablet.

PROBLEM OCCUR DURING COATING OF TABLET FROM AQUEOUS COATING



Figure 7.11: Twinning of Tablet.



Figure 7.12 Spores formation of Tablet.

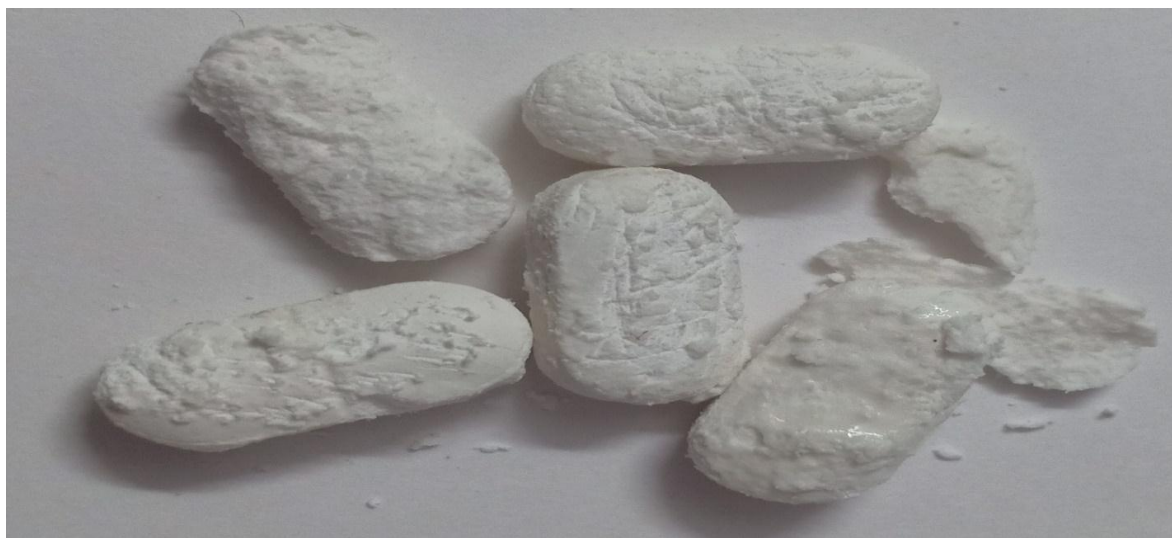
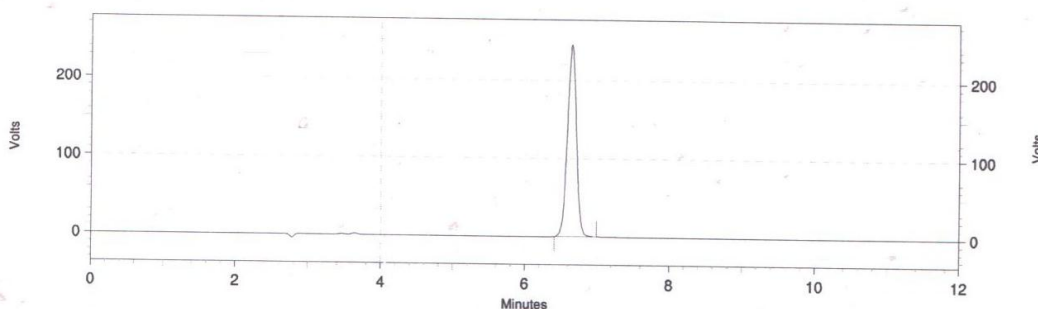


Figure 7.13: Capping & Melting of Tablet.

To improve the dissolution and coating of the tablet, formulation SAD-002 was formed in which percentage of starch were changed for paste formation as well as for mixing.

Sample Name: Linezolid Tabs Test Solution (F-140519003)
 Data File: D:\HPLC 2019\Result\Surbi\Linezolid Tablet 14052019.rslt\Linezolid Test Solution
 Method: D:\HPLC 2019\Method\linezolid Tab Assay.met
 Run Time: 5/14/2019 8:17:09 PM (GMT +05:30)



VWD: Signal
 A, 250 nm
 Results

Name	Retention Time	Area	Area %	Height	Height %
	6.647	35846759	100.00	4124088	100.00
Totals		35846759	100.00	4124088	100.00

Figure 7.14: Assay of Formulation No 2 (Sad-02).

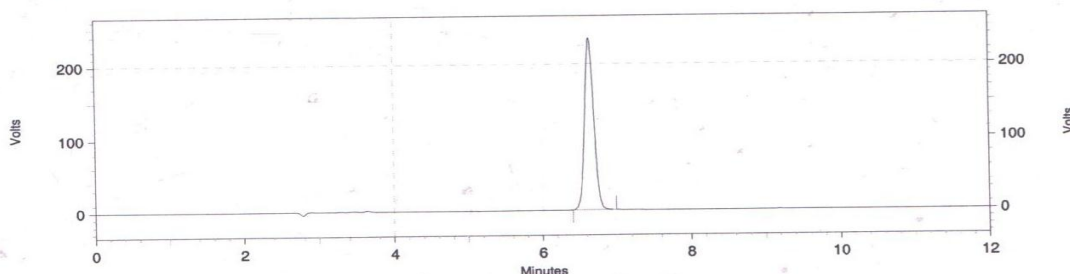
It was taken as 2% and 3% for paste formation and for mixing respectively. Due to these changes, the hardness of the tablet was reduces which was not under acceptance criteria during in-process control. Whenever hardness of tablet comes with in specification, the dissolution of the tablet was failed and vice versa.

tablet. Same procedure is used only the ratio of starch was changed where starch was used as 2.5% and 2.5% for paste and mixing respectively. After that the wet mass get dried and then was shifted through 20#.

3rd trial was formulated **SAD-03**, to improve the hardness, dissolution release profile and coating of the

The hardness of the tablet was passed & under acceptance criteria but due to large granules, dissolution of the core tablet was failed.

Sample Name: Linezolid Tabs Test Solution (F-140519005)
 Data File: D:\HPLC 2019\Result\Surbi\Linezolid Tablet 14052019.rslt\Linezolid Test Solution
 Method: D:\HPLC 2019\Method\linezolid Tab Assay.met
 Run Time: 5/14/2019 8:43:10 PM (GMT +05:30)



VWD: Signal
 A, 250 nm
 Results

Name	Retention Time	Area	Area %	Height	Height %
	6.647	34268308	100.00	3944407	100.00
Totals		34268308	100.00	3944407	100.00

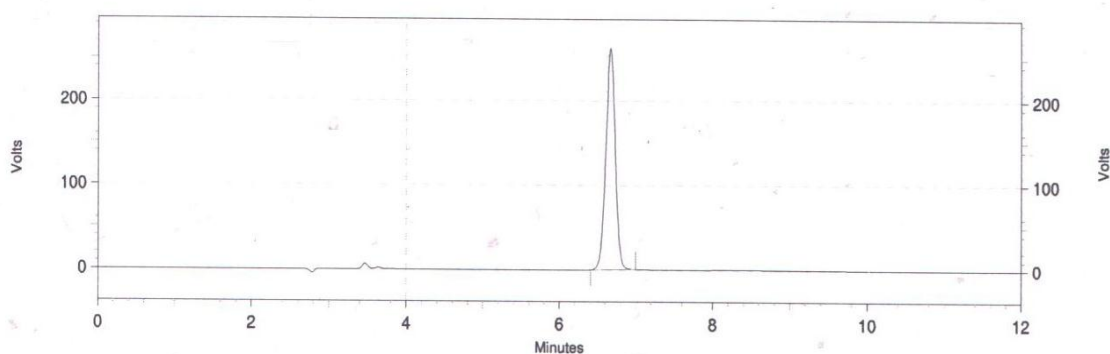
Figure 7.15: Assay of Formulation No 3 (Sad-03)

So to improve the dissolution of the core tablet, the granules were passed through 14# mesh and some extra material were added by which the hardness and dissolution were passed but the final assay was decreased as according to other two last formulations.

Again to improve hardness and dissolution of the tablet without addition of extra granules, the coating solvent for

the next trial (**4th formulation**) was changed. A new formulation was prepared SAD-004, in which the coating was done from non-aqueous solvent i.e IPA (Isopropyl Alcohol). During granulation process, starch was used in the ratio of 2% and 3% and SLS was used in the ratio of 70% and 30%.

Sample Name: Linezolid Tabs Test Solution (F-140519002)
 Data File: D:\HPLC 2019\Result\Surbi\Linezolid Tablet 14052019.rsl\Linezolid Test Solution
 Method: D:\HPLC 2019\Method\linezolid Tab Assay.met
 Run Time: 5/14/2019 8:04:11 PM (GMT +05:30)



VWD: Signal

A, 250 nm

Results

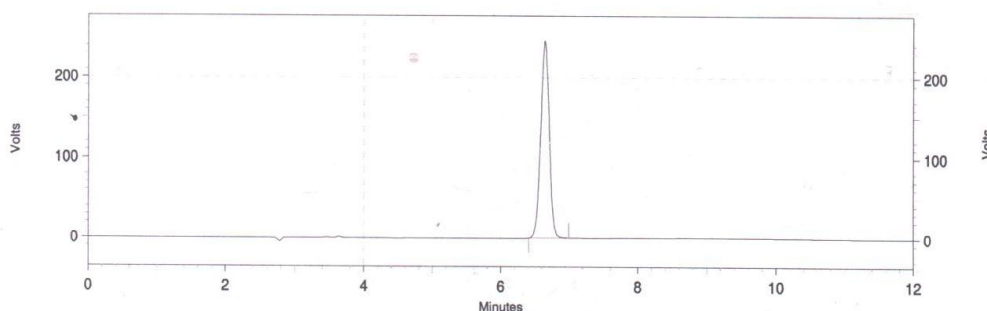
Name	Retention Time	Area	Area %	Height	Height %
	6.667	38448555	100.00	4400360	100.00
Totals		38448555	100.00	4400360	100.00

Figure 7.16: Assay of Formulation No 4 (SAD-04)

During granulation process, starch was used in the ratio of 2% and 3% and SLS was used in the ratio of 70% and 30% and some extra quantity of SLS was added to improve the dissolution release profile which lighten the weight of the powder and help to disintegrate the tablet easily. By addition of SLS, the dissolution of tablet was passed but it minimizes the hardness of the tablet.

To improve the hardness, dissolution & coating appearance, **5th trial SAD-05** was formed using same formulations, where starch was used in the ratio of 2% and 3% and SLS was used in the ratio of 20% and 80% for mixing & blending respectively. Temperature of FBD was changed according to other formulations (inlet and outlet temperature), which were taken as 70^o C & 60^o C respectively.

Sample Name: Linezolid Tabs Test Solution (F-140519004)
 Data File: D:\HPLC 2019\Result\Surbi\Linezolid Tablet 14052019.rsl\Linezolid Test Solution
 Method: D:\HPLC 2019\Method\linezolid Tab Assay.met
 Run Time: 5/14/2019 8:30:09 PM (GMT +05:30)



VWD: Signal

A, 250 nm

Results

Name	Retention Time	Area	Area %	Height	Height %
	6.643	35864436	100.00	4123475	100.00
Totals		35864436	100.00	4123475	100.00

Figure 7.17: Assay of Formulation No 5 (SAD-05)

SLS makes the powder weight lighten which is useful to disintegrate the tablet easily as well as help in fast dissolution and high temperature increase the hardness of tablet.

The core tablet passes all the in-process parameters including hardness, disintegration, friability and dissolution release profile. The hardness & assay was found to be 6.45 kg/cm² & 104.0% respectively which is under acceptance criteria and is better than other above four formulations. Then compressed tablet was proceed for coating of tablet where coating was done with non-aqueous solvent. Film coating from IPA was done successfully and no defect were found after coating of tablet in formulation SAD-05.

Formulation SAD-05 passes all the parameters during its formulation and was taken as ideal formulation.