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Review on Formulation and Evaluation of Immediate Release tablets of Bedaquiline

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ABSTRACT

Bedaquiline, an anti-tubercular agent used in the treatment of multidrug-resistant tuberculosis (MDR-TB). Due to its low aqueous solubility and poor bioavailability, formulation development focused on enhancing the dissolution rate of bedaquiline to achieve rapid therapeutic action. Tablets were prepared using wet granulation method, employing various solubility-enhancing excipients such as surfactants and disintegrants. The prepared formulation was evaluated for pre-compression parameters, including bulk density, tapped density, and flow properties, as well as post-compression parameters such as hardness, friability, weight variation, disintegration time, and in-vitro drug release profiles.

The optimized formulation exhibited a disintegration time of less than 3 minutes and a drug release of over 85% within 30 minutes, confirming its suitability for immediate -release purposes. Compatibility studies using Fourier-transform infrared (FTIR) spectroscopy indicated no significant interactions between bedaquiline and excipients. Stability studies conducted as per ICH guidelines revealed no significant changes in physical or chemical properties, ensuring the formulation's robustness. The findings suggest that the formulated immediate-release bedaquiline tablets are a promising strategy to improve patient compliance and achieve rapid therapeutic efficacy in MDR-TB treatment.

Key words: Bedaquiline, Multi-Drug -Resistant tuberculosis MDR-TB, (FTIR)Fourier-transforminfrared spectroscopy

I. INTRODUCTION

Tuberculosis is a disease that results from infection with the bacteria Mycobacterium tuberculosis. It most commonly affects the lungs but can also affect other areas of the body. The infection can be active or latent, withapproximately 10% of latent infections progressing to active status. The disease is spread by droplets from speaking, coughing, and sneezing. In the past, the disease was colloquially known by the name consumption. Diagnosis is via chest X-ray, micro bacterial cultures, and tuberculin skin test [1].

MULTI-DRUG-RESISTANT TUBERCULOSIS (MDR-TB)

Multi-drug–resistanttuberculosis (MDR-TB) is a form of TB disease caused by a strain of M. Tuberculosis complex that is resistant to rifampicin and isoniazid.[2]

This contagious infection contributes to a major cause of illness and deaths occurring in India [3]. India has the highest global burden of TB which accounts for almost a quarter of cases of TB from all over the world [4]. The occurrence of drug-resistant strains is one of the major issues with pharmacotherapy of this disease. Resistance to only Rifampicin is known as rifampicin-resistant TB (RR-TB). Multidrug-resistant TB (MDR-TB) is characterized by resistance to rifampicin (R) as well as isoniazid (H) with or without resistance to first-line antitubercular drugs [5]. Resistance to rifampicin, isoniazid, and any of the fluoroquinolone (FQ) along with at least any one of the group A drugs is resistance to all medications is known as totally drug-resistant TB (TDR-TB) [6]. It takes years and costs a lot to treat drug-resistant TB (DRTB) as compared to treating ordinary diseases.

As a result, novel Anti-tubercular medicines with a distinct mode of action are urgently needed. Rifapentine, an antitubercular drug was approved in 1998. After this, no other antitubercular drug was approved for a long duration. The US Food and Drug Administration (FDA) on 28 December 2012 granted accelerated

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approval to Johnson and Johnson'sdrug bedaquiline to treat resistant tuberculosis (TB) [7]. There are numerous medications for better management of TB, Bedaquiline is one such drug that is first in class and can help in the better management of TB. Initially, this drug had been available to individual patients under "compassionate use" with pre-approval of the Drug Controller General of India (DCGI) [8]. Now, the National Tuberculosis Elimination Program (NTEP)[8]. WithProgrammatic Management of Drug-Resistant TB (PMDT) services has approved bedaquiline-containing regimens for the treatment of DRTB and bedaquiline has been rolled out for all DRTB centers in India. Every registered medical practitioner in India must know about bedaquiline in detail which is an important drug in the treatment of DRTB [9].

Multidrug-resistant-tuberculosis medications:

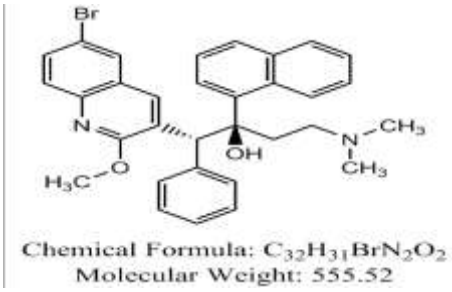
World Health Organization released a new treatment for multidrug-resistant/rifampicin-resistant tuberculosis (MDR/RR-TB) guideline. The main novelty of this update is two new recommendations (i) a 6-month treatment regimen composed of bedaquiline, pteromalid, linezolid (600 mg), and moxifloxacin (BPaLM) is recommended in place of the 9-month or longer (18-month) regimens in MDR/RR-TB patients, now including extensive pulmonary TB and extrapulmonary TB (except TB involving central nervous system, miliary TB and osteoarticular TB); (ii) the use of the 9-month all-oral regimen rather than longer (18-months) regimen is suggested in patients with MDR/RR-TB . The new guidelines represent a milestone in MDR/RR-TB treatment landscape, setting the basis for a shorter, all-oral, more acceptable, equitable, and patient-centered model for MDR/RR-TB management [10,11]

NEWER DRUGS
Bedaquiline
Delamanid
Linezolid
Pteromalid

FLUOROQUINOLONES
Levofloxacin
Moxifloxacin

INJECTABLE AGENTS
Amikacin
Kanamycin
Capreomycin

CHEMISTRY:



Bedaquiline is a diarylquinoline having alcohol and amine groups on its side chains. its antimycobacterial effect is due to these two side chains. It has a quinolinic central heterocyclic nucleus [12]. Molecular formula: C32H31BrN2O2. Molecular weight: 555.504 g/mol. ATC Code: J04AK05 –Bedaquiline [13]. Fumaric acid in ratio 1:1 isused with bedaquiline to prepare bedaquiline fumarate [14]. In enantiopure bedaquiline, there are two chiral centers in it. There is a mixture of four isomers. Bedaquiline is isolated from it. It's the most effective stereoisomer against several mycobacterial strains. The configuration of bedaquiline is identified through conformational analysis along with x-ray diffraction researches [15].

DRUG EXCIPIENT PROFILE
BEDAQUILINE:
SUMMARY:

BEDAQUILINE is a diarylquinoline antimycobacterial used in combination with other antibacterials to treat pulmonary multi drug resistant tuberculosis

BRAND NAME:
Sirturo
GENERIC NAME:
BEDAQUILINE

DRUG BANK ACCESSION NUMBER:
DB08903
HALF LIFE:
164 days.

BACKGROUND

Bedaquiline is a bactericidal antimycobacterial drug belonging to the class of diarylquinoline. The quinolinic central heterocyclic nucleus with alcohol and amine side chains is responsible for bedaquiline-mediated antimycobacterial activity. Bedaquiline to treat pulmonary MDR-TB, following favourable results

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in multiple pre-clinical and clinical studies. It is the first drug that was approved in the last 40 years by the FDA for TB unresponsive to current treatments on the market Currently, bedaquiline is the anti-TB drug and must only be used in an appropriate combination regimen [16].

MECHANISM OF ACTION

Bedaquilinepossesses antimycobacterial activity that is both distinct and specific. It inhibits mycobacterial adenosine triphosphate (ATP) synthase's proton pump. Prokaryotic as well as eukaryotic cells require the production of ATP for cell life. It is done with the help of ATP synthase. Bedaquiline inhibits the generation of ATP. It binds to mycobacterial ATP synthase at subunit c which is oligomeric and proteolipid. As a result, it causes bacterial death. Bedaquiline binds to mycobacterial ATP synthase with more than 20,000 times more affinity than it binds to human mitochondrial ATP synthase. It is the reason for specific action in mycobacterium only and minimum host cell damage [17].

Bedaquiline
↓
Binds to c subunit of ATP synthase (enzyme complex)
↓
Inhibits proton pump function of ATP synthase
↓
Disruption of ATP production
↓
Energy depletion in Mycobacterium tuberculosis
↓
Cell death

Antimicrobial spectrum

By blocking mycobacterial ATP synthase, bedaquiline kills dormant as well as actively reproducing mycobacteria. It inhibits drug-resistant mycobacterium along with drug-sensitive mycobacterium. Bedaquiline has a substantial inhibitory impact on a wide range of nontuberculous mycobacteria (NTM), including Mycobacterium avium, Mycobacterium ulcers, Mycobacterium abscesses, and Mycobacterium intracellular**.** Bedaquiline has a mild inhibitory effect on Gram-positive bacteria and Gram-negative bacteria [18].

IMMEDIATE RELEASE OF BEDAQUILINE

The multi-source product is a white to off - white, round uncoated tablet, they are biconvex (rounded on top and bottom). The objective was to develop stable, robust, IMMEDIATE release dosage form. Wet granulation was selected as method of product manufacture to achieve the desire powder flowability, powder containment, and satisfactory product performance [19].

Composition

Each IMMEDIATE-release tablet typically containsBedaquiline fumarate equivalent to 100 mg of bedaquiline [20].

Indication

Bedaquiline is indicated for the treatmentof:
Pulmonarymultidrug-resistant tuberculosis (MDR-TB) as part of combination therapy with other antitubercular agents.

Dosage and Administration

Adults and Adolescents (≥12 years and ≥30 kg):
First 2 weeks: 400 mg once daily.
Weeks 3 to 24: 200 mg three times per week (at least 48 hours between doses).
Must be taken with food to enhance absorption [21].

Common Side Effects

Nausea
Arthralgia
Headache
Increased liver enzymes
QT prolongation [22]

Contraindications

•Clinically significant ventricular arrhythmia.
•A QTcF interval of >500 Ms (confirmed by repeat ECG).
•Severe liver disease.
•Use with other QT prolonging drugs
•A history of torsade de pointes
•A history of congenital long QT syndrome
•A history of hypothyroidism and bradyarrhythmia's
•A history of uncompensated heart failure
•Serum calcium, magnesium or potassium levels below t [23].

Important Considerations:

ECG should be obtained before initiation of treatment, and at least two, 12 and 24 weeks after starting treatment with bedaquiline. ECGs should be done at least monthly (more...) The QT interval must always be corrected for heart rate [24].
Hepatic Effects: Liver test abnormalities occur in 8% to 12% of patients treated with multiple drug regimens that include bedaquiline Elevations in

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liver enzymes have been observed. Regular monitoring of liver function tests is advised [25].
Drug Interactions: Caution is advised when co-administering bedaquiline with other QT-prolonging drugs or strong CYP3A4 inhibitors/inducers [26].

MATERIALS AND METHODS: Bedaquiline, sodium starch glycolate crospovidone microcrystallinecellulose, Magnesiumsterate.

Pre formulating studies:

The Pre-formulation studies are the first step in the rational development of dosage form of a drug substance. The objective of pre-formulation studies is to develop a portfolio of information about the drug substance, so that this information is useful to develop formulation.
Pre-formulation can be defined as investigation of physical and chemical properties of drug substance alone and when combined with excipients.

The powder blends were evaluated for angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio etc. as following
Bulk Density: Bulk density is defined as the ratio of total mass of powder to the bulk volume of powder. Bulk density is calculated according to the formula which is mentioned below. RT56
Bulk Density = Mass of powder/Volume of powder
Tapped Density: It is the ratio of total mass of the powder to the tapped volume of the powder
Tapped Density = mass of powder(mg)/volume of tapped power(ml)
Angle of Repose Angle: It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane.

It can be expressed as fallows
tan (è) = h/r
Where, (è) = angle of repose
h = height in cms,
r = radius in cms.

Carr's Index & Hausner's Ratio: Carr's index and Hausner's ratio measure the propensity of powder to be compressed and the flow ability of powder. Carr's index and Hausner's ratio can be calculated from the bulk and tapped density.
Carr's Index = Tapped density–Bulk density / Tapped density × 100
Hausner's Ratio = Tapped density / Bulk density

Sieving, Mixing & Lubrication: Bedaquiline was sieved through mesh 100 (#100); mannitol, microcrystalline cellulose PH 102, croscarmellose sodium and orange DC 100 PH were sieved through mesh 40 (#40). Bedaquiline was first mixed geometrically with mannitol and then with all other excipients manually in a polybag for 5 minutes.

Magnesium Stearate and Aerosol were sieved through mesh 60 (#60) and lubrication was done with the above mixed powder manually in a polybag for 45 seconds. The moisture content of the lubricated powder was observed in Denever digital moisture analyzer at 105°C. The pre-compression parameters of the bulk lubricated powder were performed using Electrolab Tapped Density Tester USP.
The pre compression parameters revealed good flow property of powder for both 0.2 and 0.3 mg of Bedaquiline tablets.

Compression: After performing the pre-compression parameters, the lubricated powder was subjected for punching using tablet punching machine. The average punch weight of the tablets was 110 mg. The hardness, thickness, weight variation and friability of the punched tablets were maintained in the desired range.

Preparation of immediate Release of Bedaquiline tablets:

Bedaquiline, Microcrystalline cellulose, and super disintegrants (sodium starch glycolate, crospovidone) were shift through sieve No.40 thoroughly mixed in a rapid mixer granulator for 10 Min. PovidoneK-30 Dissolved in sufficient quantity of water, used as a binder solution. Mix bedaquiline with fillers and disintegrants in a blender. Add the binder solution to the mixture to form a dump mass.Pass the dump mass through a sieve to produce granules. Granulation was done in rapid mixer granulator. Granules were dried in fluid bed dryer at 6065^0c till a LOD (loss on drying) of dried granules obtained not more than 2.5% w/w. Dried granules were passed through sieve No.24.

The dried granules were blended in a blender with microcrystalline cellulose and super disintegrants for 5mins which was already passed through sieve No 40. Above mixer was lubricated for 5mins with magnesium stearate which was already passed through sieve N60.
The lubricated granules were then compressed into tablets on a 16-station rotatory machine to get a tablet of 400mg weight.

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EVALUATIONOF IMMEDIATERELEASE OF BEDAQUILINE TABLETS:

1. Uniformity of weight:

Twenty tablets were selected at random from the lot, weighed individually and the average weight was determined. The percent deviation of each tablets weight against the average weight was calculated.

Hardness test:

The prepared tablets were subjected to hardness test28,38. It was carried out by using hardness tester and expressed in kg/cm2.

Friability test:

Friability is the measured of tablets strength Roche friabilator was used for testing the friability using the following procedure six tablets were weighted accurately and placed in the plastic chamber that revolves at 25 rpm, dropping the tablets at a reweighted and the percentage loss in weight was determined

% Friability = Initial Weight-Final Weight-Initial weight × 100

Content Uniformity Test: Ten Tablets accurately weighted and powdered a quantity of the powder equivalent to 10 mg of Bedaquiline was weighted accurately and dissolved in buffer solution. After filtration and sufficient dilution with phosphate buffer solution, sample were analysed UV spectrophotometrically at 282 nm against buffer solution as a blank

Disintegration Test: Tablets were taken and introduced in each tube of disintegration apparatus, and the tablets rack of the disintegration apparatus in to a 1-liter beaker containing 900 ml of distilled water and the time of disintegration was recorded. The discrimination between disintegration was done at room temperature and disk was not used for the study

Wetting Time: Five circular tissue paperof 10cm diameter are placed in Petri dish with 9.8 cm internal diameter. 10 ml of water added to Petri dish. A tablet is carefully placed on the surface of the tissue paper. Time required for water to reach upper surface of the tablet was noted as wetting time **of tablet defects**

Capping
Lamination
Chipping
Sticking
Picking
Cracking
Binding / Binding in the die
Edging / Flashing of tablet
Mottling
High friability
Weight Variation
Hardness Variation
Aging of tablets/ Loss of hardness
Protracted Hardness (Hardness increases with time)
Disintegration time too long
Uneven Breakage
Black Spot/Stain
Double Impression
Bisected/ Score line/ break line or imprint or logo not sharp or well-defined
Splitting of Layered tablets or layer separation

1. **Capping**

Capping is a term used to describe the partial or complete separation of the top or bottom crowns of a tablet from the main body of the tablet [1]. In other words, capping is a laminar splitting along the edge of the crown or band of a compressed tablet [2]. Generally, capping is a common tablet defect during tablet manufacturing.

Causes:

- Air-entrapment in the granular materials.
- Toodry granules.
- High quantity of fine powder materials in the granules.
- Presence of too much lubricant.
- Too soft granules

2. **Lamination:**

Lamination is the separation of a tablet into two or more distinct horizontal layers. It is a tablet defect in which a tablet splits or separates into layers.

Causes:

- High quantity of fine powder materials in the granules.
- Oily, elastic, or waxy excipients in granules.
- Air-entrapment in the granular material
- Presence of too much lubricant.

3. Chipping:

Chipping is the breaking of tablet edges during the pressing process or during the subsequent handling and coating.

Causes:

- Too dry granules.
- Too much or too low binding.
- Sticking on punch faces

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4.Sticking:

Sticking is a defect of the tablet where the tablet surface sticks to the punch face or adhesion of tablet material to the die wall during compression. Simply, sticking is the adherence of material to the faces of tablet press punches or dies after compression [2]. In sticking, the tablet surface sticks to the lower punch face but a small portion of the tablet surface is not detached or the pitted surface will not occur.

Causes:

- Excess moisture in granules.
- Inadequate lubrication.
- Too much binder.
- Too much hygroscopic excipients.
- Too much hygroscopic excipients.
- Sticky API or sticky excipient.

5.Packing:

Picking is the term used when a small amount of material from a tablet is sticking to and being removed from the tablet surface by a punch [1]. In other words, the removal of material from the surface of the tablet, and its adherence to the face of the punch is called picking.

Causes:

- Inappropriate dried granules.
- Inadequate lubrication.
- Too much binder.
- Too warm granules when compressing.

6.**Cracking:**

Cracking is a defect of tablets where small, fine cracks are observed on the upper and lower central surface of tablets, or very rarely on the sidewall. Easily visible in the tablet that contains pigment dye.

Causes:

- Large size of granules.
- Too dry granules.
- Inadequate binder.
- Rapid expansion of tablets.
- Elastic excipients in granules.
- Granulation too cold.

7.**Binding / Binding in the die**

Binding is a tablet defect where a tablet adheres, seizes, or tears in the die, or a film is formed on the die area and hindered the ejection of the tablet or splits during the molding/pressing process. The powder adheres to punch edges and dies punches may bind in dies difficult ejection.

Causes:

- Too moist granules.
- Excessive binder.
- Inadequate lubrication.
- Too hard granules for the lubricant to be effective.
- Granular material very abrasive and cutting into dies.
- Use of hygroscopic Ingredients Use of Hygroscopic Ingredients

8.Edging / Flashing of tablet

Edging is a defect of tablets in which burrs (raised edges)/ sharp edges appear on the final compressed tablet. This type of tablet defect also known as collaring of the tablet or flashing.

Causes:

- Waxy or elastic API or excipients in formulation.
- Moisture in granules.
- Higher compression pressure
- Poor design punch or wear punch.

9.Mottling

Mottling is the term used to describe an unequal distribution of color on a tablet, with light or dark spots standing out on an otherwise uniform surface [1]. This type of tablet defect occurs in tablet formulation with a dry coloring agent. Simply, mottling is a tablet defect where dark and light patches on the tablet surface occur.

Causes:

- The unequal particle size of the coloring agent or pigment.
- A colored drug used along with colorless or white-colored excipients.
- A dye migrates to the surface of granulation while drying.
- Improperly mixed dye, especially during 'Direct Compression'.
- Too small amount of colorant.
- Preferential absorption of soluble dye by component of mix.

10.Weight Variation

Weight variation is a common defect of tablets that occurs during tablet manufacturing where the average or individual weight of the tablet may be outside of the accepted limit.

Causes:

- Poor or erratic flow of granules from the hopper.

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- Improper amount of glidant
- Particle size ranges too wide.
- Improper drying.
- Abnormal uniform mixing of all excipients.
- Particle segregation as press RPMs increase
- Particle size not suitable for die diameter
- Improper tool setting of the machine. Hi-speed running of the machine.

11.Hardness Variation:

Tablet hardness does not remain constant but it has a range. Hardness variation is a common defect of tablets where individual hardness of tablets may be outside the accepted limit. Unlike weight variation, the hardness variation limit is determined by a prototype trial of that tablet.

Causes:

- Over-blending.
- Weight variation in granules filled in die.
- Improper mixing of lubrication
- Uneven die-fill

12.Aging of tablets/ Loss of hardness

It is a tablet defect where the hardness of the tablet decreases with time.

Causes:

- Over-lubrication.
- Tablets with microcrystalline cellulose (MCC) lose some hardness with time at high humidity, but most of the hardness is quickly regained at normal humidity.
- Compression force (pressure) too low
- Granulation too soft
- Moisture content too high

13.Uneven Breakage

Many tablets are designed to be broken into smaller dosages with functional score-line / break lines. It is a tablet defect where the tablet breaks unevenly into two parts.

Causes:

- Coarse granules.
- Improper mixing.
- Air-entrapment in the granular materials.
- Unequal sizes of granules.

14.Double Impression:

Double impression is one of the most common tablet problems. This defect is characterized by the presence of two or more imprints on a single tablet. It occurs when the tablet material is subjected to multiple impressions during compression, resulting in overlapping or duplicated markings.

Causes:

- The punches are not properly aligned within the die cavity.
- The rotation of lower punches is not properly controlled.
- Clearance between the punches and dies is not properly adjusted.

15.Black Spots:

Black spots on tablets refer to the dark or black-colored specks or dots on the tablet surface. These spots are considered defects and can negatively impact the appearance and quality of the tablets.

Causes:

- Foreign particles or impurities are in the raw materials used for tablet manufacturing.
- The equipment, compression tooling, and manufacturing environment are poorly cleaned.
- Inadequate lubricant mixing results in agglomeration.
- The tablet formulation is not properly granulated.
- Oxidation of formulation components or exposure to unfavorable conditions causes the formation of black spots or discoloration.

16.Inconsistent Thickness:

- Inconsistent thickness is one of the most common defects in tablets.
- It refers to variations in the tablet thickness within a batch or across different tablets.
- Inconsistent thickness can impact the overall quality, functionality, and appearance of the tablets.

17.Twining:

Twinning is one of the common tablet problems. It presents as two distinct tablets fused together. Twinning occurs when two tablets stick together during the compression process.

Causes:

- The tablet material and the punches and dies are not adequately lubricated.
- Formulations are not properly granulated, resulting in tablets with excessive porosity.
- Tablets with flat or parallel faces are more likely to experience twinning.
- Inconsistent compression force causes tablets to merge instead of being individually formed.

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- ❖ The ejection mechanism of the tablet press is not functioning optimally.

II. RESULT AND DISCUSSION:

Bedaquiline were prepared by Wet granulation method using differentconcentrationof microcrystalline cellulose, mannitol, croscarmellose sodium, magnesium stearate.

FTIR spectral study FT-IR spectroscopy study was carried out separately to find out the compatibility between the drug bedaquiline and Microcrystalline cellulose, mannitol, croscarmellose sodium. The FT-IR was performed for drug, the physical mixture of drug-polymer. The spectral obtained from FT-IR spectroscopy studies shows in andthe peaks obtained in the spectra of drug mixtures. This indicates that the drug was compatible with the formulation components. IR studies indicated no interaction between drug and polymers.

The International Pharmaceutical Excipients Council (IPEC) defines excipients as "Substances, other than the Active Pharmaceutical Ingredient (API) in finished dosage form, which have been appropriately evaluated for safety and are included in a drug delivery system to either aid the processing or to aid manufacture, protect, support, enhance stability, bioavailability or patient acceptability, assist in product identification, or enhance any other attributes of the overall safety and effectiveness of the drug delivery system during storage or use". Solvents used for the production of a dosage form but not contained in the final product are considered to be excipients, i.e. the granulation fluids, which might be dried off later, should comply with relevant requirements of Pharmacopoeia unless adequately justified. Excipients no longer maintain the initial concept of "inactive support" because of the influence they have both over biopharmaceutical aspects and technological factors.

The wet granulation process significantly enhanced tablet hardness and reduced friability, minimizing breakage during transportation.

Dissolution Rate: Wet granulation improved the dissolution rate of bedaquiline due to better wettability and uniform distribution of the API with excipients, leading to enhanced bioavailability.

Drug Stability: The process ensured minimal API degradation, confirmed by stability studies, suggesting compatibility between bedaquiline and excipients All the bedaquiline drugs are white odour less some are pink depending upon colour and circular shape with smooth shinning.

Thickness and hardness of all formulations are 4.04kg\cm^2 approximately.

Rapid disintegration test is done assist swallowing and also plays a key role in fast absorption of drug. Tablets have disintegration time less than 2 mins. passed disintegration test.

Super disintegrating agents is greater in proportion to the other batches which lead to improved dissolution tablets.

Two types of super disintegrating agents are used.it can be conclude from the study that formulation of dispersed tablet using sodium starch glycolate as super disintegrating agent and hence it shows better disintegration.

III. CONCLUSION:

Bedaquiline- a groundbreaking drug for multidrug-resistant tuberculosis (MDR-TB), plays a critical role in combating the global TB epidemicThe formulation and evaluation of bedaquiline are pivotal for ensuring its effectiveness and safety as a treatment for multidrug-resistant tuberculosis (MDR-TB). Through optimized drug formulation strategies, the bioavailability, stability, and therapeutic efficacy of bedaquiline can be significantly enhanced. Proper excipient selection and drug delivery systems contribute to reducing side effects while maintaining the drug's potency. Comprehensive evaluation processes, including physicochemical characterization, stability testing, and in vitro and in vivo studies, ensure that the drug meets quality standards and performs effectively in clinical settings. Analytical techniques such as FTIRisintegral for quality control, stability analysis, and compatibility studies. In conclusion, meticulous formulation and evaluation practices are essential to achieving a stable, effective, and safe bedaquiline formulation. This ensures its continued success in treating MDR-TB, improving patient outcomes, and contributing to global efforts in tuberculosis eradication.

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CONFLICT OF INTREST:
The author declares no conflict of interest.

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