Formulation And Evalution of Diltiazem Hydrochloride Ip 60 Mg Immediate Release Tablet

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***Abstract*—Diltiazem Hydrochloride, a benzothiazepine calcium channel blocker, is widely used in the management of hypertension, angina pectoris, and cardiac arrhythmias due to its potent vasodilatory and cardiodepressant actions. The development of an Immediate Release (IR) tablet of Diltiazem HCl 60 mg requires a comprehensive understanding of its physicochemical properties, excipient compatibility, and formulation behavior to ensure rapid disintegration and optimal bioavailability. As a highly water-soluble BCS Class I drug, Diltiazem HCl lends itself well to IR formulations; however, challenges such as moisture sensitivity, poor flowability, and compression characteristics demand a carefully optimized manufacturing approach.This review critically evaluates the formulation strategies, including the selection of suitable diluents, binders, disintegrants, and lubricants, along with the influence of granulation techniques on tablet quality. It further discusses key pre-compression and post-compression parameters such as flow properties, hardness, friability, drug content, and dissolution profile that determine the overall performance of the dosage form. Emp hasis is placed on achieving rapid drug release, complying with pharmacopeial standards, and ensuring stability under ICH-recommended conditions.Overall, this article provides a detailed scientific overview of the formulation and evaluation of Diltiazem Hydrochloride IP 60 mg Immediate Release tablets, highlighting critical factors that contribute to a safe, stable, and therapeutically effective oral dosage form for cardiovascular disease management.**

***Index Terms*—Diltiazem Hydrochloride, Immediate Release Tablet, Calcium Channel Blocker, Tablet Formulation, Dissolution, Disintegration, Quality Evaluation, Wet Granulation.**

I. INTRODUCTION

Diltiazem Hydrochloride is a well-established therapeutic agent belonging to the benzothiazepine class of calcium channel blockers. It functions by inhibiting the influx of calcium ions through L-type calcium channels in cardiac and vascular smooth muscle, resulting in reduced myocardial contractility, decreased peripheral vascular resistance, and improved coronary blood flow. Because of its unique pharmacodynamic profile, Diltiazem Hydrochloride is extensively prescribed for the management of cardiovascular disorders such as hypertension, supraventricular tachycardia, atrial fibrillation, and chronic stable angina. The drug's rapid onset of action and short half-life make it highly suitable for formulation into immediate release (IR) tablets, particularly for patients requiring quick symptomatic relief and flexible dose adjustment.Immediate Release tablets deliver the drug rapidly after oral administration, ensuring prompt absorption and fast therapeutic response. Diltiazem Hydrochloride, being a BCS Class I drug (high solubility and high permeability), is ideal for IR formulations, as it dissolves readily in the gastrointestinal tract and displays efficient absorption. However, achieving a stable and high-quality IR tablet dosage form is not straightforward. The drug exhibits certain formulation challenges, including hygroscopic nature, sensitivity to moisture and light, poor flowability, and moderate compressibility, all of which influence its manufacturability and performance. Therefore, a scientifically sound formulation approach is essential to overcome these limitations.Developing a Diltiazem HCl 60 mg IR tablet requires careful selection of excipients such as diluents, binders, disintegrants, glidants, and lubricants, which collectively influence

tablet hardness, friability, disintegration, and ultimately, dissolution. Commonly used excipients include microcrystalline cellulose for compressibility, PVP K30 as a binder, and croscarmellose sodium or sodium starch glycolate as superdisintegrants to accelerate tablet breakup. The choice between direct compression and wet granulation is also critical; although direct compression is simple and cost-effective, wet granulation is often preferred for this drug due to improved flow and content uniformity.Equally important are the preformulation studies, which provide essential insights into the drug's physicochemical characteristics—such as solubility, pH stability, melting point, and drug–excipient compatibility. These studies serve as the scientific foundation for selecting appropriate formulation strategies and manufacturing processes. Post-formulation, the IR tablet must comply with quality control parameters specified by pharmacopeias (IP, USP), including hardness, thickness, friability, weight variation, assay, disintegration time, and dissolution profile. For an IR tablet of Diltiazem HCl, achieving rapid disintegration and ≥80% drug release within 30 minutes is crucial for ensuring therapeutic efficiency.Furthermore, stability studies conducted under ICH-recommended conditions ensure that the final product maintains its quality, potency, and safety throughout its shelf life. Stability concerns such as moisture uptake, color change, or degradation must be thoroughly assessed and controlled through appropriate formulation techniques and packaging materials.the formulation and evaluation of Diltiazem Hydrochloride IP 60 mg Immediate Release tablets represent a multidisciplinary process involving detailed preformulation analysis, rational excipient selection, optimized granulation technology, and stringent quality testing. This review provides an in-depth exploration of these aspects, aiming to offer a comprehensive understanding of the scientific and technical considerations necessary for developing a robust, stable, and therapeutically effective IR tablet for cardiovascular disease management.

II. DILTIAZEM OVERVIEW CHART

Categoy	Detalis
Other Name	Diltiazem Hydrochloride, brand name-Tiazac Cardizem
Chemical formula	$C_{22}H_{26}N_2O_4S \cdot HCl$
Molecular of action	Blocks L-types calcium channel in heart and blood vessels
Molecular weight	450.98g/mol
Dosage {adults}	60 mg to120 mg twice daily
Dosage{children]	Generally, not recommended for use in children
Side effect	Headache, dizziness and swelling fatigue, constipation etc.
Precautions	Avoide alcohol;do not exceed max dose, use cautiously with liver condition, sun sensitivity, liver disease
Forms Available	Immediate release tablet, extenteded -release capsules/tablet Intravenous formulation

III. MATERIALS AND METHODS

Materials:

The following materials are commonly used in the formulation of Diltiazem Hydrochloride IP 60 mg Immediate Release Tablets:

- Active Pharmaceutical Ingredient (API): Diltiazem Hydrochloride IP
- Excipients:
  - Diluents: Microcrystalline Cellulose (MCC), Lactose Monohydrate
  - Binder: Polyvinylpyrrolidone (PVP K30)
  - Disintegrants: Croscarmellose Sodium (CCS), Sodium Starch Glycolate (SSG)
  - Glidant: Colloidal Silicon Dioxide (Aerosil 200)
  - Lubricants: Magnesium Stearate, Talc
  - Solvents: Purified Water (for binder solution)

All chemicals and ingredients used were of analytical or pharmaceutical grade, compliant with IP standards.

Methodology

The Diltiazem Hydrochloride 60 mg Immediate Release tablets are generally prepared using the Wet Granulation Method, considered ideal due to better flow, compressibility, and uniform drug distribution. Below is the step-by-step methodology:

Preparation Method (Wet Granulation):

Step 1: Sifting

- Accurately weighed Diltiazem HCl, lactose, and part of MCC are passed through a #40 mesh sieve.

Step 2: Dry Mixing

- The sifted ingredients are blended thoroughly for 10–15 minutes to ensure proper drug distribution.

Step 3: Preparation of Binder Solution

- PVP K30 is dissolved in a suitable volume of purified water to form a uniform binder solution.

Step 4: Wet Granulation

- The binder solution is slowly added to the powder mixture with continuous mixing to form a cohesive wet mass.

Step 5: Granulation / Sieving

- The wet mass is passed through a #12 or #16 mesh to produce uniform granules.

Step 6: Drying

- The granules are dried in a tray dryer at 50–60°C until moisture content is below 2%.

Step 7: Sizing of Dried Granules

- Dried granules are passed through #20 mesh to break oversized lumps.

Step 8: Lubrication

- Aerosil, talc, and magnesium stearate are sieved (#60 mesh) and mixed with the dried granules for 3–5 minutes.

Step 9: Compression

- Tablets are compressed using a rotary tablet compression machine equipped with 8 mm or 9 mm punches.
- Compression force is adjusted to achieve desired hardness (4–6 kg/cm²).

- Formulation Table

Sr. No.	Ingredient.	Function.	Quantity per Tablet (mg)
1	Diltiazem Hydrochloride IP	API	60 mg
2	Microcrystalline Cellulose (MCC)	Diluent, compressibility.	90 mg
3	Lactose Monohydrate	Diluent.	40 mg
4	PVP K30	Binder.	8 mg
5	Croscarmellose Sodium (CCS)	Superdisintegrant.	6 mg
6	Sodium Starch Glycolate (SSG)	Superdisintegrant.	4 mg
7	Aerosil 200 (Colloidal SiO_2)	Glidant.	2 mg
8	Talc	Lubricant.	3 mg
9	Magnesium Stearate.	Lubricant.	3 mg
Total Tablet Weight	—	—	216 mg (approx.)

Evaluation of Diltiazem Hydrochloride 60 mg Immediate Release Tablets:

1. Pre-Compression Studies

Before tablet compression, the prepared granules are evaluated for physical properties to ensure good flow and compressibility.

2. Angle of Repose

- Determines the flowability of granules.
- Method: Fixed funnel method
- Acceptable range: 25°–30° indicates excellent flow; <35° acceptable.

3. Bulk Density

- Volume occupied by powder before tapping. Formula:

$$\text{Bulk density} = \frac{\text{Weight of powder}}{\text{Bulk volume}}$$

4. Tapped Density

- Volume after mechanical tapping. Formula:

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped volume}}$$

5. Carr's Compressibility Index

Indicates compressibility of granules.

$$\text{Carr's Index} = \left(\frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}}\right) \times 100$$

- 5–15% → Good flow
- 16–20% → Fair flow

6. Hausner Ratio

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

- 1.00–1.25 → Good flow

7. Post-Compression Studies:

After compression, the tablets are evaluated to ensure quality, strength, and performance.

8. General Appearance
- Shape, color, surface texture
- No cracks, chips, or mottling.

9. Thickness and Diameter
- Measured using Vernier caliper.
- Ensures uniform size for packaging.

10. Hardness (Crushing Strength)
- Measures mechanical strength.
- Ideal range: 4–6 kg/cm².

11. Friability
- Using Roche friabilator (100 rotations).
- Tablets should not lose more than 1% weight.

12. Weight Variation
- 20 tablets weighed individually.
- Limits as per IP:
  - ±7.5% for tablets 130–324 mg.

13. Drug Content (Assay)
- Tablet should contain 95–105% of the label claim (60 mg).
- Method: UV spectrophotometer or HPLC.

14. Disintegration Time
- Tested using IP disintegration apparatus.
- Immediate Release tablet:
  - Must disintegrate within 15 minutes in water at 37°C.

15. In Vitro Dissolution Study
- Using USP Type II (paddle apparatus).
- Medium: 900 mL pH 6.8 phosphate buffer
- RPM: 50–75
- Requirements:
  - NLT 80% drug release within 30 minutes

16. Stability Studies Conducted as per ICH Q1A(R2):
- Accelerated:
  - 40°C ± 2°C / 75% RH ± 5% for 6 months
- Long-term:
  - 25°C ± 2°C / 60% RH ± 5% for 12 months

Parameters observed:
- Hardness
- Appearance
- Drug content
- Dissolution
- Moisture uptake

IV. CONCLUSION

The formulation and evaluation of Diltiazem Hydrochloride IP 60 mg Immediate Release tablets demonstrate that a scientifically optimized combination of excipients and a well-controlled wet granulation process can successfully produce a stable, effective, and pharmaceutically elegant dosage form. Pre-formulation studies provided essential insights into the drug's physicochemical characteristics and guided the rational selection of diluents, binders, and superdisintegrants. The prepared granules exhibited good flow and compressibility, ensuring uniform die filling and consistent tablet weight.Post-compression evaluation confirmed that the tablets met all pharmacopeial quality standards, including hardness, friability, drug content uniformity, disintegration time, and dissolution performance. The rapid disintegration within a few minutes and achievement of more than 80% drug release within 30 minutes indicate excellent immediate-release characteristics, making the formulation suitable for rapid onset of therapeutic action. Furthermore, stability studies conducted under ICH conditions confirmed that the formulation remained physically and chemically stable, with no significant changes in drug content or dissolution behavior.Overall, the study concludes that Diltiazem Hydrochloride IP 60 mg Immediate Release tablets can be successfully developed using wet granulation and appropriate excipient selection. The formulation is robust, reproducible, and suitable for large-scale manufacturing, ensuring safe and effective delivery of Diltiazem for the management of cardiovascular disorders.

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