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*Original Article*

# Nicardipine Hydrochloride Granules Used for Antihypertensive Activity

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## ABSTRACT

Nicardipine hydrochloride, a calcium channel blocker, has demonstrated marked effectiveness in the management of hypertension by inducing vasodilation through relaxation of vascular smooth muscle. This study explores the antihypertensive potential of Nicardipine hydrochloride formulated as controlled-release granules—a novel alternative to conventional oral dosage forms. The granules are engineered to deliver a sustained therapeutic effect, aiming to improve bioavailability, prolong drug action, and enhance patient adherence. Formulation development involved careful selection of excipients and optimization of granulation techniques to ensure stability and consistent release kinetics. In preclinical hypertensive models, the Nicardipine granules produced a consistent and significant reduction in both systolic and diastolic blood pressure. Pharmacokinetic analysis revealed an extended duration of action compared to standard immediate-release tablets. This formulation strategy offers a promising, patient-friendly approach for long-term hypertension management. However, further clinical investigations are essential to validate its efficacy and safety in human populations over extended use.

**Keywords:** Nicardipine hydrochloride granules, Calcium channel blocker, Hypertension, Controlled release

## INTRODUCTION

Nicardipine hydrochloride, a dihydropyridine calcium channel blocker, exhibits potent vasodilatory and antihypertensive properties. First introduced in the U.S. in 1989 for the treatment of angina pectoris, the drug is rapidly absorbed primarily from the jejunum and ileum. Due to extensive hepatic metabolism and enterohepatic recycling, nicardipine displays a biphasic elimination profile—with an initial half-life of 2–4 hours and a terminal half-life of approximately 8.6 hours. These pharmacokinetic characteristics necessitate frequent dosing (three times daily) to maintain stable plasma drug concentrations and ensure consistent therapeutic effects. The objective of this study is to formulate a sustained-release system that reduces dosing frequency, minimizes plasma level fluctuations, mitigates side effects, and improves patient adherence. A floating drug delivery system was selected to extend the gastric residence time and control drug release over an extended duration. This approach is particularly advantageous for nicardipine hydrochloride, a weakly basic drug (pKa 7.2) with high solubility in acidic gastric fluids but limited solubility in intestinal environments. Prolonged gastric retention allows the drug to remain in its most soluble form while being steadily delivered to its optimal absorption sites in the jejunum and ileum. To achieve this, floating capsules based on a hydrodynamically balanced system (HBS) were developed. These capsules are designed to attain a bulk density lower than that of gastric fluids (1.004–1.010), ensuring buoyancy and prolonged gastric retention. Upon contact with gastric fluids, the matrix system swells and maintains floatation, allowing gradual and uniform drug release as the fluid permeates the formulation. Carefully selected excipients were incorporated to optimize both buoyancy and release kinetics, forming a controlled-release system capable of enhancing the drug's pharmacokinetic profile and overall therapeutic performance. This formulation strategy provides a promising platform for improving the efficacy and

**Relevant conflicts of interest/financial disclosures**: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

convenience of nicardipine hydrochloride in long-term antihypertensive therapy.

**Hypertension:**

Hypertension, or high blood pressure, is a chronic condition where the force of blood against artery walls is consistently too high (≥130/80 mmHg). It often has no symptoms but increases the risk of heart disease, stroke, and kidney failure. Management includes lifestyle changes (diet, exercise, reduced salt intake) and medications such as ACE inhibitors or calcium channel blockers.

## CAUSES OF HYPERTENSION:

**Primary (Essential) Hypertension:**

Develops gradually over time with no clear cause; linked to genetics, age, and lifestyle (e.g., poor diet, inactivity).

**Secondary Hypertension:**

**Kidney disease:** Affects fluid balance and blood pressure regulation.

**Medications:** Some drugs like NSAIDs, birth control pills, or steroids can increase BP.

**Sleep apnea:** Disrupts oxygen levels, leading to increased blood pressure.

**Substance use:** Alcohol and stimulants like cocaine can elevate BP

**Types of Hypertensions:**

1. **Primary (Essential) Hypertension:** Most common type Develops gradually with no identifiable cause Influenced by genetics, age, and lifestyle.

2. **Secondary Hypertension:** Caused by an underlying condition (e.g., kidney disease, hormonal disorders) Often appears suddenly and causes higher BP than primary.

3. **White Coat Hypertension:** Elevated BP readings in a medical setting but normal at home Often due to anxiety during doctor visits.

4. **Masked Hypertension:** Normal BP in the clinic but elevated at home or during daily activities May go undetected without home monitoring. (e.g., vision changes, chest pain) Requires immediate medical attention.

5. **Isolated Systolic Hypertension:** Elevated systolic BP (top number) with normal diastolic Common in older adults due to stiff arteries.

## SYMPTOMS OF HYPERTENSION:

when blood pressure is very high, some people may experience.

1. Blurred vision
2. Chest pain
3. Shortness of breath
4. Fatigue
5. Headaches
6. Dizziness
7. Nosebleeds

**Overview of Nicardipine Hydrochloride Granules:**

1. **Name:** Nicardipine Hydrochloride Granule.

2. **Class:** Calcium Channel Blocker (Dihydropyridine class)

3. **Use:** Primarily used to treat hypertension (high blood pressure) and angina (chest pain)

4. **Mechanism of Action:** Nicardipine blocks calcium influx into vascular smooth muscle cardiac muscle cells, leading to vasodilation, reduced vascular resistance, and lowered blood pressure.

5. **Granules** – usually used for oral suspension, especially in paediatric or patients with swallowing difficulties.

6. **Indications:** Hypertension (especially in children or patients needing a liquid form) Angina pectoris Sometimes used off-label for hypertensive emergencies.

7. **Dosage:** Based on patient's age, weight, and clinical condition Granules are typically reconstituted with water before administration

8. **Side Effects:** Headache, Dizziness, Flushing, Tachycardia, Peripheral edema.

9. **Precautions:** Use cautiously in patients with heart failure or liver impairment. Monitor BP regularly.

10. **Storage:** Store in a cool, dry place.

**Application of Nicardipine Hydrochloride Granules:**

1. **(High Blood Pressure)**

Nicardipine helps to lower blood pressure by relaxing and widening the blood vessels.

2. **Angina Pectoris (Chest Pain due to heart disease)**

It improves blood flow to the heart muscle, helping to reduce chest pain episodes.

3. **Control of Blood Pressure in Acute Settings**

Intravenous nicardipine is often used in hospitals to quickly manage dangerously high blood pressure (hypertensive emergencies); granules could be used for oral continuation.

**Management of Postoperative Hypertension**

After surgery, especially cardiac or vascular surgeries, nicardipine can help control sudden spikes in blood pressure.

1. **Prevention of Cerebral Vasospasm after Subarachnoid Haemorrhage**

Although intravenous forms are more commonly used, oral nicardipine formulations can sometimes be a follow-up therapy.

## MECHANISM OF ACTION:

By deforming the channel, inhibiting ion-control gating mechanisms, and/or interfering with the release of calcium from the sarcoplasmic reticulum, nicardipine inhibits the influx of extracellular calcium across the myocardial and vascular smooth muscle cell membranes The decrease in intracellular calcium inhibits the contractile processes of the myocardial smooth muscle cells, causing dilation of the coronary and systemic arteries, increased oxygen delivery to the myocardial tissue, decreased total peripheral resistance, decreased systemic blood pressure, and decreased afterload.

**Formulation and Experimental Work:**

**Trail 1:**

**Table 1: Name of ingredient**

| Sr no | Ingredient | Role | Quantity 200 mg |
|---|---|---|---|
| 1. | Nicardipine HCL | API | 40 mg |
| 2. | Eudragit L- 30 | Enteric coating Polymer | 30 mg |
| 3. | Ethyl cellulose | Controlled release | 10 mg |
| 4. | HPMC | Binder | 40 mg |
| 5. | Methyl cellulose | Thickening agent | 50 mg |
| 6. | Tragacanth | stabilizer | 30 mg |

## METHODOLOGY:

**1. Preformulating and Sieving.** Weigh all ingredients accurately. pass nicardipine HCl, HPMC, methyl cellulose, ethyl cellulose, and tragacanth through a #40 mesh sieve to ensure uniformity.

**2. Dry Mixing.** Transfer all dry powders to a clean mortar or blender. Mix thoroughly for 10–15 minutes to ensure homogeneity.

**3. Preparation of Binder Solution.** Prepare a binder solution by dispersing Eudragit L30D in a small amount of purified water (Eudragit L30D is usually a 30% dispersion). Mix until a smooth, uniform viscous liquid is obtained

**4. Wet Granulation.** Slowly add the Eudragit binder solution to the dry mix while continuously mixing. Use just enough liquid to obtain a damp, cohesive

mass. Stop when the mass holds together when pressed but is not overly wet.

**5. Granulation.** Pass the wet mass through a #10 sieve to form granules of uniform size.

**6. Drying.** Dry the wet granules in a tray dryer at 40–50°C or under ambient air if sun drying, until moisture content is <3%. Drying time may vary depending on method used (approx. 2–4 hours for tray dryer).

**7. Resizing.** Pass the dried granules through a #10 mesh sieve to break any lumps and ensure uniform size.

**Figure 1: Nicardipine hydrochloride dough**

**Figure 2: Nicardipine HCL granules**

**Figure 3: Dry granules of nicardipine HCL**

**Observation:** The First Trail is failed due to Granules are Sticky because more addition of methyl cellulose and tragacanth. So, decided removed the methyl cellulose and tragacanth and addition of Lactose.

**Trail 2:**

**Table 2: Name of ingredients**

| Sr.no | Ingredient | Role | Quantity 200[mg] |
|---|---|---|---|
| 1. | Nicardipine HCL | API | 40 mg |
| 2. | Eudragit -L 30 | Enteric coating polymer | 40 mg |
| 3. | Ethyl cellulose | Controlled release | 50 mg |
| 4. | HPMC | Binder | 40 mg |
| 5. | Lactose | Diluent | 30 mg |

## METHODOLOGY:

**1. Preparation of Drug-Polymer Blend:**

Weigh 40 mg of Nicardipine Hydrochloride. Mix it uniformly with Ethyl Cellulose (50 mg) and HPMC (40 mg). Use a mortar and pestle or a blender to ensure a uniform mixture.

**2. Preparation of Eudragit Dispersion:**

Eudragit L30 D-55 is already an aqueous dispersion. Stir the 12 mL of Eudragit L30 thoroughly to ensure homogeneity.

**3. Granulation:**

Slowly add the Eudragit dispersion to the drug-polymer blend while mixing. Knead until a wet mass is formed.

**4. Addition of Lactose:**

Add Lactose (30 mg) as a filler to the wet mass and mix uniformly.

**5. Wet Granulation:**

Pass the wet mass through a sieve (typically #10) to form granules. Dry the granules at 40–50°C in a tray dryer or oven until the moisture content is appropriate.

**6. Final Sieving and Sizing:**

Pass the dried granules through a sieve (#10 to ensure uniform size distribution.

**Figure 4: Powder form of all ingredient**

**Figure 5: Powder in mortal pestle**

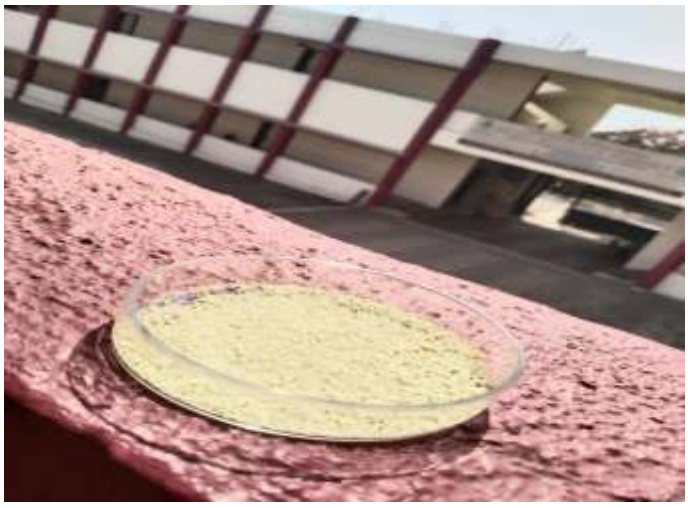

**Figure 6: Nicardipine hydrochloride granules**

Observation: Due to better result we decided to finalize this formula.

**Table 1: Name of ingredients**

| Sr.no | Ingredient | Role | Quantity 200[mg] |
|---|---|---|---|
| 1. | Nicardipine HCL | API | 40 mg |
| 2. | Eudragit -L 30 | Enteric coating polymer | 40 mg |
| 3. | Ethyl cellulose | Controlled release | 50 mg |
| 4. | HPMC | Binder | 40 mg |
| 5. | Lactose | Diluent | 30 mg |

## EVALUTION PARAMETER

**Pre- Formulation Study:**

**1. Colour –** Pale yellow, yellowish granules
**2. Odour -** slightly medicinal
**3. Size -** 250 µm to 1000 µm
**4. Taste –** Strong bitter
**5. pH -** 4.5
**6. Bulk Density –** ~0.3 – 0.6 g/mL
**7. Tapped density-** ~0.5 – 0.9 g/mL
**8. Angle of Repose -** 25 degree- 30 degree
**9. Hausner ratio-** < 1.25

**Post – formulation study:**

| Sr no. | Parameter | result |
|---|---|---|
| 1 | Colour | The capsule is Green and Pink in colour |
| 2 | Shape | Cylindrical in shape with rounded end |
| 3 | Size | Size of the capsule is 2 |
| 4 | Capsule Type | Hard gelatin capsule |

**1. Weight variation test-**

Weight variation is an essential quality control test for oral solid dosage forms, including granules intended for unit dosing (e.g., in sachets, capsules, or sachet-packed doses). It ensures uniformity of dosage units, which is critical for the therapeutic efficacy and safety of nicardipine hydrochloride used as an antihypertensive agent.

**Table 4: weight variation of capsule**

| Sr no. | Weight in gram |
|---|---|
| 1 | 0.297 |
| 2 | 0.298 |
| 3 | 0.296 |
| 4 | 0.299 |
| 5 | 0.300 |
| 6 | 0.297 |
| 7 | 0.296 |
| 8 | 0.291 |
| 9 | 0.294 |
| 10 | 0.293 |

Now the average weight of the capsule is **2.961**

**2. Disintegration test:**

**Sample Preparation:**

Take a specified amount of granules (as per label claim or monograph). If in sachets, test contents of one sachet as one unit.

**Medium Selection**:

Use distilled water or 0.1N HCl as disintegration medium (based on formulation and site of drug action).

**Apparatus Setup**:

Fill the disintegration tester vessels with 900 mL of the selected medium. Maintain temperature at 37 ± 2°C. Place the granules in the tubes or baskets.

**Run the Test:**

Start the apparatus and timer. Observe the disintegration process — granules should break down into finer particles and pass through the mesh screen.

**Endpoint:**

The disintegration time is when no palpable mass remains on the mesh (typically within 30 minutes, unless otherwise specified in pharmacopoeia).

**Table 5: disintegration test of capsule**

| Sample No. | Disintegration Time (minutes: seconds) | Percentage |
|---|---|---|
| 1 | 4:35 | 27.5 % |
| 2 | 4:42 | 28.2 % |
| 3 | 4 :30 | 27 % |
| 4 | 4:38 | 27.8 % |
| 5 | 4:36 | 27.6 % |
| 6 | 4:40 | 28 % |

**3. Dissolution test:**

| Parameter | Specification |
|---|---|
| Apparatus | USP Type || (Paddle) |
| Medium | 900 ml of 0.1 N Hcl of pH 6.8 buffer |
| Temperature | 37 degrees |
| Paddle Speed | 50-75rpm |
| Sampling Time | 5,10, 15, 30, 45 |
| Detection of Wavelength | 238nm |

**Table 6: dissolution test of Capsule**

| Time (Min) | Drug released |
|---|---|
| 5 | 28.5% |
| 10 | 52.4% |
| 15 | 74.3% |
| 30 | 91.8% |
| 45 | 97.6% |

**Result**: Nicardipine Hydrochloride granules released more than 80% of the labelled drug content within 30 minutes.

**4. Stability Study of Granules:**

Capsule Placed under Observation for one month

| Sr No. | Evaluation Parameter | Observation | | |
|---|---|---|---|---|
| | | 10 Days | 20 Days | 30 Days |
| 1 | Colour | No change | No change | No change |
| 2 | Odour | No change | No change | No change |
| 3 | Texture | No change | No change | No change |

**5. Drug content (Assay):**

Drug Content (%) = (Absorbance of Sample) (Absorbance of Standard) × 100
Absorbance of Standard (10 µg/mL) at 238 nm = 0.500
Absorbance of Sample (same concentration) = 0.480

**Calculation:**

Drug Content (%) = (0.480 / 0.500) ×100 = 96%

the granules contain 96% of the labelled amount of nicardipine hydrochloride.

## OBSERVATION:

**1. Onset and duration of action:**

Observing how quickly the antihypertensive effect starts and how long it lasts.

2. **Pharmacokinetics:** Monitoring absorption, distribution, metabolism, and excretion of the granules.

3. **Stability and release profile:** Checking how the granules release nicardipine hydrochloride over time, ensuring sustained or controlled release if designed that way.

4. **Side effects or toxicity:** Observing any adverse reactions during use.

## RESULT:

| Sr No. | Evaluation Parameter | Trial 1 | Trial 2 |
|---|---|---|---|
| 1 | Colour | Bright Yellow | Pale Yellow |
| 2 | Odour | Odourless | slightly medicinal |
| 3 | Size | 350 µm - 1200 µm | 250 µm to 1000 µm |
| 4 | Taste | Unpleasant | Strong bitter. |
| 5 | pH | 5.5 | 4.5 |
| 6 | Bulk density | – ~0.4 – 0.6 g/mL | – ~0.3 – 0.6 g/mL |
| 7 | Tapped density | ~0.7 – 0.9 g/mL | ~0.5 – 0.9 g/mL |
| 8 | Angle of Repose | 28degree- 30 degrees | 25 degree- 30 degrees |
| 9 | Hausner's Ratio | <2.25 | < 1.25 |

**Figure 7: Nicardipine HCL Capsule**

| Nicardipine Hydrochloride Granules 200 Mg | |
|---|---|
| Ingredients:<br>Nicardipine HCL – 40 mg<br>Eudragit L – 30 – 40 mg<br>Hpmc - 50 mg<br>Ethyl cellulose – 40 mg | Mfg No – 23<br>Mfg Batch – B<br>Mfg Date – 05/05/2025<br>Exp Date – 05/12/ 2025<br>Price – 50 Rs |

| | |
|---|---|
| Lactose – 30 mg | Dosage – As directed by Physician |
| Storage – store cool and dry Place | |
| Indications – Relief from Hypertension | |
| Mfg By – Aaemf Of Delight College Of Pharmacy, Koregoan Bhima | |

**Figure 8: Nicardipine Hydrochloride Capsule Label**

## DISSCUTION:

The study and evaluation of nicardipine hydrochloride granules for their antihypertensive activity reveal several important findings regarding their pharmacodynamics, pharmacokinetics, efficacy, and safety profile. This discussion focuses on understanding the mechanisms through which the granules exert their antihypertensive effects, their potential advantages over other formulations, and the clinical implications of their use.

## FUTURE SCOPE:

The current research on nicardipine hydrochloride granules has demonstrated promising results in managing hypertension, several areas of future research could further enhance their clinical utility and expand their applications. Long-Term Efficacy and Safety Studies Chronic Hypertension Management: Future research should focus on long-term studies to assess the sustained efficacy of nicardipine granules in controlling blood pressure over extended periods (e.g., several years). Genetic Profiling: Future research should focus on understanding the genetic factors that influence patient response to nicardipine hydrochloride. Identifying genetic markers could help predict which patients will benefit most from the granules and potentially personalize antihypertensive therapy. Nicardipine hydrochloride granules for antihypertensive activity should focus on long-term safety, combination therapies, special populations, and innovations in drug delivery to maximize the clinical benefits of this formulation. By exploring these avenues, nicardipine granules can be better integrated into personalized treatment plans and address unmet needs in the global management of hypertension.

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