SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

REVIEW ON SUSTAINED RELEASE NIFEDIPINE TABLET

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ABSTRACT

This study been designed to assess bioequivalence of the newly developed delayed-release oral tablets (test) 30 mg nifedipine compared to its marketed counterpart (30 ing: reference) in healthy adult Chinese volunteers. Methode We conducted randomised, open-label, four-period, crossover trials, including a fasting trial and a fed trial. The anhjects. administered the test or reference products in a 1:1 ratio at random throughout each period with 7 days washout period. Then in the next ansidon, they got the alternate products. Lipid chromatography-tandem mass spectrometry and WinNonlin software were used to evtluste the bioequivalence of nifedipine peak blood concentration (Cmax) and area under the concentration-time (AUC). Result A total of 46 subjecta participated in the fasting trial ami 48 subjects in the postprandial trial. In both auses the 90% CL of the geometrica ratios of Cmax, AUCU and AUCH were in the equivalence range (80-125%), When nifedipine was given concomitantly with a high-fat meal, tmax was approximately twofold earlier, absorption was approximately 4.8% less and Conax changed little compared to fasting conditions. In addition, no serious adverse events were observed in the subjects. Conclusion: This study confirus the hioequivalence of the test and reference formulations of nifedipine extended mlense tablets under fasting and postprandial conditions. Food giving kende much earlier Tmax, which is different from the results of other studies. The effect of food effect on the pharmacokinetics of nifedipine needs to be further explored

KEYWORDS: *Nifedipine, Matrix tablet, HPMC,Sustained release, HEC Ethyl cellulose, Eudragit RS100, Wet granulation.*

INTRODUCTION

Nifedipine (NFP) is a short-acting dihydropyridine calcium channel blocker1. Nifedipine can selectively blockL-type calcium channels on cardiac and smooth muscle cells, organize the inward flow of extracellular calciumions, reduce the intracellular calcium ion concentration, relieve the effect of vascular smooth muscle spasm,reduce peripheral vascular resistance, reduce myocardial oxygen consumption, and lower diastolic and systolicblood pressure in hypertensive patients2. At the same time, nifedipine can diastole the coronary arteries,and its application in small doses can have a very good anti-anginal effect. It is currently used clinicallyfor the prevention and treatment of various types of coronary artery disease and angina pectoris, is alsoindicated for various types of hypertension, and has good efficacy in persistent and severe hypertension3,4Nifedipine is almost completely absorbed from the gastrointestinal tract after oral administration and undergoes first-pass metabolism in the liver and intestinal wall, and its oral bioavailability reaches 43%-77%.Nifedipine is highly bound to plasma proteins, metabolized by the liver, and excreted primarily in the urine,with only less than 1% of the dose being excreted in its original form5Regular nifedipine tablets havelow and irregular bioavailability, and short-acting calcium antagonists cause increased sympathetic tone and reflex tachycardia, along with adverse effects such as headache, palpitations, flushing, and dizziness6-78. In contrast, nifedipine extended-release and controlled-release formulations do not have the ”sudden release” phenomenon of ordinary tablets, which can reduce the gastrointestinal stimulation of the drug and avoidthe adverse reactions caused by high peak blood concentrations, making the onset of nifedipine smooth and blood pressure control more stable9. Nifedipine extended-release tablets III, in the size of 30 mg, are capableof releasing nifedipine at a near-constant rate for 24 hours, similar to controlled-release tablets. Nifedipine extended-release tablets I and II are generally taken on an empty stomach, whereas nifedipine extendedrelease tablets III are not restricted by meal times because they are not affected by gastrointestinal motility or pH10.

NEED OF WORK

Sustained-release (SR) nifedipine tablets are designed to provide a controlled release of the drug over an extended period, which helps maintain a steady level of medication in the bloodstream. This formulation is particularly useful for treating conditions like hypertension (high blood pressure) and angina (chest pain) by:

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1**. Improved Blood Pressure Control**: Sustained-release nifedipine helps maintain a consistent effect over 24 hours, reducing the need for multiple doses and ensuring more stable blood pressure control.
2. **Fewer Side Effects**: By avoiding peak concentrations in the blood, sustained-release formulations can minimize side effects such as dizziness, headaches, or flushing that may occur with immediate-release versions.
3. **Convenience:** Patients may prefer the sustained-release form due to fewer doses per day, which can improve adherence to the prescribed regimen.
4. **Reduced Risk of Tachycardia**: The controlled release of nifedipine can help prevent sudden drops in blood pressure, reducing the risk of reflex tachycardia (a rapid heart rate) that can occur with immediate-release nifedipine.

PLAN OF WORK
for sustained-release (SR) nifedipine tablets typically involves a comprehensive approach, starting from formulation development to clinical use. Below is an outline for a work plan focusing on different stages of development, testing, and therapeutic application of SR nifedipine tablets.

1. Formulation Development
Objective: Design and optimize the sustained-release formulation of nifedipine.
Steps:
a. Choice of Release Mechanism: Select the appropriate mechanism of release (e.g., matrix system, osmotic pump, or coated systems).
b. Excipients Selection: Choose polymers, binders, and other excipients that control the rate of nifedipine release.
c. Drug-Excipient Compatibility: Conduct stability studies to ensure nifedipine is compatible with chosen excipients.
d. Formulation Trials: Prepare small batches to determine optimal drug loading, release profile, and tablet hardness.
e. Scale-Up: Increase batch size while maintaining consistent release properties.

2. Pre-Clinical Studies
Objective: Evaluate the pharmacokinetics, pharmacodynamics, and safety of the SR formulation.
Steps:
a. In Vitro Release Testing: Conduct dissolution testing using various media to simulate the gastrointestinal conditions.
b. Stability Testing: Test the formulation under various temperature and humidity conditions to assess shelf life.
c. Animal Studies: If necessary, perform animal studies to confirm the controlled release profile and assess systemic exposure.

3. Clinical Trials (Human Studies)
Objective: Ensure the safety and efficacy of SR nifedipine tablets in humans.
Phases:
a. Phase I (Safety and Pharmacokinetics):
b. Administer the formulation to a small group of healthy volunteers.Assess the pharmacokinetics, including half-life, Tmax (time to reach peak concentration), and Cmax (maximum concentration). Monitor for adverse effects.
c. Phase II (Efficacy and Dose-Response):
d. Test on patients with conditions like hypertension or angina.Evaluate the effectiveness of the sustained release in controlling blood pressure or preventing chest pain.
e. Phase III (Large-Scale Efficacy and Safety):
f. Conduct large-scale, multicenter trials to assess long-term safety and efficacy in a diverse patient population.Collect data on adverse events and side effects.

4. Regulatory Approval
Objective: Obtain regulatory approval for the SR nifedipine formulation.
Steps:
a. Compile Data: Gather all preclinical, clinical, and manufacturing data for submission to regulatory bodies (e.g., FDA, EMA).
b. Documentation: Ensure compliance with Good Manufacturing Practices (GMP) and Good Clinical Practices (GCP).
c. Regulatory Submission: Submit the New Drug Application (NDA) or Marketing Authorization Application (MAA) for approval.
d. Manufacturing and Quality Control
e. Objective: Produce the SR nifedipine tablets on a commercial scale, ensuring quality and consistency.

Steps
a. Batch Production: Manufacture large-scale batches under GMP conditions.

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b. Quality Control (QC): Perform QC tests to ensure tablet uniformity, release profile, and stability.
c. Packaging: Package tablets in a manner that protects them from environmental factors like moisture or light, ensuring long shelf life.

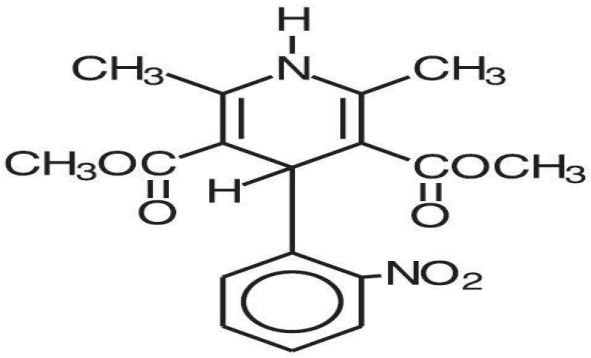
6. Post-Marketing Surveillance (Phase IV)
Objective: Monitor the long-term safety and effectiveness of SR nifedipine tablets once they are on the market.
Steps:
a. Adverse Event Reporting: Collect data on any new adverse effects or long-term side effects.
b. Post-Market Studies: Conduct additional studies to observe the drug's effectiveness in real-world settings.
c. Patient Education: Provide information on how to use the medication safely and effectively, including possible interactions and side effects.

7. Patient Management Objective: Ensure the correct use of SR nifedipine tablets by patients.
Steps:
a. Dosing Instructions: Educate patients on proper dosing intervals (usually once or twice daily).
b. Monitoring: Regularly monitor patients' blood pressure and heart rate to ensure the drug's effectiveness and adjust the dosage if needed.
c. Follow-Up: Schedule periodic follow-up visits to track patient progress, especially for chronic conditions like hypertension and angina.

8. Marketing and Distribution
Objective: Ensure the widespread availability and accessibility of SR nifedipine tablets.
Steps:
a. Distribution Channels: Establish partnerships with wholesalers and pharmacies.
b. Promotion: Educate healthcare providers about the benefits of SR nifedipine for long-term treatment.
c. Global Reach: Depending on the regulatory approvals, expand distribution to other countries or regions.

DRUG PROFILE **STRUCTURE**





Uses:- Nifedipine is used to treat high blood pressure and to control angina (chest pain).
AVAILABLE FORMS OF DRUG
ROUTE: ORAL

AVAILABLE FORMS
TABLETS: 20mg, 30mg, 60 mg,90 mg
CAPSULES: 10mg, 20mg
concentration, minimizing side effects.
Enhanced Efficacy**:** Provides prolonged therapeutic effects

DRUG DESIGN
1. Selection of Formulation Approach
The sustained-release mechanism can be achieved using various approaches, each providing different release profiles. Common strategies include:

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Matrix Systems: The drug is dispersed in a hydrophilic or lipophilic polymer matrix, where the drug is gradually released as the matrix swells or erodes over time.

Hydrophilic Matrix (e.g., HPMC, Xanthan gum): This type of system forms a gel barrier around the tablet core as it comes in contact with water, controlling the drug release.

Hydrophobic Matrix (e.g., ethylcellulose): These systems rely on the drug's diffusion through the polymer matrix, which slowly releases the drug over time.

Reservoir Systems: A drug core is surrounded by a rate-controlling membrane, typically made of polymers such as ethylcellulose or cellulose acetate, which regulates the release rate of nifedipine. Osmotic Pump Systems: In these systems, the drug is released through a controlled orifice due to osmotic pressure. A semipermeable membrane surrounds the tablet, and water enters, causing the drug to be released at a controlled rate.

2. Selection of Drug Release Mechanism
Diffusion-Controlled Release: In a matrix or reservoir system, nifedipine is released via diffusion through the polymer.Swelling-Controlled Release: In a hydrophilic matrix, water uptake leads to the swelling of the polymer, which slows the drug release.
Erosion-Controlled Release: Some hydrophobic matrices will erode over time, slowly releasing the drug.Combination Systems: A combination of these mechanisms can be used to achieve the desired release profile.

3. Choice of Polymers
The choice of polymers is critical for controlling the release rate. Commonly used excipients include: Hydrophilic Polymers: Hydroxypropyl methylcellulose (HPMC), polyethylene oxide (PEO), or carbopol. These polymers swell in water, forming a gel that gradually releases the drug. Hydrophobic Polymers: Ethylcellulose, Eudragit, or cellulose acetate. These polymers can provide a more consistent release by slowing down the drug's diffusion.Other excipients: Pore-formers like sodium chloride or magnesium stearate may be used to enhance drug release through diffusion channels.

4. Tablet Core Design
Drug Loading: Nifedipine should be carefully loaded into the matrix to ensure uniformity in content and release characteristics. Granulation Process: Wet or dry granulation techniques may be used to ensure uniform distribution of the drug and excipients.Compression: The tablet should be compressed to an optimal hardness to ensure mechanical integrity, but not so hard as to inhibit drug release.

5. Optimization of Release Profile
To achieve the desired release profile, it's essential to optimize factors such as: Polymer concentration and ratio (hydrophilic to hydrophobic) Particle size of nifedipine (smaller particles tend to have faster release) Tablet hardness and porosity, which affect the rate of water uptake and drug release.Coating thickness (for membrane-controlled systems) or use of pore formers (for diffusion-controlled release).

6. Preformulation Studies: Before the final formulation, preformulation studies such as solubility, stability, and compatibility tests are conducted on nifedipine and the excipients to ensure that the drug and excipients do not interact in a way that compromises the drug's release or stability.

7. In Vitro Release Testing
In vitro dissolution testing is a critical step to evaluate the performance of the sustained-release tablet. The dissolution medium and test conditions (e.g., USP Apparatus II at 50 or 75 rpm) should mimic gastrointestinal conditions. The goal is to ensure that nifedipine is released at a controlled rate and meets the target profile for a once-daily dosage.

8. Stability Testing
The stability of the tablet needs to be assessed under accelerated conditions (e.g., 40°C/75% RH) to ensure the drug remains stable over time and the release profile is maintained**.**

9. Clinical Considerations
Therapeutic Range: Nifedipine is used to treat conditions such as hypertension and angina. Sustained-release formulations should maintain plasma concentrations within the therapeutic range for extended periods.Side Effects: The sustained-release form aims to minimize peaks and troughs in drug concentration, which can reduce side effects such as dizziness, flushing, or palpitations associated with nifedipine**.**

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10. Regulatory Requirements

Ensure the formulation complies with regulatory standards for sustained-release dosage forms, including the FDA's guidelines on controlled-release drug products.Perform necessary bioavailability and bioequivalence studies to demonstrate that the SR formulation provides therapeutic benefit. Summary of Key Design Considerations: Formulation strategy: Matrix, reservoir, or osmotic system.Polymers: Hydrophilic (e.g., HPMC) or hydrophobic (e.g., ethylcellulose) based on desired release profile.Tablet compression and hardness: Balanced to ensure mechanical integrity without compromising drug release.Dissolution testing: To optimize the release rate and ensure compliance with therapeutic goals.By carefully balancing the drug, excipients, and release mechanisms, it's possible to design a nifedipine sustain release tablet that provides controlled, consistent drug delivery over a prolonged period, improving therapeutic outcomes and patient adherence.

SAFATY ASSESSMENT

A safety assessment of sustained-release (SR) nifedipine tablets involves evaluating the potential risks associated with the drug's formulation, pharmacokinetics, and its clinical use. Nifedipine is a calcium channel blocker commonly prescribed for hypertension, angina, and other cardiovascular conditions. The sustained-release formulation aims to provide a steady, controlled release of the drug over an extended period, reducing the frequency of dosing and improving patient compliance.

Key factors in the safety assessment of sustained-release nifedipine include

1. Pharmacokinetic Considerations

Absorption and Bioavailability: Sustained-release formulations are designed to release the drug slowly, which impacts the peak plasma concentrations and the overall bioavailability. This slower absorption can reduce the risk of adverse events associated with rapid peaks in drug levels, such as hypotension or tachycardia. Steady-State Concentration: The controlled release allows for more consistent plasma concentrations, which can be beneficial for maintaining therapeutic effects while minimizing side effects. Risk of Dose Dumping: There is a potential risk of "dose dumping" where the sustained-release mechanism fails, leading to a rapid release of the drug. This can result in overdosing and heightened risks of adverse effects, such as hypotension, dizziness, or even heart failure.

2. Adverse Effects

Common Side Effects: The most common side effects of nifedipine, including SR formulations, are related to its vasodilatory effects and may include:

- Headache
- Dizziness
- Flushing
- Edema (particularly peripheral edema)
- Palpitations
- Gingival hyperplasia

Serious Side Effects: In rare cases, more severe side effects could include:

- Reflex tachycardia (due to vasodilation)
- Severe hypotension (especially with overdose or in patients with preexisting low blood pressure)
- Cardiac arrhythmias
- Acute myocardial infarction (with high doses or improper use)
- Exacerbation of heart failure (particularly in patients with existing heart conditions)

Tolerability: Sustained-release nifedipine may offer better tolerability compared to immediate-release formulations, as the slower onset of drug action can reduce the intensity of side effects like flushing or palpitations.

3.Patient-Specific Considerations

Renal and Hepatic Function: Nifedipine is metabolized by the liver, so patients with liver impairment may have altered drug metabolism, leading to increased plasma concentrations and a greater risk of side effects. Renal function can also impact the excretion of the drug. Cardiovascular Conditions: In patients with heart failure or aortic stenosis, nifedipine may exacerbate symptoms due to the drug's vasodilatory effects.

Drug Interactions: Nifedipine can interact with other medications, such as beta-blockers (increasing the risk of bradycardia), CYP3A4 inhibitors (increasing nifedipine plasma levels), and antihypertensive drugs (leading to excessive lowering of blood pressure).

4. Formulation Issues

Tablet Integrity: The safety of sustained-release tablets depends on the integrity of the formulation. If the tablet is damaged (e.g., crushed or chewed), it could lead to a rapid release of the drug, significantly increasing the risk of side effects and

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overdose.Bioequivalence: Different brands or generics of sustained-release nifedipine might have variations in how the drug is released, which could affect both efficacy and safety. It is important to ensure that the SR formulations are bioequivalent to prevent inconsistent therapeutic effects.

5. Long-Term Safety
Chronic Use: The long-term use of nifedipine SR tablets generally appears to be safe for most patients when prescribed appropriately. However, as with any chronic medication, regular monitoring for signs of adverse effects

EXESSIVE HYPERTENSION IN PATIENT WITH ANGINA
Excessive hypertension in a patient with angina while using sustained-release (SR) nifedipine tablets could be due to several factors related to the drug's pharmacodynamics, the patient's underlying conditions, or drug interactions. Here's a breakdown of potential causes and considerations:
1. Nifedipine and Blood Pressure Control
Mechanism of Action: Nifedipine is a calcium channel blocker that works by relaxing vascular smooth muscle, leading to vasodilation and, ideally, a reduction in blood pressure. In patients with angina, this helps reduce myocardial oxygen demand by lowering systemic vascular resistance and decreasing heart workload.Sustained-Release Formulation: The SR formulation is designed to provide a gradual release of the drug over time, helping maintain stable blood levels and preventing sharp fluctuations in blood pressure. This should ideally prevent both excessively high and low blood pressure.

2. Potential Reasons for Excessive Hypertension
Dose Adjustment Issues: If the initial dose of SR nifedipine is too low or inadequate for the patient's needs, it may not sufficiently lower blood pressure, particularly in a hypertensive patient. This could result in uncontrolled hypertension despite using the drug.
Tachyphylaxis or Tolerance: Although rare with SR nifedipine, some patients may develop tolerance over time, where the drug becomes less effective at controlling blood pressure. This might cause inadequate blood pressure lowering, especially in patients with higher baseline hypertension.

Dose Dumping or Absorption Issues: If the SR formulation fails due to improper tablet integrity (e.g., crushing, chewing, or improper dissolution), there could be rapid release of the drug, leading to a sudden drop in blood pressure followed by rebound hypertension as the body tries to compensate.

Inappropriate Use in Severe Hypertension: If the patient's hypertension is particularly severe or if they are on other medications that increase blood pressure (e.g., corticosteroids, sympathomimetics), SR nifedipine may not be sufficient as a sole agent to control the elevated pressure.

BETA-BLOCKER WITHDRAWAL
Beta Blocker Withdrawal with Sustained-Release Nifedipine Tablets
Beta blockers and calcium channel blockers like nifedipine are often prescribed for various cardiovascular conditions, such as hypertension, angina, and arrhythmias. Nifedipine belongs to a class of drugs known as calcium channel blockers, and when used in a sustained-release (SR) formulation, it provides a gradual release of the drug into the bloodstream over an extended period, which helps maintain a consistent therapeutic effect.

When discussing beta blocker withdrawal specifically, it's important to note that beta blockers (e.g., metoprolol, atenolol) are a different class of drugs from nifedipine, but they are often prescribed together in cardiovascular conditions. Therefore, the withdrawal effects from beta blockers (if discontinued suddenly) and the management of nifedipine (particularly in its sustained-release form) must be understood within the broader context of cardiovascular treatment.

1. Beta Blocker Withdrawal
Beta blockers are commonly used to treat hypertension, arrhythmias, heart failure, and angina. They work by blocking the effects of adrenaline on beta receptors, slowing the heart rate and reducing the force of heart contractions, which ultimately lowers blood pressure. When beta blockers are stopped abruptly or reduced too quickly, it can lead to withdrawal symptoms. These may include: Rebound hypertension: Beta blockers have a blocking effect on the sympathetic nervous system. Discontinuing them suddenly can lead to an overreaction of the sympathetic system, resulting in a significant increase in blood pressure (rebound hypertension).

Tachycardia (rapid heart rate): The heart rate may increase significantly as the body's natural sympathetic response is no longer moderated by the beta blockers.

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Angina or chest pain: Withdrawal may lead to increased workload on the heart, which can precipitate angina in individuals with underlying coronary artery disease.

Anxiety, sweating, and tremors can also be symptoms as the sympathetic nervous system is suddenly unopposed.
Increased risk of arrhythmias: The sudden loss of beta blockade may expose the heart to a higher risk of arrhythmias, especially in individuals with a history of heart disease.

Because of these potential risks, beta blockers should be tapered gradually under medical supervision if discontinuation is necessary.

2. Sustained-Release Nifedipine (SR Nifedipine) Overview
Nifedipine is a calcium channel blocker that works by inhibiting the influx of calcium ions into smooth muscle cells and cardiac muscle cells. This action causes vasodilation, which can lower blood pressure and relieve angina.

In the sustained-release (SR) formulation, nifedipine is designed to release the drug slowly over a prolonged period. This helps maintain a steady drug concentration in the blood and avoids peak concentrations that could cause adverse effects.

Key Points about SR Nifedipine:
It is used primarily for hypertension and angina.
SR nifedipine helps in managing these conditions with fewer fluctuations in blood drug levels.
Sudden cessation of SR nifedipine can lead to a rebound effect, but this is more commonly associated with the vasodilatory effects (e.g., sudden increases in blood pressure or worsening of angina) rather than direct withdrawal symptoms like those seen with beta blockers.

3. Impact of Beta Blocker Withdrawal on SR Nifedipine Therapy
While SR nifedipine itself does not cause withdrawal symptoms in the traditional sense, the withdrawal of beta blockers can impact how nifedipine works. Te effects of discontinuing a beta blocker while on nifedipine include:
Increased Heart Rate: Without the beta blocker to counteract the tachycardia caused by nifedipine, patients may experience a significant increase in heart rate, especially when they transition to standing or during physical activity.

Worsening Angina: In patients who use beta blockers for angina, withdrawing the beta blocker may increase the risk of angina attacks due to a combination of higher heart rate and potential rebound hypertension.

Rebound Hypertension: As mentioned, stopping beta blockers abruptly can cause an increase in blood pressure, which could exacerbate the hypertensive effects in a patient on SR nifedipine.

4. Management of Withdrawal Symptoms and Cessation of Beta Blockers
If beta blockers are being withdrawn in a patient on SR nifedipine, the withdrawal should be gradual. A tapering plan is usually recommended to minimize the risk of rebound hypertension, tachycardia, and arrhythmias.
Monitor heart rate and blood pressure closely during the tapering period.

If angina worsens during this process, additional medications or adjustments to nifedipine doses might be necessary.
In some cases, an alternative anti-hypertensive or anti-anginal therapy might be introduced to support the patient during the transition.

CLINICAL TRIALS AND ADVERSE DRUG REACTION
Adverse Drug Reactions (ADRs) in Clinical Trials for Sustained-Release Nifedipine Tablets
Sustained-release nifedipine is commonly used in the treatment of hypertension and angina, providing a more controlled release of the active ingredient compared to immediate-release formulations. While nifedipine is generally well-tolerated, clinical trials have identified a range of adverse drug reactions (ADRs) that can occur with its use. The side effects are typically dose-dependent and can vary in frequency and severity. Here's a detailed look at the clinical trial data for sustained-release nifedipine:

Common Adverse Drug Reactions
1. Cardiovascular
Peripheral edema (swelling): One of the most common side effects, especially in elderly patients. This occurs due to nifedipine's vasodilatory effect on peripheral blood vessels.

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Hypotension (low blood pressure): Due to its vasodilatory effects, nifedipine can lower blood pressure too much, leading to symptoms like dizziness, light-headedness, and fainting. This is more likely to occur if a patient is volume-depleted or is on high doses.

2. Gastrointestinal

Constipation: Although less common than with other calcium channel blockers, some patients may experience constipation

DO NOT USE NIFEDIPINE TABLET

There are several clinical situations where nifedipine tablets, particularly the sustained-release formulation, may not be recommended or should be avoided due to safety concerns. Here are some of the key reasons why nifedipine tablets might be contraindicated or should be used with caution:

1.Severe Hypotension (Low Blood Pressure):

Nifedipine is a calcium channel blocker that works by relaxing blood vessels, which can significantly lower blood pressure. In individuals with already low blood pressure or severe hypotension, nifedipine can exacerbate this condition, leading to life-threatening situations such as dizziness, fainting, or shock.

2. Acute Myocardial Infarction (Heart Attack)

Nifedipine should generally be avoided in patients who are experiencing a heart attack, particularly in the acute phase. There is a risk that it could worsen the heart's condition due to reflex tachycardia (increased heart rate), which might increase the oxygen demand of the heart, potentially leading to further ischemia (lack of blood flow to the heart).

3. Unstable Angina

Nifedipine should not be used in patients with unstable angina because its vasodilatory effects could lead to reflex tachycardia, which might worsen the angina symptoms. The condition could deteriorate, leading to more severe chest pain or a heart attack.

4. Severe Aortic Stenosis

Aortic stenosis, a condition where the aortic valve is narrowed, can be exacerbated by nifedipine, which dilates blood vessels. In such patients, the decrease in vascular resistance can lead to impaired blood flow to the coronary arteries, which could precipitate severe complications.

5. Hypersensitivity (Allergy) to Nifedipine or its Components

Individuals with a known allergy to nifedipine or any of the excipients in the formulation should avoid the drug. Allergic reactions could range from mild skin rashes to severe anaphylactic reactions, which can be life-threatening.

HOW TO TAKE SUSTAINED RELEASE NIFEDIPINE TABLET

When taking sustained-release nifedipine tablets, it's important to follow the prescribed instructions to ensure the medication works effectively and to minimize the risk of side effects. Here's how to take sustained-release nifedipine correctly:

1. Follow the Prescribed Dose and Schedule

Always take the medication exactly as prescribed by your healthcare provider. The typical dosing for sustained-release nifedipine will vary depending on your condition (e.g., hypertension, angina) and individual factors (e.g., age, other health conditions).
Don't adjust the dose on your own. If you feel that the dose is too high or too low, talk to your doctor.

2. Take with or without Food

Sustained-release nifedipine can generally be taken with or without food. However, taking it with food might help reduce some gastrointestinal side effects (like nausea) for some people.
If you experience stomach upset, try taking it with food to see if it helps.

3. Swallow the Tablet Whole

Do not crush, chew, or break the tablet. The tablet is designed to release nifedipine gradually over time, so crushing or breaking it could release too much of the drug at once, increasing the risk of side effects like severe low blood pressure or other adverse reactions.
Always swallow the tablet whole with a glass of water.

4. Take at the Same Time Every Day

To help remember to take your medication consistently, try to take your nifedipine tablet at the same time each day. This helps maintain a steady level of the drug in your system.

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5. Do Not Take More Than Prescribed
Never take more than the prescribed dose. Taking extra tablets or doses can lead to dangerous side effects such as severe hypotension (low blood pressure), tachycardia (fast heart rate), or other heart-related issues.
If you miss a dose, do not double the next dose. Instead, take the missed dose as soon as you remember, unless it's almost time for your next dose. In that case, just skip the missed dose and continue with your regular schedule.

6. Stay Hydrated
It's a good idea to stay well-hydrated when taking nifedipine, as dehydration can increase the risk of side effects like dizziness and hypotension.

7. Monitor Blood Pressure and Heart Rate
If you're taking nifedipine for hypertension or angina, it's important to regularly monitor your blood pressure and heart rate. Your doctor may ask you to check these regularly to ensure that the medication is working as expected.
Report any significant changes in your blood pressure or heart rate to your doctor.

8. Avoid Grapefruit and Grapefruit Juice
Grapefruit and grapefruit juice can interact with nifedipine and increase its concentration in the blood, which may increase the risk of side effects like low blood pressure or heart problems. Avoid consuming grapefruit products while taking nifedipine.

9. Stay Alert for Side Effects
Some people may experience dizziness, headache, or swelling while taking nifedipine. If you feel light-headed or dizzy, avoid standing up too quickly and be careful when driving or operating heavy machinery.

Peripheral edema (swelling in the ankles or feet) is a known side effect of nifedipine, especially in the lower extremities. If this becomes bothersome or severe, talk to your doctor.

10. Keep Regular Appointments
Regular follow-up appointments are important to monitor your response to the medication and to check for potential side effects. Your doctor may adjust your dose or change your medication if needed.

Key Points to Remember:
Do not crush or chew the sustained-release tablet.
Take as prescribed, and do not alter your dosage without consulting your doctor.
Monitor your blood pressure and heart rate, especially when starting the medication.
Stay hydrated and avoid grapefruit.
If you miss a dose, do not double the dose—just take the next scheduled dose.
By following these guidelines, you can help ensure that sustained-release nifedipine works effectively and safely for your condition. Always consult your healthcare provider if you have any questions or concerns about taking the medication.

CONCLUSION

In conclusion, sustained-release nifedipine tablets represent a significant advancement in the management of hypertension and angina by providing a controlled, prolonged release of the medication. This formulation not only helps maintain consistent blood drug levels, improving therapeutic outcomes, but also enhances patient compliance by reducing the frequency of dosing. While generally well-tolerated, careful monitoring of patients is essential to manage potential side effects, particularly in those with preexisting cardiovascular conditions. Ongoing research into the pharmacokinetics and long-term effects of sustained-release nifedipine will further refine its role in clinical practice and expand its therapeutic applications

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SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 11 | November 2024 - Peer Reviewed Journal

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