INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD)
© 2026 IJNRD | Volume 11, Issue 4, April 2026 | ISSN: 2456-4184 | IJNRD.ORG

A Review On: Formulation Development And Evaluation Of Valsartan Nanoemulsion: Bioavailability

Gulshan, Rajesh Kumar, Pradeep Kumar,
[1]Designation of 1st ***Scholar-Ch. Sughar Singh Pharmacy College, Jaswantnagar, Etawah, 206245 Uttar Pradesh India***
[2]Designation of 2nd ***Faculty-(Department of Pharmaceutics) -Ch. Sughar Singh Pharmacy College, Jaswantnagar, Etawah, 206245 Uttar Pradesh India***
, [3]Designation of 3rd ***Professor (Dr.)-Ch. Sughar Singh Pharmacy College, Jaswantnagar, Etawah, 206245 Uttar Pradesh India***
*Department of Pharmacy****: Ch. Sughar Singh Pharmacy College, Jaswantnagar, Etawah, 206245 Uttar Pradesh India***
Corresponding author at:
Gulshan, **Ch. Sughar Singh Pharmacy College, Jaswantnagar, Etawah, 206245 Uttar Pradesh India**
Email address: gulshan992742@gmail.com

ABSTRACT
Valsartan is a strong and selective drug used to lower blood pressure, taken orally. However, its effectiveness is limited because of its poor water solubility and slow dissolution, which lower its absorption and bioavailability. This study aimed to develop and test a self-nanoemulsifying drug delivery system (SNEDDS) for Valsartan to overcome these issues and improve its bioavailability.
The SNEDDS formulations were created using a spontaneous emulsification technique. First, we examined the saturation solubility of Valsartan in different oils, surfactants, and co-surfactants to find suitable ingredients. Based on these findings, we chose triacetin and castor oil as the oil phase, Tween 80 as the surfactant, and PEG 600 as the co-surfactant.
We then characterized the formulations by looking at droplet size, morphology, differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR), and in vitro drug release. We also conducted pharmacokinetic evaluations using Wistar rats. When diluted with 500-fold Milli-Q water, the SNEDDS formulations showed nanosized droplets, with average sizes of 139.29 ± 10.5 nm (triacetin-based) and 142.6 ± 18.6 nm (castor oil-based). Transmission electron microscopy (TEM) confirmed the spherical shape and uniform distribution of the droplets.
Stability studies under accelerated conditions showed that the formulations remained stable over time. In vivo results indicated a significant increase in maximum plasma concentration (Cmax) and area under the curve (AUC) compared to pure Valsartan, suggesting improved bioavailability.
Key words: Valsartan, Nano emulsion, SNEDDS, Surfactant, Co-surfactant, Oil phase.

INTRODUCTION

Valsartan is a commonly used drug for lowering blood pressure, part of the angiotensin II receptor blocker (ARB) class. Doctors widely prescribe it for treating high blood pressure, heart failure, and for patients recovering from heart attacks. While the drug is effective and well tolerated, its potential is limited by poor water solubility and relatively low oral bioavailability, usually between 20% and 25%. This lower bioavailability mainly occurs due to its slow dissolution in gastrointestinal fluids and significant first-pass metabolism, which both reduce the amount of drug entering systemic circulation. Improvement of bioavailability in poorly water soluble drug like Valsartan remains a significant challenge in pharmaceutical research.

To tackle this problem, several innovative drug delivery systems have been introduced in recent years. Lipid-based formulations, including self-emulsifying drug delivery systems (SEDDS), self-nanoemulsifying drug delivery systems (SNEDDS), and their solid forms, have shown significant promise. These systems enhance drug solubility, improve lymphatic transport, and reduce first-pass metabolism, thus enhancing overall drug absorption. Besides lipid-based carriers, alternative formulation methods such as solid dispersions, nanosuspensions, nanocrystals, inclusion complexes, and polymeric micelles have also been investigated to improve Valsartan's dissolution rate and bioavailability. These strategies primarily focus on increasing the drug's effective surface area, improving wettability, and keeping the drug in a solubilized or amorphous state within the gastrointestinal tract. Among these methods, SNEDDS and solid SNEDDS have gained particular attention due to their simple formulation process, thermodynamic stability, and ability to spontaneously create fine oil-in-water nano emulsions under gentle agitation in the gastrointestinal environment. The formation of nanosized droplets offers a large surface area for drug release, leading to faster dissolution and better absorption. This review highlights various formulation strategies used to boost Valsartan's oral bioavailability, focusing specifically on lipid-based nano formulation approaches like SNEDDS. It also discusses recent developments, evaluation methods, and both in vitro and in vivo performance of these systems, providing useful insights into how they enhance therapeutic effectiveness.

COMPONENTS OF NANOEMULSION

Nano emulsions consist of a mix of carefully selected components that together form a stable system of nanometer-sized droplets. Choosing the right ingredients and their proportions is crucial for determining physical stability, droplet size distribution, drug loading capacity, and overall bioavailability of the formulation.

1. Oil Phase

The oil phase acts as the main solubilizing medium for lipophilic drugs like Valsartan, which have poor water solubility.

Functions

- Enhances solubility of hydrophobic drugs.
- Affects droplet size and physical stability.
- Influences drug release behavior.

Examples

- Medium-chain triglycerides (MCT oil).
- Long-chain triglycerides.
- Oleic acid.
- Caproyl 90.

2. Surfactants

Surfactants are molecules that lower the tension between oil and water phases, helping form stable nano-sized droplets.

Functions

- Promote nano emulsion formation.
- Stabilize droplets, preventing aggregation and merging.
- Enhance dispersion and uniformity.

Examples

- Tween 80 (Polysorbate 80).
- Span 20.
- Cremophor EL.

3. Co-surfactants

Co-surfactants are used alongside surfactants to improve film flexibility and further lower interfacial tension, making emulsification more efficient.

Functions

- Enhance emulsification.
- Help achieve smaller droplet sizes.
- Improve thermodynamic stability.

Examples

- Ethanol.
- Propylene glycol.
- Polyethylene glycol (PEG 400).

4. Aqueous Phase

The aqueous phase serves as the continuous external phase in oil-in-water (o/w) nano emulsion systems.

Functions

- Provides a medium for dispersion.
- Affects viscosity, pH, and stability.

Examples

- Distilled water.
- Purified water.
- Buffer solutions.

5. Active Pharmaceutical Ingredient (API)

The drug is added based on its properties, especially solubility.

Example

- Valsartan (a lipophilic drug classified as BCS Class II).

6. Auxiliary Additives (Optional Components)

a. Preservatives

Prevent microbial contamination and extend shelf life.

Example: Methyl paraben.

b. Antioxidants

Prevent oxidative degradation of the formulation.

Example: Butylated hydroxytoluene (BHT).

c. Flavoring and Coloring Agents

Mainly added in oral formulations to enhance patient acceptability and compliance.

Conclusion

The effectiveness of a nano emulsion system heavily relies on selecting and optimizing its components. Each ingredient has a unique role, and their combined effects determine the formulation's efficiency, stability, and therapeutic performance.

FORMULATION DEVELOPMENT OF NANOEMULSION

Developing a nano emulsion involves a systematic, multi-step process aimed at selecting the right components and optimizing their ratios to create a stable, effective, and reproducible formulation. This process is especially useful for poorly soluble drugs like Valsartan, as it improves solubility and oral bioavailability.

1. Preformulating Studies

Preformulating studies are the initial stage, providing insights into the drug's physicochemical characteristics.

Key Considerations

- Solubility in different oils, surfactants, and co-surfactants.
- Partition coefficient.

- Stability under various environmental conditions.

These factors guide the choice of suitable excipients for the formulation.

2. Solubility Screening

The drug's solubility is tested in various components to find the best excipients.

Methodology

- Add an excess amount of the drug to selected components.
- Mix samples and allow them to reach equilibrium.
- Determine drug concentration using techniques like UV spectroscopy or HPLC.

Result

Components showing higher drug solubility are selected for further development.

3. Selection of Surfactant and Co-surfactant

Surfactants and co-surfactants are chosen for their ability to improve solubilization and reduce interfacial tension, as well as their safety and compatibility.

We prepare different ratios of surfactant and co-surfactant (Smix), such as 1:1, 2:1, and 3:1, for optimization.

4. Construction of Pseudo-Ternary Phase Diagram

This step is crucial to determine the composition range that results in a stable nano emulsion.

Procedure

- Combine oil and Smix in varying proportions.
- Gradually add water while mixing continuously.
- Observe the system for transparency and phase behavior.

Outcome

The clear and isotropic region indicates nano emulsion formation and helps identify the best formulation composition.

5. Preparation of Nano emulsion

a. High-Energy Techniques

These methods apply external energy to reduce droplet size:

- High-pressure homogenization.
- Ultrasonication.

b. Low-Energy Techniques

These methods rely on the system's intrinsic properties:

- Phase inversion temperature (PIT) method.
- Spontaneous emulsification method.

Low-energy techniques are usually simpler and more cost-effective.

6. Optimization of Formulation

Different formulations are prepared by adjusting:

- Oil concentration.
- Smix ratio.
- Amount of aqueous phase.

Optimization focuses on parameters such as:

- Droplet size.
- Polydispersity index (PDI).
- Physical stability.

7. Characterization During Development

The prepared nano emulsions are evaluated to select the most suitable formulation.

Evaluation Parameters

- Droplet size measurement.
- Zeta potential determination.
- Drug content analysis.
- In vitro drug release studies.

These evaluations help in selecting an optimized and stable nano emulsion formulations.

EVALUATION PARAMETERS OF NANOEMULSION

Characterizing nano emulsions is essential to verify their stability, homogeneity, and overall performance. A range of physicochemical parameters are systematically assessed to ensure the quality and reliability of the developed formulation.

1. Droplet Size Determination

Droplet size significantly affects drug dissolution and absorption. This is often measured using dynamic light scattering (DLS). Nano emulsions generally show droplet sizes of 20 to 200 nm, where smaller droplets offer a larger surface area, improving bioavailability.

2. Polydispersity Index (PDI)

PDI measures the uniformity of droplet sizes within the system. It ranges from 0 to 1, where values below 0.3 indicate a narrow and uniform size distribution. Higher values suggest heterogeneity and potential instability.

3. Zeta Potential

Zeta potential reflects the electrical charge on the droplet surfaces, which is important for stability. Higher absolute values (whether positive or negative) enhance repulsion between droplets, decreasing the likelihood of aggregation.

4. Drug Content Estimation

This parameter measures the amount of active pharmaceutical ingredient in the formulation. It ensures consistency and is usually assessed using analytical techniques like UV spectroscopy or HPLC.

5. In Vitro Drug Release Studies
These studies evaluate how the drug is released from the nano emulsion system. Generally, nano emulsions show a quicker and more effective drug release profile compared to traditional dosage forms.
6. Thermodynamic Stability Testing
Thermodynamic stability studies assess how resistant the formulation is to stress conditions. These include: - Heating and cooling cycles -Centrifugation - Freeze-thaw cycles A stable nano emulsion does not show signs of phase separation, creaming, or cracking.
7. Viscosity Measurement
Viscosity is an important factor that affects the flow characteristics and drug release behavior. It is measured with a viscometer and should be suitable for the intended route of administration.
8. pH Measurement
The formulation's pH is evaluated to ensure it is compatible with biological systems and stable. The pH of the sample was measured using a properly calibrated pH meter.
9. Morphological Examination
Morphological analysis helps understand the shape and structural features of the droplets. Techniques like Transmission Electron Microscopy (TEM) and Scanning Electron Microscopy (SEM) are often used to confirm nanoscale size and uniformity.
10. Refractive Index and Transparency
The refractive index is measured to check the clarity and isotropic nature of the nano emulsion. Transparent systems usually indicate uniform dispersion and nanoscale droplet size. Merits of valsartan nano emulsion Nano emulsion-based formulations of valsartan offer a promising way to tackle the issues related to its low water solubility and limited oral bioavailability.
These systems provide several pharmaceutical and therapeutic advantages compared to traditional dosage forms.
1. Improved Solubility
Valsartan has poor water solubility, which limits its dissolution. Inclusion in a nano emulsion significantly increases its solubilization capacity, thus enhancing its availability in the gastrointestinal tract.
2. Enhanced Bioavailability
Nanosized droplets expand the surface area for absorption, which leads to better drug uptake and improved oral bioavailability.
3. Rapid Drug Release and Onset
Nano emulsions allow for quicker drug dispersion and dissolution, resulting in a faster onset of pharmacological action compared to standard formulations.
4. Increased Surface Area for Absorption
The very small droplet size offers a larger interfacial surface, promoting efficient drug absorption across biological membranes
5. Protection from Degradation
Nano emulsion systems can shield valsartan from chemical and enzymatic degradation in the gastrointestinal tract, thereby enhancing its stability.
6. Dose Reduction Potential
Better bioavailability may enable the use of lower therapeutic doses, which can help reduce adverse effects and improve patient safety.
7. Better Patient Compliance
These formulations can be designed into patient-friendly dosage forms, such as liquids or soft gelatin capsules, improving ease of use.
8. Uniform Drug Distribution
Nano emulsions ensure even distribution of the drug within the formulation, leading to consistent therapeutic performance.
9. Possibility of Targeted Delivery
With the right modifications, nano emulsions can be tailored for site-specific drug delivery, enhancing therapeutic efficiency and reducing systemic exposure.
10. Ease of Formulation and Scale-Up
Nano emulsions can be created using relatively simple and scalable methods, making them suitable for industrial production.
LIMITATIONS
Despite the many benefits of nano emulsion systems in enhancing valsartan's solubility and bioavailability, several challenges exist regarding their formulation and practical use.
1. Physical Instability Over time, nano emulsions may face instability issues like phase separation, creaming, or Ostwald ripening, especially during long-term storage.
2. Requirement of High Surfactant Levels Typically, these systems need higher concentrations of surfactants and co-surfactants, which can cause irritation or potential toxicity, particularly with oral use.
3. Restricted Drug Loading The ability to include the drug is often limited by its solubility in the chosen oil phase, which can constrain the overall drug content.
4. Sensitivity to External Conditions Nano emulsions can be affected by changes in temperature, pH, and dilution, which may impact their stability and performance.
5. Difficulties in Scale-Up While making them in the lab is relatively easy, large-scale production can be tough due to the need for specialized equipment and precise control over process parameters.
6. Increased Production Cost Using refined excipients and specialized processing methods can increase the overall formulation cost compared to traditional dosage forms.
7. Possibility of Drug Precipitation After administration, dilution in gastrointestinal fluids may lead to drug precipitation, possibly lowering the expected bioavailability.
8. Packaging Constraints To maintain stability, nano emulsions often need protective packaging, such as light-resistant and airtight containers.

9. Shorter Shelf Life Compared to solid formulations; nano emulsions may have a shorter shelf life because they are more vulnerable to physical and chemical degradation.

10. Regulatory and Safety Challenges Introducing new excipients and nanoscale systems may involve strict regulatory requirements and safety evaluations before approval.

APPLICATION

Nano emulsion-based delivery systems have received significant attention for improving valsartan's therapeutic performance. Since they enhance solubility and absorption, these systems are widely studied for various pharmaceutical uses.

1. Oral Drug Delivery

Nano emulsions are mainly used for the oral administration of valsartan to boost its solubility and bioavailability. The nanosized droplets improve dissolution and aid absorption in the gastrointestinal tract.

2. Enhancement of Bioavailability

Valsartan nano emulsions greatly increase systemic availability by enhancing drug dissolution and reducing absorption variability.

3. Rapid Onset of Action

Thanks to quicker drug release and improved absorption, nano emulsions help achieve a faster therapeutic response, which is beneficial for managing hypertension.

4. Controlled and Sustained Release Systems

Nano emulsions can be modified for controlled or prolonged drug release, keeping therapeutic levels steady over a longer time. 5. Targeted Drug Delivery With suitable formulation strategies, nano emulsions can be designed for targeted delivery, boosting drug concentration at the desired site while minimizing systemic side effects.

6. Reduction of Dose and Side Effects

Better bioavailability provides the chance for lower doses, which might decrease the risk of side effects and improve patient safety.

7. Use in Combination Therapy

Nano emulsion systems can deliver valsartan alongside other antihypertensive drugs to enhance therapeutic results.

8. Alternative Dosage Forms

Valsartan nano emulsions can be made into various dosage forms such as: - Soft gelatin capsules - Liquid formulations - Oral sprays This adds flexibility in how the drug can be administered.

9. Improved Patient Compliance

Easier administration and better therapeutic efficiency lead to greater patient adherence to treatment.

10. Potential for Transdermal Delivery (Research Stage)

Nano emulsion systems are being studied for transdermal delivery of valsartan, offering a non-invasive option compared to oral administration.

FUTURE PERSPECTIVE

1. Targeted Drug Delivery

Future advancements may focus on designing nano emulsion systems for site-specific delivery, allowing valsartan to effectively reach targeted tissues while limiting unwanted systemic effects.

2. Integration with Novel Nanocarriers

Combining nano emulsions with advanced nanocarrier systems like polymeric nanoparticles, liposomes, and solid lipid nanoparticles could further enhance drug delivery and therapeutic results.

3. Enhancement of Stability and Shelf Life

Ongoing research aims to improve the physical and chemical stability of nano emulsions to extend storage life and ensure their commercial viability.

4. Advancement in Scale-Up Techniques

Innovations in manufacturing processes are likely to enable efficient large-scale production, making nano emulsion formulations more suitable for industrial use.

5. Alternative Routes of Administration

There is rising interest in developing nano emulsions for non-oral delivery methods, such as transdermal, nasal, and parenteral systems, to provide more flexible treatment options

6. Personalized Drug Delivery

Future formulations may be tailored to meet individual patient needs, improving therapeutic response and minimizing treatment variability.

7. Combination Drug Therapy

Nano emulsion systems could be developed to deliver valsartan with other therapeutic agents, creating synergistic effects in managing hypertension.

8. Regulatory and Safety Developments

As research continues, clearer regulatory frameworks and safety assessments for nano emulsion formulations are anticipated, supporting their broader clinical use.

9. Application of Artificial Intelligence

Artificial intelligence and computer modeling can help with formulation optimization, predicting stability, and designing processes, which may shorten development time and cut costs.

10. Clinical Translation and Commercialization

Additional preclinical and clinical studies will be crucial to move nano emulsion technologies from research labs to commercially available pharmaceutical products.

CONCLUSION

Nano emulsion-based drug delivery systems offer an effective way to tackle the challenges associated with poorly water-soluble drugs like valsartan. The reduction of droplet size to the nanoscale boosts drug solubility, dissolution, and oral bioavailability, ultimately enhancing therapeutic results. The success of these systems largely depends on careful formulation design, including the right choice of components, understanding phase behavior, and systematic optimization. Furthermore, thorough evaluations ensure the stability, consistency, and effectiveness of the developed nano emulsion. While some limitations like physical instability, high surfactant needs, and scale-up challenges remain, ongoing advancements in nanotechnology and formulation methods are expected to address these issues. In conclusion, valsartan nano emulsion holds great promise as an effective drug delivery strategy with significant potential for future development, clinical application, and commercial success.

REFERENCES

1. Pouton, C. W. (2000). Lipid formulations for oral administration of drugs. European Journal of Pharmaceutical Sciences, 11(Suppl 2), S93–S98.
2. Porter, C. J. H., Trevaskis, N. L., & Charman, W. N. (2007). Lipid-based formulations as a means to improve oral drug delivery. Nature Reviews Drug Discovery, 6(3), 231–248.
3. Savjani, K. T., Gajjar, A. K., & Savjani, J. K. (2012). Drug solubility: importance and enhancement techniques. ISRN Pharmaceutics, 2012, 195727.
4. Date, A. A., & Nagarsenker, M. S. (2007). SNEDDS for poorly soluble drugs. Journal of Pharmaceutical Sciences, 96(3), 650–658.
5. Kawabata, Y., Wada, K., Nakatani, M., Yamada, S., & Onoue, S. (2011). Formulation strategies for poorly soluble drugs. International Journal of Pharmaceutics, 420(1), 1–10.
6. Gupta, S., et al. (2011). Self-nanoemulsifying systems for oral delivery. Colloids and Surfaces A, 392, 145–155.
7. Tadros T. et al. Formation and stability of nano emulsions. Advances in Colloid and Interface Science.
8. Gupta A., Eral H.B., Hatton T.A., Doyle P.S. Nanoemulsions: Formation, properties and applications. Soft Matter.
9. Date A.A., Nagarsenker M.S. Design and evaluation of self-nanoemulsifying drug delivery systems. Journal of Pharmacy and Pharmacology.
10. Constantinides P.P. Lipid-based systems for improving drug solubility and bioavailability. Pharmaceutical Research.
11. Shakeel F., Ramadan W. Nano emulsions as drug delivery systems. Saudi Pharmaceutical Journal.
12. Beg S., Swain S., Singh H.P., Patra C.N., Rao M.B. Development and characterization of valsartan-loaded self-nanoemulsifying drug delivery systems. AAPS PharmSciTech. 2012;13(4):1416–1427.
13. Dixit R.P., Rajput S.J., Patel S.G. Preparation and bioavailability enhancement of valsartan using SMEDDS. AAPS PharmSciTech. 2010;11(1):314–321.
14. Date A.A., Nagarsenker M.S. Design and evaluation of self-nanoemulsifying drug delivery systems (SNEDDS). Journal of Pharmacy and Pharmacology. 2007;59:1–12.
15. Constantinides P.P., Chaubal M.V., Shorr R. Advances in lipid-based drug delivery systems for improving bioavailability. Pharmaceutical Research. 2008;25:1381–1390.
16. Porter C.J.H., Trevaskis N.L., Charman W.N. Lipid-based formulations as enabling drug delivery systems. Nature Reviews Drug Discovery. 2007;6:231–248.
17. Cholakova D., Vinarov Z., Tcholakova S., Denkov N. Advances in self-emulsification technologies. Chemical Engineering Review. 2022
18. McClements D.J. Nanoemulsions versus microemulsions: future trends. Soft Matter. 2012.
19. Mason T.G., Wilking J.N., Meleson K., Chang C.B. Nano emulsions: structure and emerging applications. J Phys Condens Matter. 2006.
20. Solans C., Izquierdo P., Nolla J., et al. Nano emulsions: future pharmaceutical applications. Curr Opin Colloid Interface Sci. 2005.
21. Nasr A.M., et al. Transdermal delivery approaches of valsartan using nanocarriers. Pharmaceutics. 2022