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Solid Lipid Nanoparticles for Enhanced Oral Bioavailability of Valsartan in the Management of Hypertension

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Abstract: Hypertension is a major chronic cardiovascular disorder affecting millions of people worldwide and is a leading cause of heart disease, stroke, and kidney failure. Valsartan, an angiotensin II receptor blocker, is widely used in the management of hypertension; however, its poor water solubility and low oral bioavailability limit its therapeutic effectiveness. Solid Lipid Nanoparticles (SLNs) have emerged as a promising nanocarrier system to overcome these limitations. Valsartan-loaded SLNs enhance drug solubility, improve bioavailability, provide controlled and sustained drug release, and protect the drug from degradation. SLNs are composed of biocompatible and biodegradable lipids, offering advantages such as improved stability, reduced dosing frequency, and enhanced patient compliance. Various preparation methods including hot homogenization, cold homogenization, and solvent emulsification-evaporation, ultra sonication, and microemulsion techniques are used for SLN formulation. Important characterization parameters include particle size, polydispersity index, zeta potential, entrapment efficiency, and in vitro drug release studies. The improved pharmacokinetic and therapeutic performance of valsartan-loaded SLNs makes them a promising approach for effective hypertension management and prevention of associated cardiovascular complications. Future advancements in targeted delivery and large-scale production may further expand their clinical applications.

Key Words: Hypertension, Valsartan, Solid Lipid Nanoparticles (SLN), Nanoparticles, Solubility Enhancement

1. INTRODUCTION;

Hypertension is a long-lasting illness when the arterial blood pressure stays constantly above typical levels. Among the main risk factors for heart attack, stroke, heart failure, and kidney problems cardiovascular diseases it is The World Health Organization estimates that more than one billion individuals globally have hypertension sometimes referred to as a "silent killer" as it might not manifest symptoms early on. Genetic variables, being overweight, too much salt intake, stress, smoking, drinking alcohol, and not enough exercise are all frequent reasons.

Hypertension usually falls under primary hypertension and secondary hypertension. Chronic high blood pressure over time affects essential organs and blood vessels.

Controlling hypertension depends on changes in lifestyle including good diet, frequent exercise, weight management, and low salt intake.

Commonly used treatments are antihypertensive drugs such beta blockers, calcium channel blockers, diuretics, and ACE inhibitors.

Early diagnosis and proper management can significantly reduce complications and improve quality of life. Recent research also focuses on nanotechnology-based drug delivery systems to improve the efficacy and safety of antihypertensive medications. [1,2,3]

Valsartan is a potent, orally active nonpeptide tetrazole derivative and selectively inhibits Angiotensin II Receptor type 1 which causes reduction in blood pressure and is used in treatment of hypertension.

It was first developed by Novartis and has a wide market in the developed and the developing countries. It is also available in combination with other antihypertensive drugs. It is a lipophilic drug and possesses moderate onset of action than other drugs of the same category.

Valsartan is not extensively metabolized and is mainly excreted by non-renal routes. Valsartan is effective in treatment of pediatric, adolescents and the elderly patients with mild to moderate hypertension. [4,5,6]

Solid lipid nanoparticles have several benefits over other nanocarriers, such as biodegradability, biocompatibility, and the capacity to change a drug's physicochemical characteristics. Additional advantages include ease of use, low cost, organic solvent-free processing, good stability, and controlled release features.

Compared to alternative nanocarriers, the composition has greater bioavailability and stability. These carriers are able to load both hydrophilic and lipophilic drugs without affecting their active component. SLNs are made up of solid lipid, emulsifier and water/solvent. [7,8]

1.1 OVERVIEW OF HYPERTENSION;

Hypertension is a frequent, chronic, age-related disorder, which often entails debilitating cardiovascular and renal complications. Blood pressure is usually noted in combination with other cardiovascular risk factors. [9]

Fig 1: Hypertension

Etiology;

Most cases of hypertension are idiopathic, which is also known as essential hypertension. It has long been suggested that an increase in salt intake increases the risk of developing hypertension. One of the described factors for the development of essential hypertension is the patient's genetic ability to salt response. About 50% to 60% of the patients are salt sensitive and therefore tend to develop hypertension. [10,11,12]

Epidemiology;

More than one billion adults worldwide have hypertension, with up to 45% of the adult populace being affected by the disease. The high prevalence of hypertension is consistent across all socio-economic and

income strata, and the prevalence rises with age, accounting for up to 60% of the population above 60 years of age.

In the year 2010, the global health survey report published in Lancet, which was comprised of patient data from 67 countries, reported Hypertension as the leading cause of death and disability-adjusted life years worldwide since the year 1990.

In the United States, HTN alone accounts for more cardiovascular disease-related deaths than any other modifiable risk factor and is second only to cigarette smoking as a preventable cause of death for any reason.

Recent estimates have suggested the number of patients with hypertension could increase as much as 15% to 20%, which could reach close to 1.5 billion by 2025. [13,14]

1.1 TYPES OF HYPERTENSION;

1. Basic (Essential) Hypertension

The most frequent kind of hypertension, primary hypertension which accounts for almost 90–95% of all cases Over many years, it progresses without any discernible medical reason. Genetics, obesity, stress, high salt intake, smoking, drinking, and sedentary Behaviour all help it to develop.

2. Secondary Hypertension

An underlying medical condition or medicine causes secondary hypertension. Common reasons include kidney diseases, endocrine disorders, thyroid dysfunction, obstructive sleep apnea, and several medicines including oral contraceptives or corticosteroids. Addressing the underlying reason can support blood pressure management.

3. Solitary systolic hypertension

In this condition, only the systolic blood pressure is elevated above 140 mmHg; the diastolic pressure stays normal. Stiffening of arteries is a common cause in older adults that raises their risk of cardiac events.

4. Malignant Hypertension

Severe and potentially lethal hypertension known as malignant hypertension presents very high blood pressure usually above 180/120 mm Hg together with organ damage. Headache, fuzzy vision, chest discomfort, and renal failure can all be symptoms. Medical attention is urgently needed.

5. Resistant Hypertension

Resistant hypertension is high blood pressure that stays unmanaged even after three or more antihypertensive drugs have been used. Common contributing elements are poor medication adherence, kidney illness, and obesity.

6. Pulmonary hypertension

Pulmonary hypertension is right-sided heart high blood pressure that impacts the arteries of the lungs. It can cause shortness of breath, exhaustion, chest discomfort, and if left untreated, heart failure. [15,16,17,18]

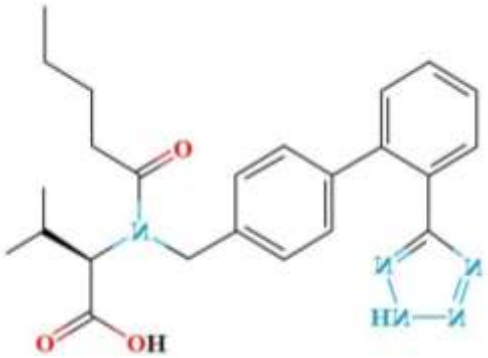
2. DRUG PROFILE;

DRUG NAME: Valsartan
IUPAC NAME: (2S)-3-methyl-2-[pentanoyl-[[4-[2-(2H-tetrazol-5- yl) phenyl] phenyl]methyl]amino]butanoic acid

MOLECULAR WEIGHT: 435.53 G MOL

CHEMICAL FORMULA: (C24H29N5O3)

CAS NUMBER: 137862-53-4. [19]



2.1 SOLID LIPID NANOPARTICLES:

Lipid nanoparticles are strong colloidal carriers composed of lipids that remain solid at room temperature as well as at body temperature. They consist of a solid lipid core in which the medicine is dissolved or dispersed, protected by a surfactant. They are colloidal transporters with a size range of 50 nm to 1 m, which is below the micron level.

Triglycerides and phospholipids, which are nano-meter in size, make up the very promising medication delivery system known as solid lipid nanoparticles, which have just been researched for regulated release. Solid lipid nanoparticles have several benefits over other nanocarriers, such as biodegradability, biocompatibility, and the capacity to change a drug's physicochemical characteristics. Additional advantages include ease of use, low cost, organic solvent-free processing, good stability, and controlled release features.

Compared to alternative nanocarriers, the composition has greater bioavailability and stability.

These carriers are able to load both hydrophilic and lipophilic drugs without affecting their active component. SLNs are made up of solid lipid, emulsifier and water/solvent. The lipids used may be triglycerides (tri-stearin), partial glycerides (Imwitor), fatty acids (stearic acid, palmitic acid), and steroids (cholesterol) and waxes (cetyl palmitate). Various emulsifiers and their combination (Pluronic F 68, F 127) have been used to stabilize the lipid dispersion. The combination of emulsifiers might prevent particle agglomeration more efficiently. [20,21]

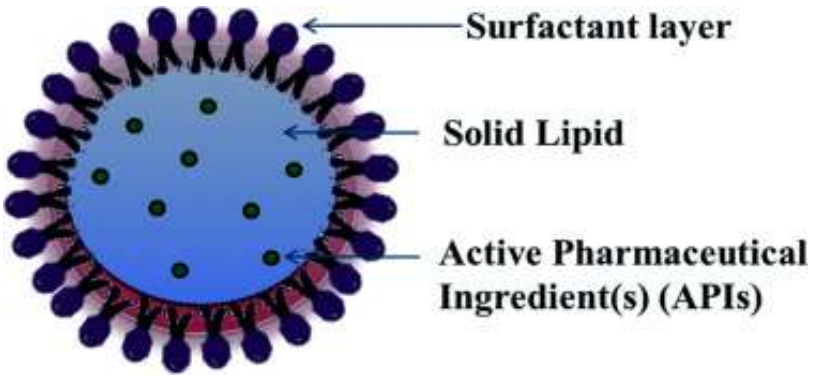


Fig 2: Solid Lipid Nanoparticles

2.2 VALSARTAN LOADED SLN

A lipid-based nanocarrier system created to enhance the delivery of valsartan, an often used antihypertensive medication, valsartan-loaded Solid Lipid Nanoparticles (SLN) Encapsulation into SLN improves valsartan's low oral bioavailability and bad water solubility by increasing its solubility, absorption, and therapeutic action. The lipid matrix guarantees controlled and ongoing medication release, therefore helping to keep blood pressure under control for longer. SLN also prevent valsartan from degrading in the digestive tract and help to lower dose frequency. These benefits position valsartan-loaded SLN as a potential strategy for enhancing hypertension management. [22]

2.3 RATIONALE FOR VALSARTAN LOADED SLN;

Valsartan exhibits poor water solubility and low oral bioavailability. Incorporation of valsartan into solid lipid nanoparticles offers several advantages.

1) Enhancement of Solubility

Valsartan is a poorly water-soluble drug, which reduces its dissolution in gastrointestinal fluids and limits absorption after oral administration. Incorporation of valsartan into solid lipid nanoparticles significantly improves the surface area of the drug particles, thereby increasing dissolution rate and solubility. Nano-sized particles provide better interaction with gastrointestinal fluids and improve drug dispersion. [23]

2) Improvement of Oral Bioavailability

One of the major reasons for selecting SLN for valsartan is enhancement of oral bioavailability. SLN improve lymphatic uptake of the drug and reduce hepatic first-pass metabolism. Studies have shown that valsartan-loaded SLN formulations exhibit better absorption and enhanced plasma drug concentration compared to conventional formulations. [24]

3) Controlled and Sustained Drug Release:

Solid lipid nanoparticles provide controlled release of valsartan because the drug remains entrapped within the solid lipid matrix. Drug release occurs gradually over a prolonged period, maintaining therapeutic plasma concentration for longer duration. Sustained release reduces fluctuations in plasma drug levels and improves antihypertensive activity. Research studies demonstrated sustained release of valsartan up to 12–72 hours depending on formulation variables.

4) Reduction in Dose Frequency

Due to prolonged release and improved bioavailability, valsartan-loaded SLN may reduce dosing frequency. Conventional valsartan formulations may require repeated dosing to maintain therapeutic levels, whereas SLN formulations maintain drug concentration for extended periods. This improves patient convenience and adherence to therapy.

5) Improved Stability and Protection of Drug

Solid lipid nanoparticles protect valsartan from chemical and enzymatic degradation within the gastrointestinal tract. The solid lipid core acts as a protective barrier against environmental factors such as pH variations and oxidative degradation. This improves stability and shelf life of the drug formulation.

6) Better Therapeutic Efficacy in Hypertension

Studies indicate that Nano formulations of valsartan provide improved antihypertensive efficacy because of enhanced absorption, sustained drug release, and better tissue distribution. SLN formulations maintain consistent blood pressure control and reduce variability in therapeutic response. Recent research also demonstrated improvement in oxidative stress pathways and cardiovascular protection using valsartan Nano formulations. [25]

2.4 MECHANISM OF DRUG RELEASE;

Valsartan Loaded Solid Lipid Nanoparticles (SLN)

↓

Administration and Contact with

Gastrointestinal Fluid

↓

Hydration of Nanoparticle Surface

↓

Initial Surface Drug Dissolution

↓

Burst Release Phase

(Drug present on or near SLN surface released)

↓

Penetration of Dissolution Medium

into Lipid Matrix

↓

Diffusion of Valsartan from

Solid Lipid Core

↓

Sustained/Controlled Release

↓

Gradual Erosion or Rearrangement

of Lipid Matrix

↓

Further Drug Liberation

↓

Continuous Drug Absorption

↓

Prolonged Antihypertensive Effect [26]

2.5 CHARACTERIZATION OF VALSARTAN LOADED SLN;

1) Particle Size & PDI

The mean particle size typically ranges from 130 nm to 170 nm, with a Polydispersity Index (PDI) between 0.3 and0.5 indicating a highly uniform and monodisperse nanocolloidal system. [27]

2) Zeta Potential

Surface charge values generally fall between -20 mV and -30 mV or highly positive depending on the surfactant, ensuring excellent physical stability and preventing particle aggregation. [28]

3) Entrapment Efficiency (EE)

Optimized formulations achieve an entrapment efficiency ranging from 75%to 85%.

4) Solid State Analysis

Differential Scanning Calorimetry (DSC) and X-ray Diffraction (XRD) confirm that Valsartan converts from a crystalline state into an amorphous state within the lipid matrix.[29, 30]

5) In Vitro Drug Release

Release profiles display a biphasic behavior characterized by an initial burst release (for quick onset of action), followed by a sustained, controlled release for up to 12 to 24 hours.[31]

6) Chemical Compatibility

Fourier-Transform Infrared Spectroscopy (FTIR) analyses confirm no chemical incompatibility between Valsartan and the lipid/surfactant systems (e.g., Compritol 888 ATO and Poloxamer 407). [32]

3. METHODS OF PREPARATION;

1) Hot Homogenization Method

Principle

In this method, valsartan is dissolved or dispersed in melted lipid. The lipid phase is mixed with a hot aqueous surfactant solution at the same temperature to form a pre-emulsion. This pre-emulsion is then subjected to high-pressure homogenization. On cooling, the lipid recrystallizes and forms solid lipid nanoparticles

Procedure

- Melt solid lipid above its melting point.
- Dissolve valsartan in the melted lipid.
- Prepare hot aqueous surfactant solution.
- Mix both phases to form a pre-emulsion.
- Subject the mixture to high-pressure homogenization.
- Cool the nano emulsion to room temperature.
- Solidification produces valsartan-loaded SLN. [33]

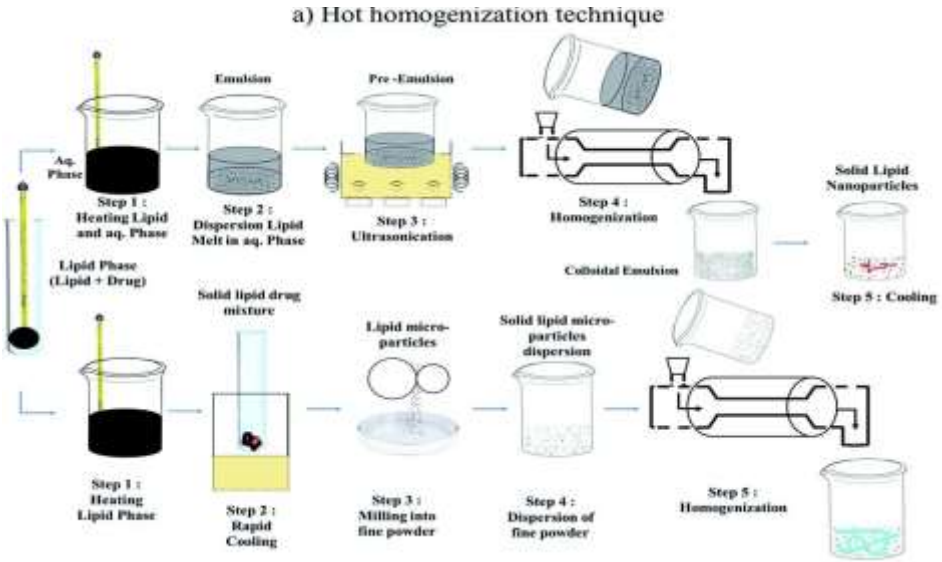


Fig 3: Hot Homogenization Method[33]

2) Cold Homogenization Method

Principle

Cold homogenization was developed to overcome problems associated with hot homogenization. Valsartan is dissolved in melted lipid, rapidly cooled using liquid nitrogen or dry ice, and then milled into microparticles. These particles are dispersed in cold surfactant solution and homogenized to form SLN.

Procedure

- Melt lipid and incorporate valsartan.
- Rapidly cool the mixture.
- Grind solidified lipid into microparticles.
- Disperse particles in cold surfactant solution.
- Perform high-pressure homogenization at room temperature.
- Obtain valsartan-loaded SLN dispersion. [34]

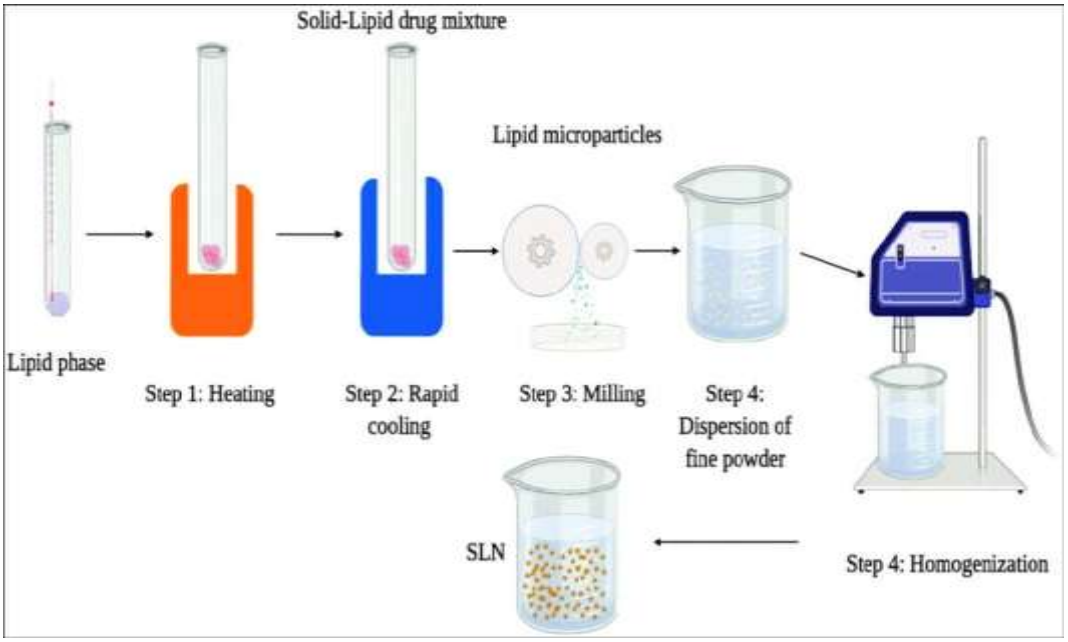


Fig 4: Cold Homogenization Method[34]

3) Solvent Emulsification - Evaporation Method

Principle

Valsartan and lipid are dissolved in a water-immiscible organic solvent such as chloroform or dichloromethane. This organic phase is emulsified in an aqueous phase containing surfactant. The solvent is then evaporated, causing lipid precipitation and formation of solid lipid nanoparticles.

Procedure

- Dissolve valsartan and lipid in organic solvent.
- Prepare aqueous surfactant phase.
- Emulsify organic phase into aqueous phase.
- Stir continuously.
- Evaporate organic solvent.
- Lipid precipitates forming SLN. [35]

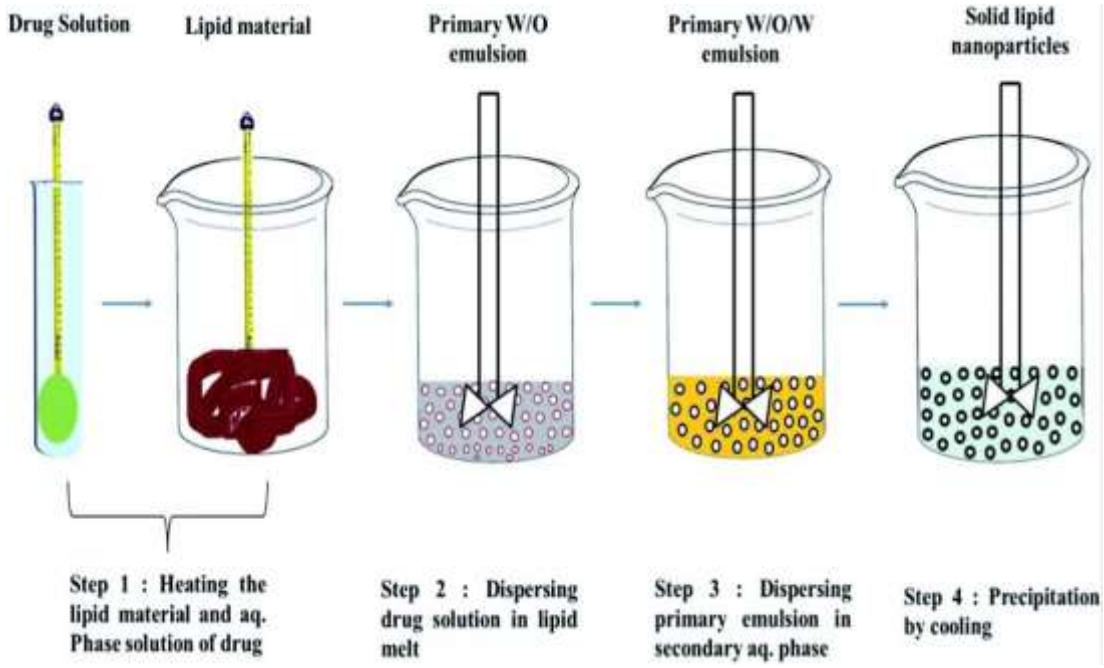


Fig 5: Solvent Emulsification – Evaporation [35]

4) Ultrasonication Method

Principle

Ultrasonication uses ultrasonic energy to reduce particle size and produce nanosized lipid particles. Molten lipid containing valsartan is dispersed into aqueous surfactant solution and subjected to ultrasonic waves, resulting in SLN formation.

Procedure

- Melt lipid and incorporate valsartan.
- Prepare aqueous surfactant solution.
- Mix both phases.
- Apply ultrasonic waves.
- Reduce particle size to nano-meter range.
- Cool dispersion to obtain SLN. [36]

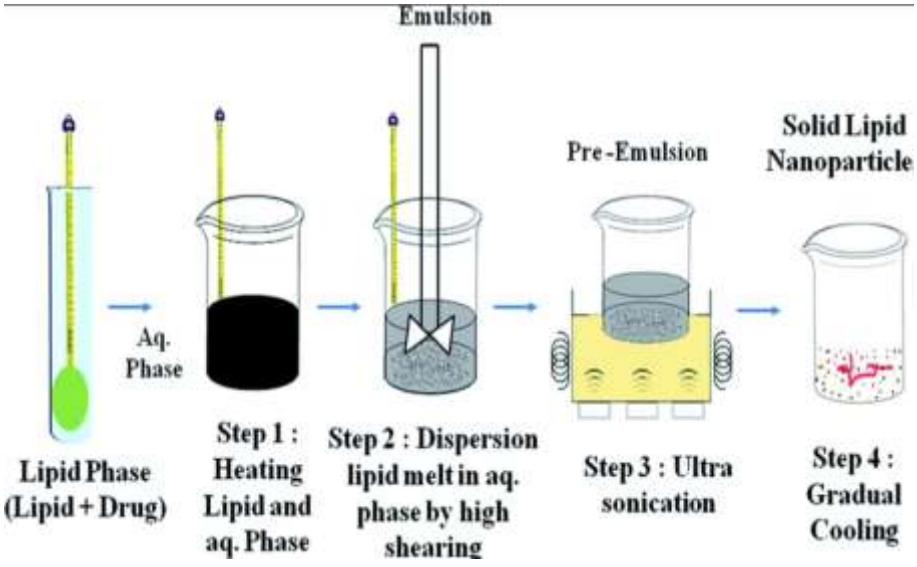


Fig 6: Ultrasonication Method[36]

5) Micro Emulsion Method

Principle

A warm microemulsion containing valsartan, lipid, surfactant, and co-surfactant is prepared and dispersed into cold water. Rapid cooling causes solidification of lipid droplets and formation of SLN.

Procedure

- Melt lipid and dissolve valsartan.
- Add surfactant and co-surfactant.
- Form warm microemulsion.
- Disperse into cold water.
- Lipid solidifies into nanoparticles. [37]

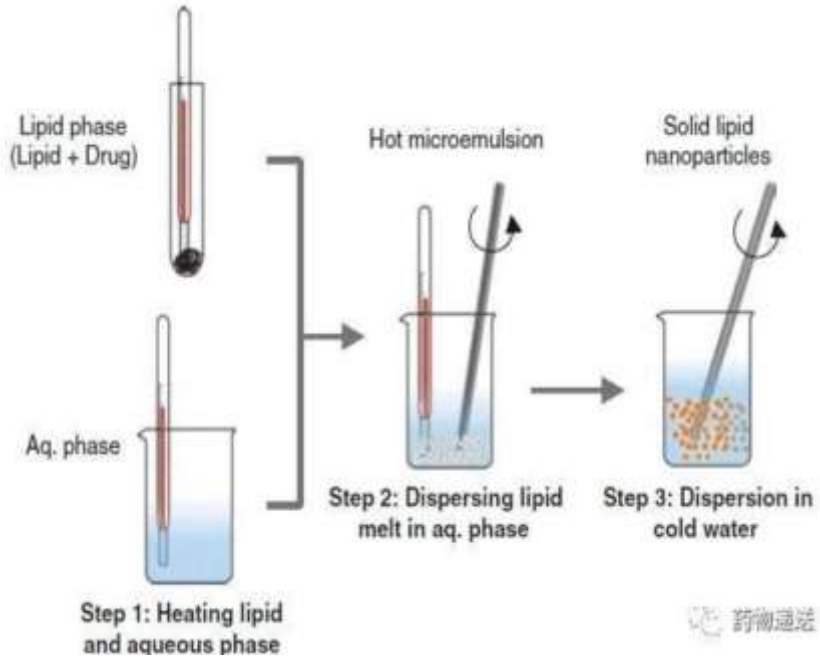


Fig 7: Micro Emulsion Method[37]

4. EVALUATION PARAMETERS FOR VALSARTAN LOADED SLN

1. Particle Size Analysis

Particle size analysis is one of the most important evaluation parameters for valsartan-loaded solid lipid nanoparticles (SLN). The particle size influences drug dissolution, bioavailability, stability, and cellular uptake. It is commonly measured using Dynamic Light Scattering (DLS). Smaller nanoparticles provide a larger surface area, leading to enhanced dissolution and absorption of valsartan. In a study by Chandana et al., the optimized valsartan-loaded SLN formulation showed a particle size of approximately 136.5 nm, indicating successful formation of nanoparticles and improved potential for oral drug delivery.

2. Polydispersity Index (PDI)

The Polydispersity Index (PDI) is used to evaluate the uniformity of particle size distribution within the nanoparticle formulation. A lower PDI value indicates a more homogeneous and stable nanoparticle system. Generally, a PDI value below 0.5 is considered acceptable for SLN formulations. Chandana et al. reported a PDI value of 0.424 for optimized valsartan-loaded SLN, indicating relatively uniform particle size distribution and good formulation stability.

3. Zeta Potential

Zeta potential is used to determine the surface charge and stability of nanoparticle dispersions. It provides information about the electrostatic repulsion between particles, which helps prevent aggregation. Higher absolute zeta potential values indicate greater stability of the formulation. Studies on valsartan-loaded SLN have reported negative zeta potential values, demonstrating adequate stability and reduced particle aggregation during storage. Stable zeta potential values contribute to prolonged shelf life and better performance of the nanoparticle system. [38]

4. Entrapment Efficiency

Entrapment efficiency (EE %) measures the percentage of valsartan successfully incorporated within the lipid matrix of the nanoparticles. High entrapment efficiency is desirable because it indicates effective drug loading and minimizes drug wastage. The entrapment efficiency depends on the type of lipid, surfactant concentration, and preparation method. Research studies have reported entrapment efficiencies ranging from 80% to 96% for valsartan-loaded SLN formulations, demonstrating the strong capacity of lipid matrices to encapsulate valsartan.

5. Surface Morphology (SEM/TEM)

Surface morphology studies are performed using Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM). These techniques provide information regarding particle shape, surface characteristics, and aggregation behaviour. TEM and SEM analyses of valsartan-loaded SLN have revealed spherical particles with smooth surfaces and uniform distribution. The spherical morphology contributes to improved stability, controlled drug release, and enhanced bioavailability of the formulation.

6. In Vitro Drug Release Study

In vitro drug release studies are performed to determine the release pattern of valsartan from SLN formulations. Most valsartan-loaded SLN systems exhibit a biphasic release profile consisting of an initial burst release followed by sustained drug release over an extended period. The initial burst release provides rapid therapeutic action, while the sustained phase maintains drug levels for up to 12–24 hours. This controlled release behavior improves antihypertensive efficacy and reduces dosing frequency. [39]

5. ADVANTAGES

1) Enhanced Oral Bioavailability

Bypasses hepatic first-pass metabolism and promotes lymphatic absorption, increasing oral bioavailability compared to conventional tablets. [40]

2) Sustained Drug Release

Exhibits an initial burst release followed by a prolonged, controlled release profile (up to 12-72 hours). This allows for reduced dosing frequency and improved patient compliance. [41]

3) Improved Solubility

Converts valsartan into an amorphous form within the lipid matrix, drastically improving its dissolution rate. [42]

4) Increased Half-Life

Maintains significantly lower systolic and diastolic blood pressure for longer durations than traditional formulations. [43]

5) Reduced Toxicity & High Biocompatibility

Uses physiological lipids and safe surfactants, avoiding the toxicities associated with certain synthetic polymers. [44]

6) Brain Targeting Potential

When administered intranasally, SLNs can effectively bypass the blood-brain barrier, which helps mitigate the secondary negative effects of hypertension and stroke. [45]

6. THERAPEUTIC USES OF VALSARTAN-LOADED SOLID LIPID NANOPARTICLES;

i. Treatment of Essential Hypertension:

Valsartan-loaded solid lipid nanoparticles are used for the effective management of essential hypertension. The SLN system enhances drug absorption and improves therapeutic efficacy by increasing oral bioavailability compared to conventional formulations. (46)

ii. Prolonged Blood Pressure Control

The sustained-release nature of SLN helps maintain therapeutic plasma concentrations of valsartan for an extended period, resulting in prolonged control of systolic and diastolic blood pressure and minimizing blood pressure fluctuations. (47)

iii. Prevention of Cardiovascular Complications

Long-term administration of valsartan-loaded SLN may reduce hypertension-associated cardiovascular complications such as myocardial infarction, ventricular hypertrophy, and heart failure due to improved drug availability and continuous antihypertensive action. (48)

iv. Reduction of Stroke Risk

Sustained antihypertensive activity achieved through SLN formulations helps maintain stable blood pressure levels and may reduce the risk of cerebrovascular events such as stroke in hypertensive patients. (49)

v. Renal Protection in Hypertensive Patients

Continuous blood pressure control provided by valsartan-loaded SLN may help prevent hypertension-induced kidney damage and reduce the progression of nephropathy by maintaining effective antihypertensive therapy. (50)

vi. Improved Patient Compliance

Due to prolonged drug release and reduced dosing frequency, valsartan-loaded SLN improve adherence to long-term antihypertensive therapy, especially in elderly patients requiring chronic treatment. (51)

vii. Enhanced Therapeutic Response in Resistant Hypertension

SLN formulations improve valsartan absorption and systemic availability, which may provide better therapeutic outcomes in patients with poorly controlled or resistant hypertension.

viii. Reduction in Dose-Related Side Effects

The controlled-release behaviour of valsartan-loaded SLN prevents sudden peaks in plasma drug concentration, thereby reducing adverse effects associated with high drug levels while maintaining therapeutic efficacy. (52)

7. FUTURE PERSPECTIVES;

Future developments in valsartan-loaded SLNs are focused on improving oral bioavailability, controlled drug release, and targeted delivery for better hypertension management. Advanced lipid-based nanocarriers may enhance therapeutic efficacy while reducing dosing frequency and adverse effects. Researchers are also exploring surface-modified and ligand-targeted SLNs to improve site-specific drug delivery. Large-scale manufacturing techniques, long-term stability studies, and clinical trials are needed to support commercialization and clinical application. Overall, valsartan-loaded SLNs represent a promising next-generation approach for safer, more effective, and patient-friendly antihypertensive therapy. (53)

8. CONCLUSION;

Valsartan-loaded Solid Lipid Nanoparticles (SLN) improve the solubility and bioavailability of valsartan. They provide sustained drug release and prolonged antihypertensive action. SLN enhance therapeutic efficacy while reducing dosing frequency and side effects. Their biocompatibility and stability make them a promising drug delivery system. Thus, valsartan-loaded SLN offer an effective approach for hypertension management.

REFERENCES;

1. World Health Organization. Hypertension [Internet]. Geneva: World Health Organization; 2023 [cited 2026 Jun 20]. Available from:
2. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension global hypertension practice guidelines. Hypertension. 2020; 75(6):1334-1357.
3. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. Hypertension. 2018; 71(6):e13-e115.
4. Criscione L, de Gasparo M, Bühlmayer P, Whitebread S, Ramjoué HP, Wood J. Pharmacological profile of valsartan: a potent, orally active, nonpeptide antagonist of the angiotensin II AT1-receptor subtype. Br J Pharmacol. 1993; 110(2):761-771.
5. Flesch G, Müller P, Lloyd P. Absolute bioavailability and pharmacokinetics of valsartan, an angiotensin II receptor antagonist, in man. Eur J Clin Pharmacol. 1997; 52(2):115-120.
6. Black HR, Graff A, Shute D, et al. Valsartan, a new angiotensin II antagonist for the treatment of essential hypertension: efficacy, tolerability and safety compared with lisinopril. J Hum Hypertens. 1997; 11(8):483-489.
7. Khatak S, Dureja H. Recent advances in solid lipid nanoparticles for drug delivery. J Pharm Investig. 2015; 45(3):219-234.
8. Zur Mühlen A, Schwarz C, Mehnert W. Solid lipid nanoparticles for controlled drug delivery: review of the state of the art. Eur J Pharm Biopharm. 2000; 50(1):161-177.
9. Franklin SS, Larson MG, Khan SA, et al. Does the relation of blood pressure to coronary heart disease change with aging? The Framingham Heart Study. Circulation. 2001; 103(9):1245-1249.
10. Frost CD, Law MR, Wald NJ. By how much does dietary salt reduction lower blood pressure? II. Analysis of observational data within populations. BMJ. 1991; 302(6780):815-818.
11. Guyton AC, Coleman TG, Cowley AV Jr, Scheel KW, Manning RD Jr, Norman RA Jr. Arterial pressure regulation. Overriding dominance of the kidneys in long-term regulation and in hypertension. Am J Med. 1972; 52(5):584-594.
12. Fagard R, Brguljan J, Staessen J, Thijs L, Derom C, Thomis M, Vlietinck R. Heritability of conventional and ambulatory blood pressures: a study in twins. Hypertension. 1995; 26(6 Pt 1):919-924.
13. Danaei G, Ding EL, Mozaffarian D, Taylor B, Rehm J, Murray CJL, Ezzati M. The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. PLoS Med. 2009; 6(4):e1000058.
14. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet. 2005; 365(9455):217-223.
15. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension global hypertension practice guidelines. Hypertension. 2020; 75(6):1334-1357.
16. Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, et al. 2017 ACC/AHA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. Hypertension. 2018; 71(6):e13-e115.
17. Carretero OA, Oparil S. Essential hypertension. Part I: definition and etiology. Circulation. 2000; 101(3):329-335.
18. Moser M, Setaro JF. Resistant or difficult-to-control hypertension. N Engl J Med. 2006; 355(4):385-392.

19. Criscione L, de Gasparo M, Bühlmayer P, Whitebread S, Ramjoué HP, Wood J. Pharmacological profile of valsartan: a potent, orally active, nonpeptide antagonist of the angiotensin II AT1-receptor subtype. Br J Pharmacol. 1993; 110(2):761-771.
20. Naseri N, Valizadeh H, Zakeri-Milani P. Solid lipid nanoparticles and nanostructured lipid carriers: structure, preparation and application. Mater Sci Eng C. 2015; 53:191-205.
21. Faraji S, Wipf P, et al. Nanotechnology-based antifungal drug delivery systems. Adv Drug Deliv Rev. 2009.
22. Parmar B, Mandal S, Petkar K, Patel LD, Sawant KK. Valsartan loaded solid lipid nanoparticles: development, characterization, and in vitro and ex vivo evaluation. Int J Pharm Sci Nanotechnol. 2011; 4(3):1483-1490.
23. Patel H, Oza V, Koli A, Ranch K, Shah D. Formulation development and evaluation of lipid-based nanoparticles of valsartan by microemulsification. 2013.
24. Das A, Gowda BHJ, Hani U, Paul K, Ahmed MG, Abdi G, et al. Solid lipid nanoparticles for the management of hypertension: advancements and challenges. Curr Pharm Des. 2025; 31(23):1823-1843.
25. Sabry SA, Abd El Razek AM, Nabil M, Khedr SM, El-Nahas HM, Eissa NG. Brain-targeted delivery of valsartan using solid lipid nanoparticles labeled with Rhodamine B: a promising technique for mitigating the negative effects of stroke. Drug Deliv. 2023; 30(1):2179127.
26. Wójcik-Pastuszka D, Musiał W, Chrząszcz A. Solid lipid nanoparticles and nanostructured lipid carriers: a review emphasizing particle structure and drug release. Eur J Pharm Biopharm. 2018; 133:285-308.
27. Hajba-Horváth E, Fodor-Kardos A, Shah N, Wacker MG, Feczkó T. Sustainable stabilizer-free nanoparticle formulations of valsartan using Eudragit® RLPO. Int J Mol Sci. 2021; 22(23):13069.
28. Amidon GL, Löbenberg R. Modern bioavailability, bioequivalence and biopharmaceutics classification system: new scientific approaches to international regulatory standards. Eur J Pharm Biopharm. 2000; 50(1):3-12.
29. Ghasemiyeh P, Mohammadi-Samani S. Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: applications, advantages and disadvantages. Res Pharm Sci. 2018; 13(4):288-303.
30. Kim MS, Jin SJ, Kim JS, et al. Fabrication and evaluation of valsartan-polymer-surfactant composite nanoparticles by using the supercritical antisolvent process. Int J Nanomedicine. 2014;9:5167-5180.
31. Kushwaha AK, Vuddanda PR, Karunanidhi P, Singh SK, Singh S. Development and evaluation of solid lipid nanoparticles of raloxifene hydrochloride for enhanced bioavailability. ScientificWorldJournal. 2013; 2013:584549.
32. Chaiklieng S, et al. pH-independent controlled release tablets containing nanonizing valsartan solid dispersions for less variable bioavailability in humans. J Drug Deliv Sci Technol. 2018.
33. Chandana M, Venkata Ramana M, Rama Rao N. Formulation and evaluation of valsartan solid lipid nanoparticles. J Drug Deliv Ther. 2021.
34. Mehnert W, Mäder K. Solid lipid nanoparticles: production, characterization and applications. Adv Drug Deliv Rev. 2001; 47(2-3):165-196.
35. Das S, Chaudhury A. Recent advances in lipid nanoparticle formulations. Pharmaceutics.
36. Khairnar SV, Pagare P, Thakre A, et al. Review on the scale-up methods for the preparation of solid lipid nanoparticles. Pharmaceutics. 2022.
37. Duan Y, Dhar A, Patel C, et al. A brief review on solid lipid nanoparticles: part and parcel of contemporary drug delivery systems.
38. Patel H, Oza V, Koli A, Ranch K, Shah D. Formulation development and evaluation of lipid-based nanoparticles of valsartan by microemulsification. Int J Pharm Sci Res. 2013.

39. Radhakrishnan A, Venkatachalam S, Paruchuri B. Design and development of valsartan-loaded solid lipid nanoparticles for enhanced protection from diabetic neuropathy. Nano Biomed Eng. 2019; 11(3):306-312.
40. Soma D, Attari Z, Reddy MS, Damodaram A, Koteshwara KBG. Solid lipid nanoparticles of irbesartan: preparation, characterization, optimization and pharmacokinetic studies. Braz J Pharm Sci. 2017; 53(4):e16084.
41. Ghasemiyeh P, Mohammadi-Samani S. Solid lipid nanoparticles and nanostructured lipid carriers as novel drug delivery systems: applications, advantages and limitations. Drug Deliv. 2023; 30(1):2179127.
42. Radhakrishnan A, Venkatachalam S, Paruchuri B. Valsartan-loaded solid lipid nanoparticles for enhanced protection from diabetic neuropathy. Nano Biomed Eng. 2019; 11(3):306-312.
43. Al-Mahallawi AM, El-Zahaby SA, Motawea A, et al. Nanotechnology-based delivery systems for antihypertensive drugs: current advances and future prospects. Pharmaceutics. 2023; 15(11):2660.
44. Khurana S, Jain NK, Bedi PMS. Solid lipid nanoparticles: a versatile carrier system for drug delivery. Res J Pharm Technol. 2019; 12(6):3021-3028.
45. Valsartan-loaded intranasal solid lipid nanoparticles for brain targeting: formulation development and evaluation. Int J Pharm. 2023; 633:122612.
46. Parmar B, Mandal S, Petkar K, Patel LD, Sawant KK. Valsartan loaded solid lipid nanoparticles: development, characterization, and in vitro and ex vivo evaluation. Int J Pharm Sci Nanotechnol. 2011; 4(3):1483-1490.
47. Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery: a review of the state of the art. Eur J Pharm Biopharm. 2000; 50(1):161-177.
48. Burnier M, Brunner HR. Angiotensin II receptor antagonists. Lancet. 2000; 355(9204):637-645.
49. Dahlof B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U, et al. Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint Reduction in Hypertension Study (LIFE): a randomised trial against atenolol. Lancet. 2002; 359(9311):995-1003.
50. Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med. 2001; 345(12):861-869.
51. Vauthier C, Bouchemal K. Methods for the preparation and manufacture of polymeric nanoparticles. Pharm Res. 2009; 26(5):1025-1058.
52. Sanad RA, Abdelmalak NS, Elbayoomy TS, Badawi AA. Formulation of a novel oxybenzone-loaded nanostructured lipid carriers (NLCs). AAPS PharmSciTech. 2010; 11(4):1684-1694.
53. Mishra V, Bansal KK, Verma A, Yadav N, Thakur S, Sudhakar K, et al. Solid lipid nanoparticles: emerging colloidal nano drug delivery systems. Pharmaceutics. 2018; 10(4):191.