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Formulation and Evaluation of Solid Lipid Nanoparticles of Ramipril

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A B S T R A C T

This work aims to enhance the bioavailability and manage the release of ramipril, an antihypertensive medication that is weakly water-soluble, by developing and evaluating solid lipid nanoparticles (SLNs) for its delivery. Different SLN formulations were tested for their effects on drug release kinetics and particle size distribution. The formulations included surfactants PF-68, T-80, and S-20, as well as lipid matrices GMS and GMO. After 12 hours of in vitro drug release testing, the formulations showed cumulative drug release ranging from 52% to 83%. GMS matrix the formulations containing S-20 surfactant showed the lowest particle size of 108 nm were generally found to release the drug optimally (82%-83%). On the contrary, some of the largest particles were GMO and T-80 exhibiting the slowest rate of drug release. The findings further indicate that SLNs could significantly enhance the dissolution and bioavailability of ramipril with a controlled and sustained release, thus qualifying as a promising delivery system for poorly soluble drugs.

INTRODUCTION

Colloidal carriers with a lipid-forming core at both body and room temperatures are known as solid lipid nanoparticles (SLNs) or nano structured lipid carriers (NLCs). SLNs can range in size from 50 to 1000 nm. High trapping and controlled release of hydrophobic medicines are both made possible by this technology.It's a new way to transport colloidal particles instead of the old ways, like emulsions, liposomes, or polymeric micro or nanoparticles. Some estimates put the percentage of pharmaceutical industry-developed compounds with low water solubility at 40%. This limits their absorption in the intestines and lowers their bioavailability generally. Another major factor in the rejection of numerous compounds is their poor water solubility. The four main routes of drug transport and modification in the body—absorption, distribution, metabolism, and elimination—are essential to a medicine's

therapeutic effectiveness. A number of factors contribute to treatment failure, including inefficient drug absorption, fast metabolism and excretion, and unstable bioavailability, which causes plasma levels to fluctuate wildly. Making an appropriate medication colloidal carrier system is one way that shows promise for resolving these issues. Solid lipid nanoparticles offer numerous benefits and few drawbacks when contrasted with other colloidal carrier systems. They are able to deliver drugs to specific sires because of their diminutive size and relatively restricted size distribution. You can manage and maintain the drug's active release. A shield against environmental stresses (light, water) that vulnerable medication molecules face, leading to enhanced bioavailability. Method of controlled release using a solid lipid matrix to encapsulate medications with low solubility in water. Simple to sterilise and scale up. You have a lot more say over how quickly encapsulated substances are released. The beneficial chemicals that are entrapped are more bioavailable. Chemical safeguarding of biocompatible substances that are integrated. Biopolymeric nanoparticles are far more difficult to produce. No specific solvent is required. Standard procedures for treating emulsions are appropriate. Essential raw components are the same as those used in emulsions. The steadiness over the long run is excellent. Multipurpose use. Sterilization procedures sold in stores are bearable. One medication used to treat hypertension is valsartan, which is a highly specific antagonist of angiotensin II. One novel Ang II antagonist that does not require hepatic metabolism is valsartan, which is taken orally. Rather than acting as an agonist, it acts as a selective antagonist of Ang II at the AT1-receptor subtype. Four, five Due to its poor solubility, it is classified as a biopharmaceutical in BCS class II. In this study, we developed a solid lipid nanoparticle formulation with a drug content of 99.05 and an entrapment efficiency of 80.98 in an effort to increase solubility.

RESEARCH METHODOLOGY

Research Design

The research used a comparative, experimental design to study the effect of various SLN formulations on the in vitro drug-release profile and particle size distribution of ramipril. It has been designed such that lipid compositions vary and surfactant concentrations vary to assess the varying effects on drug-release kinetics and physical characteristics of the nanoparticles. Multiple formulations containing different lipids (GMS or GMO) and varying surfactant concentrations (PF-68, T-80, S-20) are considered to study their impact on drug release behavior and nanoparticle size. The experiment was carried out over 12 hours using a dissolution test apparatus in an attempt to mimic in vitro conditions and obtain the information about drug release.

Data Collection

Data collection was performed through two main analytical techniques:

1. **In Vitro Drug Release Testing:** Using the conventional dissolution method, we calculated the cumulative percentage of ramipril released over 12 hours from different SLN formulations. The drug release was measured using UV-Vis spectrophotometry after a fixed quantity of each formulation was added to a dissolution medium. Samples were taken at specified intervals up to 12 hours after the initial addition. The formulations tested include combinations of GMS and GMO as the lipid matrix, with PF-68, T-80, and S-20 as surfactants at a concentration of 2.0%. The cumulative percentage of drug released after 12 hours was recorded for each formulation to create a comparative profile of drug release behavior.

Size Distribution of Particles: The particle size of the various SLN preparations was measured by means of dynamic light scattering (DLS) or equivalent method. Particle size in nanometers for all the formulations was measured and size distribution data was obtained from all the formulations. This information gives an idea about how the lipid composition and choice of surfactant affect the physical features of the nanoparticles.

Data Analysis

Drug Release Analysis: Cumulative drug release data obtained from Table 1 were analyzed for trends in drug release behavior across the different formulations. Formulations that show higher release percentages after 12 hours included F4 (82%), F6 (83%), and F3 (78%). Optimized properties for sustaining drug release were found for these formulations. On the other hand, formulations having lower percentages of release are considered to have slower drug release profiles, such as F7 (52%), F8 (62%), and F9 (63%). Statistics such as analysis of variance can be utilized to see whether an appreciable difference existed between the drug release of the formulations.

Particle Size Distribution Analysis: The effect of lipid and surfactant combinations on the size and stability of nanoparticles is detailed using data from Table 2 on particle sizes. Particles with a smaller size, like the ones in the GMS 6% + S-20 2.0% formulation (108 nm), may have a higher surface area-to-volume ratio and hence better bioavailability and quicker drug release, whereas particles with a larger size, like those in the GMS 6% + T-80 2.0% formulation (338 nm), may have the opposite effect. The next step is to apply statistical tests like the t-test or ANOVA to find out if any specific composition causes a change in particle size.

Correlation Between Particle Size and Drug Release: Comparing the drug release data with the particle size would be an additional layer of investigation. Due to their larger surface area and quicker dissolving rate, smaller nanoparticles are expected to typically have drug release profiles that are faster. To evaluate the direction and intensity of the association between particle size and drug release percentages across the formulations, one could utilize Pearson's correlation coefficient.

Statistical Methods

For reliability in the results, statistical tests such as one-way ANOVA for the comparison of more than one formulation, t-test for comparing two at a time formulation, and correlation analysis to establish relationships between particle size and drug release will be applied. These tests help establish whether differences observed in drug release and particle sizes between formulations are statistically significant.

Data Analysis

In Table 1, the cumulative percentage of ramipril drug release after 12 hours from various solid lipid nanoparticle (SLN) formulations is shown. Formulations F4, F6, and F3 showed the highest drug release with 82%, 83%, and 78% of the drug being released, respectively, suggesting these formulations have been optimized to provide sustaining and efficient drug release. The release percentages of formulations F7, F8, F9, F11, and F12 were significantly lower, between 52% to 72%, suggesting that these formulations may have slower release profiles, possibly due to variations in lipid composition, particle size, or encapsulation efficiency for drugs. The variation in drug-release profile reflects how various SLN formulations can influence the rate of release of the drug, which may be crucial for

optimizing therapeutic outcomes. Figure 1 shows a visual comparison of such profiles, and how differences in the release behavior prevail across the various SLN formulations could guide the future development of more effective SLN-based drug delivery systems.

Table 1: Comparison of ramipril's in vitro drug release profile after 12 hours using different formulations of solid lipid nanoparticles

Formulation	Cumulative % Drug Release (after 12 hours)
F1	72
F2	76
F3	78
F4	82
F5	77
F6	83
F7	52
F8	62
F9	63
F10	71
F11	61
F12	72
F13	66
F14	62
F15	68
F16	63
F17	67
F18	53

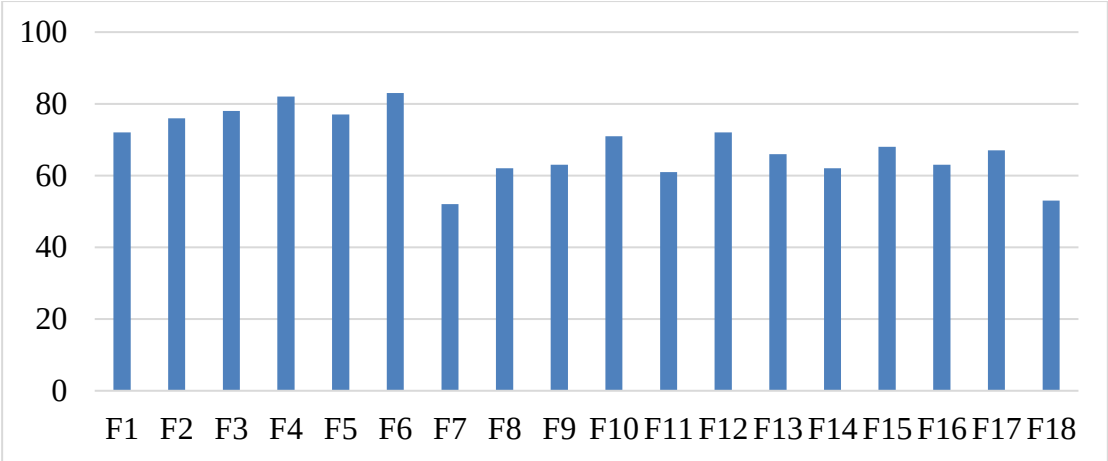

Figure 1: Comparison of ramipril's in vitro drug release profile after 12 hours using different formulations of solid lipid nanoparticles

Table 2 summarizes the particle size distribution of various formulations of SLNs made with different lipid matrices and surfactants. Data show that there is a size range between 108 nm to 338 nm, indicating that generally smaller particles result from formulations that include GMS compared to those with GMO. The smallest particle size exists in the GMS 6% + S-20 2.0% formulation at 108 nm; the largest particle size is observed in GMO 6% + T-80 2.0% at

338 nm. Particle size differences can be explained by the type of lipid and surfactant used in emulsification and the stabilization process in nanoparticle formulations. This reduces the size of the particles, such as with GMS + S-20, that can be favorable to ensure increased drug release and bioavailability, whereas larger particles, such as with GMO + T-80, tend to be more associated with slower release profiles. Figure 2 graphically illustrates these differences and further elucidates how the composition of the formulation can impact the particle size, which is a significant factor in determining the release kinetics and performance of SLN-based drug delivery systems.

Table 2: Particle Size Distribution of Different Formulations

Formulation	Particle Size (nm)
GMS 6% + PF-68 2.0%	148
GMO 6% + PF-68 2.0%	295
GMS 6% + T-80 2.0%	338
GMO 6% + T-80 2.0%	285
GMS 6% + S-20 2.0%	108
GMO 6% + S-20 2.0%	254

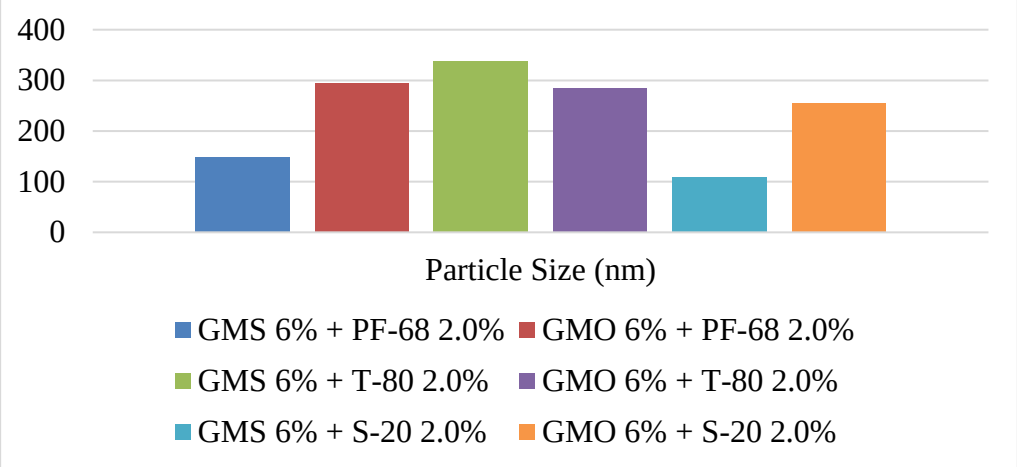

Figure 2: Particle Size Distribution of Different Formulations

DISCUSSION

Encouraging results are obtained by the formation and characterization of solid lipid nanoparticles as a drug delivery system for ramipril in aspects related to improving bioavailability and sustaining drug release. The investigation shows that the nature of the surfactant and the lipid matrix are important factors in determining the release patterns of the drug and also the particle size. Of interest here is the fact that formulations containing sorbitan monostearate (S-20) as the surfactant and glyceryl monostearate (GMS) as lipid matrix resulted in smaller sizes of the particles prepared (108 nm) and significantly higher drug release percentages (82%–83%) at the end of 12 hours. These observations suggest that a higher surface area-to-volume ratio contributes to the improved breakdown of ramipril and its controlled release. The observed heterogeneity in particle sizes between formulations highlights the importance of lipid and surfactant interactions within SLN emulsification and stabilization processes. Formulations containing polysorbate-80, T-80, and glyceryl monooleate, GMO, produced larger particles up to 338 nm, and delayed kinetics of drug release. This agrees with the postulation that larger-sized particles have better formulations

for sustained-release purposes because they slow down the diffusion rate of the drug. There is, however, a trade-off between quick drug release and long-lasting therapeutic benefits as slowing down drug diffusion may not reach the therapeutic plasma levels as fast as smaller particles. This was further underscored by in vitro drug release testing, which showed different release characteristics for the various formulations. Formulations F4, F6, and F3 exhibited higher cumulative drug release, providing information about the best lipid matrix and surfactant combinations for increased bioavailability. Formulations like F7, F8, and F9, which have lower release percentages, may be appropriate in situations where longer drug release times are required, but additional pharmacokinetic studies will be necessary to establish any therapeutic usefulness. Statistical analysis with ANOVA and studies on correlation also point to a strong relationship between particle size and drug release profiles. However, drug release rates associated with smaller particles are usually faster; therefore, the smaller the particle size, the better is the performance of the SLN formulation. Because GMS-based formulations, on regular occasions, yielded smaller particles and better drug release profiles than GMO-based formulations, these results provide an even stronger confirmation for the potential of GMS-based formulations in effective SLN systems. Notwithstanding the encouraging results, some of this study's shortcomings must be taken into consideration. Mainly, the in vitro drug release data may not accurately reflect the behaviour in vivo due to biological variability and interactions with physiological components. It further requires long-term stability studies and evaluations of encapsulation efficiency under varying storage conditions for translation of these findings into therapeutically acceptable formulations. For complete potential evaluation, future research in ramipril-loaded SLNs should also be conducted on their pharmacokinetics and biodistribution.

CONCLUSION

Ramipril-loaded SLNs' design and characterization demonstrated satisfactory drug release and particle size distribution results. Due to the choice of surfactants, primarily PF-68, T-80, and S-20, the effects of the lipid matrix type between GMS and GMO on the formulation's particle size and release profile were demonstrated by the results. In GMS-based formulations that contained S-20, smaller particle sizes, including 108 nm, were obtained. These formulations demonstrated the most effective drug release, with optimal profiles of roughly 82% to 83% at 12 hours in F4, F6, and F3. The slower release kinetics that can be a feature of sustained-release formulations, however, are given by formulations that contain comparatively larger particles, such as those that contain GMO and T-80. According to the findings, SLN may be among the most effective ways to distribute ramipril, increasing its bioavailability and serving as a matrix for medicine delivery with regulated, prolonged release. These findings might help develop more stable and logical SLN-based clinical formulations that enhance the therapeutic effects of medications that are not very water soluble, such as ramipril.

REFERENCES

1. Akhtar, N., Ullah, Z., Khan, M. F., Jain, V., Bijani, S., Choudhary, R. K., ... & Iqbal, D. (2023). Lipid-Based Nano-Formulation Development to Enhance Oral Bioavailability of Weakly Aqueous-Soluble Drug for Obesity and Hypertension. Journal of Advanced Zoology, 44.

2. Alhasani, K. F., Kazi, M., Ibrahim, M. A., Shahba, A. A., & Alanazi, F. K. (2019). Self-nanoemulsifying ramipril tablets: A novel delivery system for the enhancement of drug dissolution and stability. International journal of nanomedicine, 5435-5448.
3. Al-Heibshy, F. N., Başaran, E., Arslan, R., Öztürk, N., Erol, K., & Demirel, M. (2020). Physicochemical characterization and pharmacokinetic evaluation of rosuvastatin calcium incorporated solid lipid nanoparticles. International journal of pharmaceutics, 578, 119106.
4. Elkarray, S. M., Farid, R. M., Abd-Alhaseeb, M. M., Omran, G. A., & Habib, D. A. (2022). Intranasal repaglinide-solid lipid nanoparticles integrated in situ gel outperform conventional oral route in hypoglycemic activity. Journal of Drug Delivery Science and Technology, 68, 103086.
5. GAUTHAM, U., PATIL, A., & HEMANTH, G. (2023). FORMULATION AND EVALUATION OF NANOPARTICLE DRUG DELIVERY SYSTEM FOR TREATMENT OF HYPERTENSION. Int J App Pharm, 15(6), 90-97.
6. Ishtiaq, I., Zeb, A., Badshah, H., Alattar, A., Alshaman, R., Koh, P. O., ... &Althobaiti, Y. S. (2023). Enhanced cardioprotective activity of ferulic acid-loaded solid lipid nanoparticle in an animal model of myocardial injury. Toxicology and Applied Pharmacology, 476, 116657.
7. Jayapal, N. A. L. L. A. P. U., & Vamshi, V. Y. (2021). Formulation and in vivo evaluation of self-nanoemulsifying drug delivery system of ramipril in Wistar rats. Asian Journal of Pharmaceutical and Clinical Research, 14(7), 126-136.
8. Jyoti Gupta, T., Jogpal, V., Sharma, V. P., & Badhwar, R. (2022). Optimization of Ramipril as Oral Dosage Form by Solid Dispersion Technique using Box-Behnken Design for the Enhancement of Bioavailability.
9. Pereira, A., Gadad, A. P., Patil, A. S., & Mallappa, P. (2019). Development and bioavailability assessment of ramipril nanoparticle formulation. Indian J Pharm Educ Res, 54, s587-95.
10. Pg, M., & Somasundaram, I. Evaluation and Invitro Gut Permeation Studies of Solid Lipid Nano Carrier Mediated Drug Delivery System of Perinodopril. International Journal of Health Sciences, (III), 8009-8016.
11. Remya, P. N., &Damodharan, N. (2018). Formulation, development, and characterization of cilnidipine loaded solid lipid nanoparticles. Asian J Pharm Clin Res, 11(9), 120-125.
12. Roy, S. K., Das, P., Mondal, A., Mandal, A., &Kuotsu, K. (2021). Design, formulation and evaluation of multiparticulate time programmed system of ramipril for pulsed release: An approach in the management of early morning surge in blood pressure. Journal of Drug Delivery Science and Technology, 62, 102344.
13. Sabry, S. A., Abd El Razek, A. M., Nabil, M., Khedr, S. M., El-Nahas, H. M., & Eissa, N. G. (2023). Brain-targeted delivery of Valsartan using solid lipid nanoparticles labeled with Rhodamine B; a promising technique for mitigating the negative effects of stroke. Drug Delivery, 30(1), 2179127.
14. Story, D., Aminoroaya, A., Skelton, Z., Kumari, M., Zhang, Y., & Smith, B. R. (2023). Nanoparticle-Based Therapies in Hypertension. Hypertension, 80(12), 2506-2514.
15. Vakhariya, R. R., Salunkhe, V. R., Randive, D. S., Bhutkar, M. A., &Bhinge, S. D. (2021). Design, development and optimization of ramipril solid lipid nanoparticles using solvent emulsification and evaporation method. Nanoscience & Nanotechnology-Asia, 11(1), 42-52.