Preparation, Characterization and *In Situ* Absorption Studies of Lercanidipine Loaded Eudragit Nanoparticles

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**ABSTRACT SUMMARY**

The novel lercanidipine loaded Eudragit nanoparticles were devised using modified-emulsion-diffusion-solvent evaporation method. The nanoparticles were freeze dried and then characterized for different physicochemical parameters. The formulations possessed an average particle size of below 247.8 nm and had a positively charged surface. The encapsulation efficiency was as high as 57.90%. AFM scans recorded for lercanidipine loaded Eudragit nanoparticles showed conspicuously discrete, non-agglomerated, oval shaped, smooth particles with almost uniform distribution of lower range particle size. The *in vitro* drug release studies exhibited a biphasic release characterized by an initial rapid release followed by a extended release pattern. There has been statistically significant increase in absorption rate constant values of nanoparticle formulations as compared to free lercanidipine. The present work indicates the potential of Eudragit nanoparticles in improving the delivery efficacy of lercanidipine.

**EXPERIMENTAL METHODS**

The lercanidipine nanoparticles were produced by modified-diffusion-solvent evaporation method. In brief, lercanidipine and polymer were separately dissolved in organic solvent and were homogenized at 15000 rpm using high speed homogenizer for 15 min. The obtained organic phase containing drug and polymer were subjected to probe sonication at 60 amplitude for 6 min with 2 sec pulsar intermittently under cooling conditions. The sonicated pre-emulsion was then added to 30 mL of an aqueous phase containing 1% w/v stabilizer and subsequently homogenized at 15000 rpm for 20 min. The resulting o/w emulsion was placed on ice bath and again probe sonicated at 80 amplitude for 8 min with 2 sec pulsar intermittently. The organic phase of the preparation was evaporated with moderate magnetic stirring at room temperature and the resultant nanoparticles were further subjected to centrifugation and freeze drying step to obtain free-flowing nanoparticle powder. The obtained nanoparticles were characterized for particle size, zeta potential, encapsulation efficiency, DSC, XRD, AFM, TEM and *in vitro* drug release studies. The absorption behaviour of compliance problems. These shortcomings of lercanidipine can be overcome by developing suitable drug delivery system in the form of polymeric nanoparticles. In the present study, it was hypothesized that the novel nano-drug carriers would provide the effective means to improve the drug solubility, avoid first-pass metabolism and thereby ultimately improve the absorption and bioavailability of lercanidipine.

**INTRODUCTION**

Lercanidipine is a poorly aqueous soluble drug used in the treatment of hypertension. It has a half-life of about 2 to 5 h. Lercanidipine exhibits absolute bioavailability of only 10% due to its extensive and saturable first-pass metabolism. Further administration of lercanidipine along with food increases the absorption and hence the bioavailability. These properties are highly undesirable and can result in dose fluctuations, ineffectiveness, larger inter-patient variability and consequent patient
lercanidipine loaded nanoparticles was assessed by *in situ* single-pass perfusion technique across the rat intestine.

**RESULTS AND DISCUSSION**

The nanoparticles obtained using modified emulsion-diffusion-solvent evaporation method was dry, free-flowing and readily redispersible when reconstituted with water. The nanoparticle batches with drug: polymer ratio 1:05 to 1:60 showed a particle size in the range of 122.8 to 247.8 nm with a narrow PDI of below 0.479. The batches yielded high positive zeta potential values almost above 40 mV indicating the stable nature of the formulation. The drug encapsulation obtained was in incremental order with that of polymer concentration from 14.48 to 57.90%. DSC studies suggested amorphization of the drug in nanoparticles and same was also observed in XRD diffractograms as reflected by the amorphous humps. AFM scans recorded for lercanidipine loaded Eudragit nanoparticles showed conspicuously discrete, non-agglomerated, oval shaped, smooth particles. The TEM image analysis produced a smooth, substantially spherical to elongated type of particles with a particle size below 200 nm. Out of selected batches for dissolution study, 1:40 ratio batch showed rapid release of 44.13% within 1 h whereas batch with 1:50 ratio showed sustained fashion release of 98.73% in 24 h. The batch with 1:60 ratio on the other hand exhibited sustained but incomplete % CDR of 77.38 in 24 h. *In situ* absorption of lercanidipine nanoparticles across rat intestine showed absorption rate constant values of 2.88 (K) h⁻¹.

**CONCLUSION**

In conclusion, the study showed the important role of polymeric nanoparticles in oral delivery of lercanidipine. The novel nanoparticles exhibited desirable particle size and excellent encapsulation efficiency. The nanoparticles also illustrated extended drug release pattern for almost 24 h. The *in situ* single-pass perfusion study in wistar rats demonstrated statistically significant (*p* < 0.05) increase in absorption rate constant values of Eudragit based nanoparticles as compared to free lercanidipine. Overall, the developed nanoparticle formulation might be a novel way in improving the poor biopharmaceutical properties of lercanidipine.

**REFERENCES**


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