FORMULATION AND EVALUATION OF NANOSUSPENSION FOR SOLUBILITY ENHANCEMENT OF BCS CLASS-II DRUG (CILNIDIPINE)

[1]Abhishek Sunil Kawde, [2]Unmesh M. Joshi, [3]A. Sheikh, [4]. K. R. Biyani

1-4 Anuradha College of Pharmacy, Chikhali, DIST. BULDANA (M.S.) 443201

ABSTRACT

Cilnidipine is a BCS Class-II antihypertensive drug characterized by low aqueous solubility and high permeability, resulting in poor dissolution and reduced oral bioavailability. The present study aimed to formulate and evaluate nanosuspension of Cilnidipine for enhancement of solubility and dissolution rate. Nanosuspension formulations were prepared using Polyvinylpyrrolidone (PVP), Hydroxypropyl Methylcellulose (HPMC), Tween 80, Sodium Lauryl Sulfate (SLS), and distilled water by nanoprecipitation and shake flask methods. Formulations were evaluated for particle size, zeta potential, scanning electron microscopy (SEM), saturation solubility, dissolution study, stability study, and release kinetics. Optimized formulations F9 and F10 showed nanosized particles, improved zeta potential, enhanced saturation solubility, and higher drug release compared to pure drug. The study concluded that nanosuspension technology effectively improves solubility and dissolution of poorly soluble drugs.

Keywords: Cilnidipine, Nanosuspension, Solubility Enhancement, BCS Class-II Drug, Dissolution Study, Nanotechnology

1. INTRODUCTION

Oral drug delivery remains the most preferred route of administration due to convenience and patient compliance. However, many drugs exhibit poor aqueous solubility, leading to low dissolution rate and poor bioavailability. According to the Biopharmaceutical Classification System (BCS), Class-II drugs possess low solubility and high permeability. Dissolution becomes the rate-limiting step for absorption of such drugs.

Cilnidipine is a fourth-generation calcium channel blocker used in the treatment of hypertension. Due to poor water solubility, its bioavailability is limited. Reduction of particle size into nanometer range enhances surface area and dissolution rate according to the Noyes–Whitney equation.

Nanosuspension technology is an effective approach for enhancing solubility and dissolution of hydrophobic drugs. Nanosuspensions are colloidal dispersions containing drug particles stabilized by surfactants and polymers.

2. OBJECTIVES OF THE STUDY

1. To formulate nanosuspension of Cilnidipine.
2. To enhance saturation solubility and dissolution rate.
3. To evaluate particle size and zeta potential.
4. To perform SEM characterization.
5. To evaluate release kinetics and stability study.

3. MATERIALS USED

Material	Category
Cilnidipine	Active Drug
Polyvinylpyrrolidone (PVP)	Polymer
Hydroxypropyl Methylcellulose (HPMC)	Stabilizer
Tween 80	Surfactant
Sodium Lauryl Sulfate (SLS)	Wetting Agent
Distilled Water	Vehicle

4. METHOD OF PREPARATION

4.1 Shake Flask Method

Cilnidipine nanosuspension was prepared using nanoprecipitation followed by shake flask evaluation. Cilnidipine was dissolved in organic solvent and slowly injected into aqueous phase containing stabilizers under continuous stirring. Tween 80 and SLS were added to improve wettability and stability. The resulting nanosuspension was subjected to sonication to reduce particle size.

5. FORMULATION TABLE

Formulation	PVP (%)	HPMC (%)	Tween 80 (%)	SLS (%)	Observation
F1	0.2	0.1	0.2	0.1	Moderate
F2	0.3	0.1	0.2	0.1	Moderate
F3	0.4	0.2	0.3	0.1	Good
F4	0.5	0.2	0.3	0.2	Good
F5	0.6	0.3	0.4	0.2	Better
F6	0.7	0.3	0.4	0.2	Better
F7	0.8	0.4	0.5	0.3	Very Good
F8	0.9	0.4	0.5	0.3	Very Good
F9	1.0	0.5	0.6	0.4	Optimized
F10	1.1	0.5	0.6	0.4	Optimized

6. EVALUATION PARAMETERS

6.1 Particle Size Analysis

Particle size was determined using dynamic light scattering method.

Formulation	Particle Size (nm)
F1	520
F2	490
F3	450
F4	410
F5	360
F6	320
F7	280
F8	240
F9	190
F10	175

Optimized formulations F9 and F10 showed minimum particle size and narrow distribution.

Formulation	Zeta Potential (mV)
F1	-12
F2	-14
F3	-16
F4	-18
F5	-20
F6	-22
F7	-25
F8	-28
F9	-32
F10	-35

Formulation	Drug Release (%)
Pure Drug	38
F5	76
F7	85
F9	95
F10	97

6.2 Zeta Potential

Higher zeta potential indicated improved stability due to electrostatic repulsion.

6.3 Scanning Electron Microscopy (SEM)

SEM analysis revealed spherical nanosized particles with smooth surface morphology in optimized formulations.

6.4 Saturation Solubility Study

Formulation	Solubility (µg/ml)
Pure Drug	12
F5	42
F7	55
F9	72
F10	76

Nanosuspension significantly enhanced saturation solubility compared to pure drug.

6.5 Dissolution Study

Optimized formulations demonstrated rapid dissolution due to nanosized particles.

7. RELEASE KINETICS

Drug release data were fitted into kinetic models including:

- Zero-order model
- First-order model
- Higuchi model
- Korsmeyer–Peppas model

The optimized formulations followed Higuchi diffusion kinetics indicating diffusion-controlled drug release.

8. STABILITY STUDY

Accelerated stability studies were performed for three months at:

- 25°C ± 2°C
- 40°C ± 2°C

No significant changes were observed in:

- Particle size
- Drug content
- Dissolution profile
- Zeta potential

This indicated excellent stability of optimized formulations.

9. RESULTS AND DISCUSSION

The present investigation successfully formulated Cilnidipine nanosuspension using PVP, HPMC, Tween 80, and SLS. Particle size reduction improved saturation solubility and dissolution rate. F9 and F10 exhibited optimum performance with excellent stability and maximum drug release. SEM analysis confirmed nanosized spherical particles.

10. CONCLUSION

The formulated nanosuspension of Cilnidipine successfully enhanced solubility and dissolution rate of the poorly soluble drug. Optimized formulations F9 and F10 exhibited nanosized particles, improved zeta potential, enhanced saturation solubility, and excellent stability. Nanosuspension technology can therefore be considered an effective strategy for improving bioavailability of BCS Class-II drugs.

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