β-Cyclodextrin Nanosponges for Oral Drug Delivery Of Anti-Hypertensive Drug

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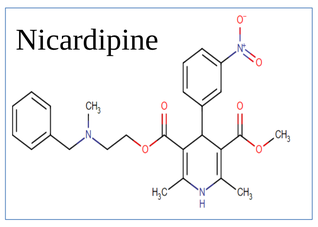
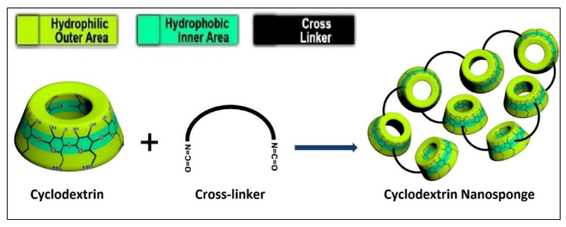
INTRODUCTION

β-cyclodextrin nanosponges (β-CDNS) are colloidal and cross-linked nanocarrier comprising of solid mesh-like structure with nanocavities for encapsulation of complex lipophilic and hydrophilic chemical substances.





AIM

Development and evaluation of β-Cyclodextrin Nanosponges for Oral Drug Delivery Of Anti-Hypertensive Drug

OBJECTIVES

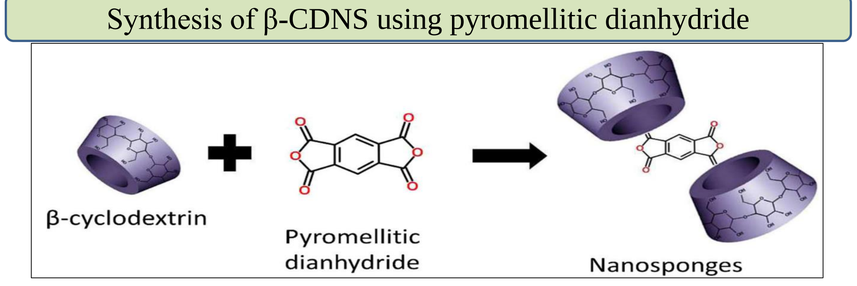
- Synthesis of drug loaded PMDA cross-linked β-CDNS.
- In vitro characterization of drug-loaded nanosponges.
- Formulation and evaluation of β-CDNS based oral drug delivery system.
- To perform Molecular dynamic study.

RATIONALE

- Nicardipine (NC) – BCS class II drug with poor bioavaibility.
- β-CDNS – an efficient nanocarrier for poorly soluble drugs.
- Solubility enhancement.
- Controlled release of the formulation.

METHODOLOGY

Synthesis of β-CDNS using pyromellitic dianhydride



Preparation of Nicardipine loaded β-CDNS

Suspended blank nanosponges and drug in 1:1 ratio in Milli Q water

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Sonicated for 15 minutes to avoid lumps

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Constant stirring for 24 hours to form complex

↓

Undissolved drug is separated by centrifugation

↓

Freeze drying

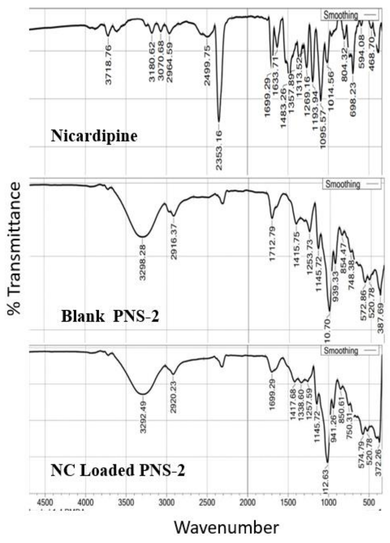
CHARACTERISATION

- The **Particle size** of PNS-2 : 411nm
- The **Polydispersity index (PDI) :** 0.392 and **Zeta Potential :** -20.9 mV.
- **Solubility** of NC in PNS-2 increased by 124.49 folds.

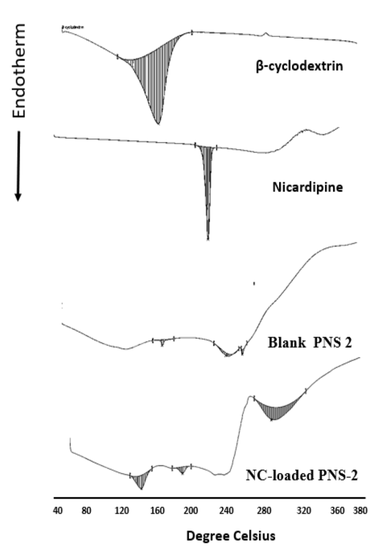
Table 1: Summary of Solubility and entrapment efficiency studies

Sample	β-CD: PMDA	Drug: Nanosponges	Solubility in distilled water (mg/ml)	Entrapment Efficiency
NC			0.00298	
PNS-1	1:2	1:1	0.224	88%
PNS-2	**1:4**	**1:1**	**0.371**	**96%**
PNS-3	1:6	1:1	0.112	75%

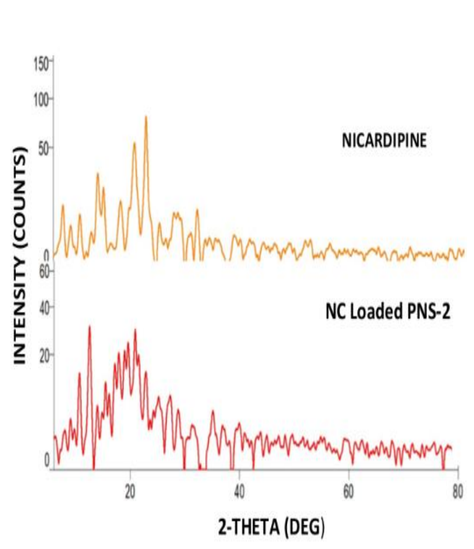
FTIR



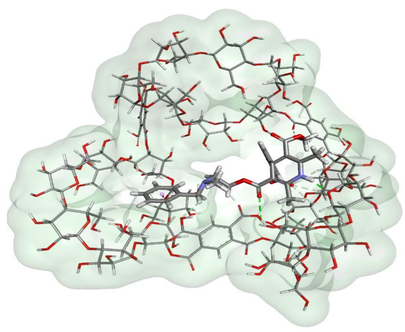
DSC



PXRD



MOLECULAR DYNAMIC STUDY



- PMDA + Nicardipine = -5.8kcal/mol

Type of Interaction	Interacting atoms
Hydrogen bonding	Keto group of ester with -CH_2OH of β-CD
Hydrogen bonding	Nitrogen of dihydropyridine with ring -O atom of β-CD
Pi-Sigma	Terminal phenyl ring with unit of β-CD
Non-classical hydrogen bonding	Multiple interactions were observed between carbon atoms of ligand with oxygen atoms of β-CD and vice versa

FORMULATION DEVELOPMENT

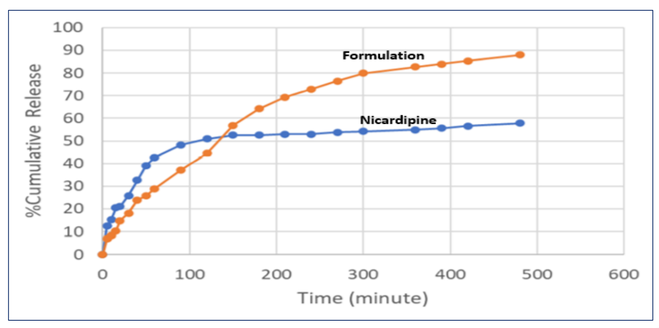
The capsules were filled with 200mg of formulation blend with 20mg of drug (NC)

Table 2: Evaluation study of the formulation

Evaluation	Results
Hausner's ratio	1.13 (Good)
Angle of repose	26.56 (Excellent)
Weight variation of capsules	±10%. (within the acceptable range)

DISSOLUTION STUDY

- USP type I basket
- The dissolution medium, was maintained at 37 ± 0.5 °C and stirred at 75 rpm.
- The release profile of NC-loaded-β-CDNS was substantially higher than pure NC in pH 6.8.
- Therefore, the formulation showed controlled release over 8 hours.



CONCLUSION

The 1:4 ratio of β-CD:PMDA showed highest solubility and entrapment efficiency with 1:1 ratio of Drug: Nanosponge. The solubility was increased significantly with controlled release of NC in vitro. The molecular dynamic studies demonstrated the interaction of NC with CDNS and suggested stability of the complexes. Thus, PMDA cross-linked CDNS can be used as a novel approach for improved oral delivery of Nicardipine.

REFERENCES: Sunil Kumar, Pooja Dalal and Rekha Rao, Cyclodextrin Nanosponges: A Promising Approach for Modulating Drug Delivery, 2019.
Atul P. Sherje*, Bhushan R. Dravyakar, Darshana Kadam, Mrunal Jadhav, Cyclodextrin-based nanosponges: A critical review ,2017.