DEVELOPMENT AND ASSESSMENT OF A BCS CLASS II - SGLT2 (SODIUM GLUCOSE COTRANSPORTER 2) INHIBITOR DRUG IN THE FORM OF SOLID LIPID NANOPARTICLES

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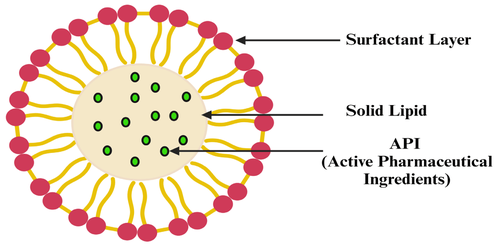
Introduction

Solid lipid nanoparticles (SLNs) represent a promising drug delivery system capable of delivering a wide variety of drugs, including both hydrophobic and hydrophilic compounds. They can be customized for specific therapeutic applications, such as targeted drug delivery, sustained release, and reduced toxicity. The research focused on developing SLN formulations using emulsification-solvent evaporation and homogenization techniques.



Solid Lipid Nanoparticle (SLN)

The SLN consists of spherical lipid particles that are dispersed in an aqueous solution containing surfactants and co-surfactants. Phospholipids create a hydrophobic core where the hydrophobic drug molecules are either entrapped or dispersed. A list of various phospholipids used to develop the SLN is provided in the table below.

Sr. No.	Lipids
1	Glyceryl behenate
2	Stearic acid
3	Glyceryl monostearate
4	Oleic acid
5	Cetyl alcohol
6	Tristearin
7	Glyceryl caprate

Materials

Material	Source / Supplier
SGLT2 inhibitor (active pharmaceutical ingredient)	Dr. Reddy's Laboratories, India
Glyceryl behenate (Compritol® 888 ATO; COM)	Gattefosse India Limited
Polysorbate 20 (Tween 20)	Gangwal Chemicals Pvt. Ltd., India
Polysorbate 80 (Tween 80)	Gangwal Chemicals Pvt. Ltd., India
Polyethylene glycol 4000	Gangwal Chemicals Pvt. Ltd., India
Soya lecithin (Leciva S90)	VAV Lipid Private Limited
Purified water (reverse osmosis)	Millipore, MD, USA
Other chemicals	Various sources

All other chemicals used were at least of reagent grade and were utilized as received.

Method

Preparation of Lipid-Based Microemulsion via High Pressure Homogenization

1. Melting of Lipids
Lipids are melted on a hot plate at a temperature approximately 50 °C above their melting point. This temperature is maintained for 5–10 minutes to ensure complete melting of the lipid phase.

2. Incorporation of Active Pharmaceutical Ingredient (API)
After melting, the active pharmaceutical ingredient (API) is added to the melted lipid and thoroughly dispersed into the aqueous phase. This dispersion is achieved by continuous stirring or sonication to form a uniform microemulsion.

3. Homogenization Process
The resulting microemulsion is subjected to homogenization using a homogenizer (PANDA PLUS 2000). This process utilizes combined mechanical forces including shear force, collision, turbulence, cavitation, and vigorous mixing to reduce particle size effectively.

4. Optimization Parameters
It is crucial to optimize both pressure and temperature during homogenization to achieve the desired particle size and stability of the microemulsion.
A schematic illustration of the high-pressure homogenization process is provided in below figure.

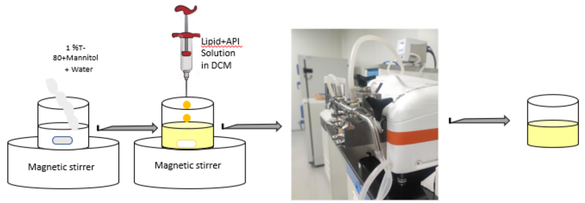


Figure: High pressure homogenization: homogenization process.

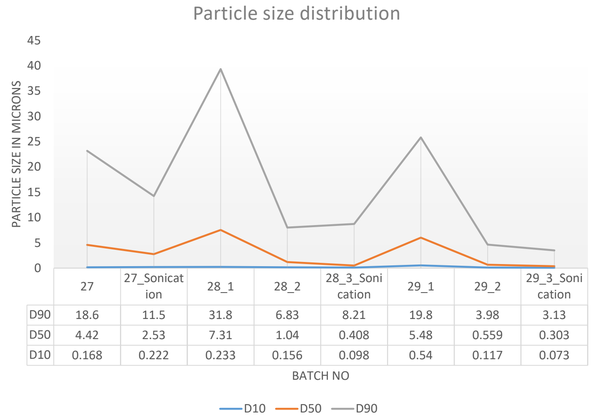
Qualitative solubility determination:

Kinetic solubility of API and various excipients was determined in aqueous solution containing surfactant, co-surfactant and lipids (qualitative). Observation of the qualitative study is provided in below table.

Sr. no	Aq. Stock solution of excipients (0.5%)	Added stock solution of drug (1mg/mL) in DCM	Observation
1	Kolliphore EL	160 µL	Range of Precipitation 120-140 µL
2	Tween -20	280 µL	Range of Precipitation 200-280 µL
3	Tween -80	300 µL	Range of Precipitation 220-300 µL
4	PEG 400	140 µL	Range of Precipitation 120-140 µL
5	Corn oil	100 µL	Range of Precipitation 80-100 µL
6	PEG 200	100 µL	Range of Precipitation 80-100 µL
7	Soyabin oil	100 µL	Range of Precipitation 80-100 µL
8	Miglyol 812	100 µL	Range of Precipitation 80-100 µL
9	Lecithin	5 mg / mL in DCM	No precipitation
10	Lecithin	5 mg / mL in Ethanol	No precipitation

Characterization and evaluation of SLN:

For high-quality solid lipid nanoparticle (SLN) development, precise physicochemical characterization is crucial. Key parameters that indicate high-quality SLN include particle size, drug loading, and drug release.



	27	27_Sonication	28_1	28_2	28_3_Sonication	29_1	29_2	29_3_Sonication
D90	18.6	11.5	31.8	6.83	8.21	19.8	3.98	3.13
D50	4.42	2.53	7.31	1.04	0.408	5.48	0.559	0.303
D10	0.168	0.222	0.233	0.156	0.098	0.54	0.117	0.073

Drug loading and release :

The Results of the % drug loaded, and drug release data were presented in the following table.

Lyophilized vials

B. No	pH	Drug loading %	Dissolution
28	6.21	Not loaded	30min - 101%
29	6.08	Not loaded	30min - 101%
32D	4.68	46%	Under evaluation
32E	4.72	52%	Under evaluation

Conclusion

The research developed Solid Lipid Nanoparticles (SLNs) as an effective drug delivery system that enhances therapeutic efficacy and stability. SLNs are biocompatible and can deliver both hydrophobic and hydrophilic drugs using various formulation techniques. The study emphasized their potential for targeted drug delivery and reduced toxicity, especially in chemotherapy and gene therapy applications.

Future work aims to optimize SLN by improving loading efficiency, decrease in particle size, scalability and stability. Overall, SLNs represent a promising, cost-effective solution for patient-friendly drug delivery.

References

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