RESEARCH PAPER

FORMULATION AND OPTIMIZATION OF SOLID LIPID NANOPARTICLES (SLNs) OF BUDESONIDE

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ABSTRACT

The present study was aimed at the formulation and optimization of Budesonide-loaded Solid Lipid Nanoparticles (SLNs) to improve the solubility, bioavailability, and sustained-release characteristics of Budesonide, a BCS Class II corticosteroid drug. SLNs were prepared using the hot homogenization technique employing Glyceryl Behenate and Glyceryl Monostearate as lipid matrices and Soya Lecithin as the surfactant. Various formulations were prepared by varying lipid-to-surfactant ratios (2:1, 2.5:1, 3.3:1, 5:1 and 10:1). The prepared formulations were evaluated for drug content, entrapment efficiency, particle size, zeta potential, in vitro drug release, and stability studies. Among all formulations, F3 containing a lipid-to-surfactant ratio of 3.3:1 showed optimum characteristics with nanosized particles, high entrapment efficiency, satisfactory zeta potential and sustained drug release up to 12 h. The optimized formulation demonstrated the suitability of SLNs as an effective carrier system for enhancing the therapeutic performance of Budesonide.

Keywords: Budesonide, Solid Lipid Nanoparticles, Hot Homogenization, Glyceryl Behenate, Glyceryl Monostearate, Sustained Release.

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1. INTRODUCTION

Nanotechnology-based drug delivery systems have revolutionized pharmaceutical research by improving therapeutic efficacy and reducing side effects. Among various nanocarriers, Solid Lipid Nanoparticles (SLNs) have attracted considerable interest due to their biocompatibility, biodegradability, controlled drug release, high drug-loading capacity, and ease of large-scale production.

SLNs are submicron colloidal carriers ranging from 10–1000 nm consisting of physiological lipids dispersed in aqueous surfactant solutions. They were introduced by Müller and Gasco in 1991 as an alternative to polymeric nanoparticles and liposomes.

Budesonide is a potent glucocorticoid used in the treatment of asthma, chronic obstructive pulmonary disease (COPD), and inflammatory disorders. It belongs to BCS Class II with high permeability but low aqueous solubility, resulting in limited oral bioavailability. Incorporation of Budesonide into SLNs can enhance dissolution, improve bioavailability, prolong drug release, and reduce dosing frequency.

Therefore, the present investigation was undertaken to formulate and optimize Budesonide-loaded SLNs using the hot homogenization technique

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2. MATERIALS AND METHODS

2.1 Materials

Material	Function
Budesonide	Drug
Glyceryl Behenate	Lipid

Material	Function
Glyceryl Monostearate	Lipid
Soya Lecithin	Surfactant
PEG-400	Co-surfactant
Distilled Water	Vehicle

2.2 Drug Profile[6-8]

Parameter	Description
Drug	Budesonide
Category	Corticosteroid
Molecular Formula	C25H34O6
Molecular Weight	430.53 g/mol
BCS Class	II
λmax	248 nm
Dosage Form	Oral/Inhalation
Bioavailability	39%
Melting Point	235–245°C

2.3 Construction of Calibration Curve of Budesonide[9-12]

A standard stock solution (1000 µg/mL) of Budesonide was prepared, and a sub-stock solution was obtained by diluting 1 mL of stock solution to 10 mL with pH 7.2 phosphate buffer. Aliquots of 0.2, 0.4, 0.6, 0.8, and 1.0 mL were transferred into separate volumetric flasks and diluted to obtain concentrations of **2, 4, 6, 8, and 10 µg/mL**, respectively. The absorbance of each solution was measured at **248 nm** using a double-beam UV–Visible spectrophotometer.

The calibration curve was constructed by plotting concentration versus absorbance. The method exhibited good linearity in the concentration range of **2–10 µg/mL** and obeyed **Beer–Lambert's law**. All measurements were performed in triplicate, and the mean values were used for calibration curve construction.

2.4 Solubility Studies:[13-15]

Solubility studies were carried out using water, methanol, ethanol, dichloromethane and acetone.

Freely soluble in water, soluble in methanol, sparingly soluble in ethanol, slightly soluble in dichloromethane, and insoluble in acetone.

2.5 Preparation of SLNs

SLNs were prepared by hot homogenization. The lipid phase containing Budesonide and lipid matrix was heated above the melting point. Simultaneously, the aqueous phase containing Soya Lecithin and PEG-400 was heated to the same temperature. The lipid phase was added dropwise into the aqueous phase under homogenization at 2700 rpm for 3 h, resulting in the formation of SLNs.

2.6 Formulation Design[16-18]

Glyceryl Behenate Formulations

Ingredient	F1	F2	F3	F4	F5
Budesonide	10 mg	10 mg	10 mg	10 mg	10 mg
Glyceryl Behenate	2 g	2.5 g	3.3 g	5 g	10 g
Soya Lecithin	1 g	1 g	1 g	1 g	1 g
PEG-400	50 mg	100 mg	150 mg	150 mg	150 mg
Water	20 mL	20 mL	20 mL	20 mL	20 mL

Glyceryl Monostearate Formulations

Ingredient	S1	S2	S3	S4	S5
Budesonide	10 mg	10 mg	10 mg	10 mg	10 mg
Glyceryl Monostearate	2 g	2.5 g	3.3 g	5 g	10 g
Soya Lecithin	1 g	1 g	1 g	1 g	1 g
PEG-400	50 mg	100 mg	150 mg	150 mg	150 mg
Water	20 mL	20 mL	20 mL	20 mL	20 mL

HOT HOMOGENIZATION METHOD

In this method, hot homogenization technique, the drug loaded melted lipid is dispersed under stirring high shear device in the aqueous surfactant solution stirring at 2700rpm. nanoparticles are been formed by which, aqueous phase is added to the oil phase with Homogenization ,10ml of water and 50mg of PEG-400 are aqueous phase The ratios of lipid and surfactant are oil

phase. The Aqueous phase was prepared by adding surfactant in to the distilled water and heated 70-80 c to the temperature of the oil phase. The prepared oil phase is added to the aqueous phase drop by drop under continuous at 2700rpm for 3 hrs. Therefore, Solid lipid nanoparticles were formed.

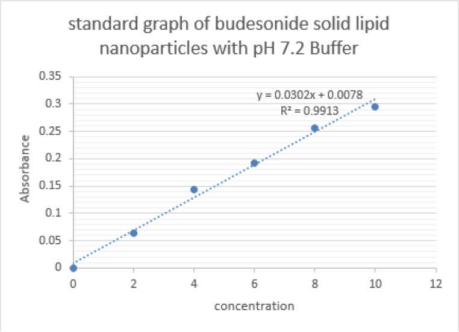
3. EVALUATION METHODS

- UV Spectrophotometric analysis
- Drug content determination
- Entrapment efficiency
- In vitro drug release
- Particle size analysis
- Zeta potential measurement
- Stability studies

4. RESULTS AND DISCUSSION

4.1 Calibration Curve of Budesonide

Standard Calibration Data

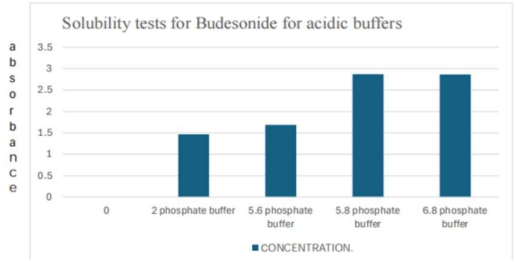


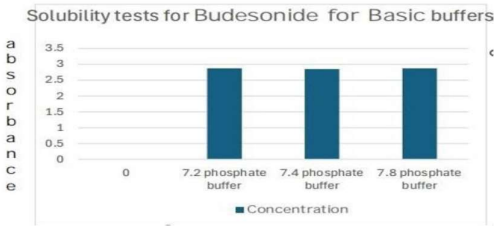
The calibration curve exhibited good linearity in the concentration range of 2–10 µg/mL and obeyed Beer-Lambert's law.

4.2 Solubility Studies

Budesonide exhibited maximum solubility in methanol and showed limited aqueous solubility confirming its BCS Class II behavior.

Solubility of the pure drug is performed by using various buffers





4.3 Optimization of Process Variables

The process variable and formulation variables like lipid polymer to Surfactant ratio, stirring speed, stirring time and sonication time were optimized by trial-and-error method.

Parameter	Optimized Value
Stirring Speed	2700 rpm
Stirring Time	3 h
Sonication Time	30 min

4.4 Characterization and Evaluation Of Budesonide Solid Lipid Nanoparticles By Employing Glyceryl Behenate Using Hot Homogenization.

The six formulations were prepared by using this technique. The prepared formulations were characterized and evaluated for drug content, entrapment efficiency, drug release studies, measurement of particle size, and measurement of zeta potential.

4.4.1 Drug content of budesonide SLN containing glyceryl behenate and soyalecithin

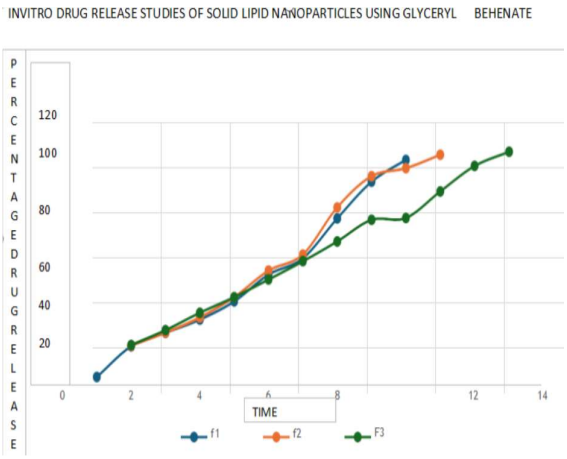
Formulation Code	Drug Content
S1	53.2±0.3
S2	43.5±0.5
S3	98.34±0.4
S4	68.9±0.6
S5	74.6±0.2

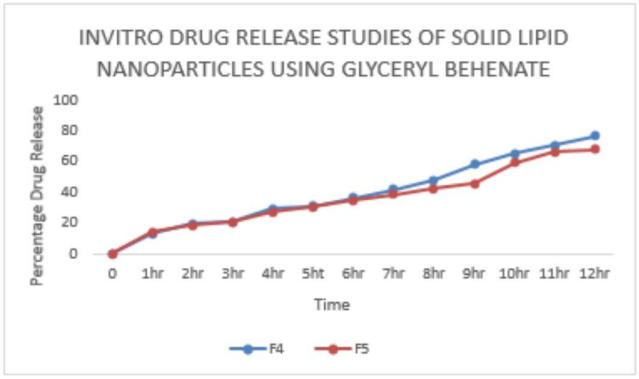
4.4.2 Entrapment Efficiency of Formulations of Budesonide Solid Lipid Nanoparticles By Using Glyceryl Behenate And Soyalechthin.

Formulation Code	Entrapment Efficiency
F1	52.61±0.5
F2	62.44±0.7
F3	98.79±0.5
F4	72.36±0.2
F5	62.15±0.4

4.4.3 In Vitro Drug Release of Glyceryl Behenate Formulations

Time (h)	F1	F2	F3	F4	F5
1	13.65	13.95	14.27	13.05	13.91
2	19.63	19.71	20.82	19.81	18.50
3	25.50	26.50	28.53	20.70	21.20
4	33.56	35.46	35.47	29.30	27.10
5	45.50	47.27	43.30	30.90	30.20
6	52.70	54.41	51.40	36.50	34.50
7	70.40	75.31	60.20	41.80	38.60
8	86.40	89.20	69.80	47.70	42.80
9	96.40	92.70	70.60	58.11	45.50
10	-	98.70	82.40	65.20	58.70
11	-	-	93.70	70.30	65.90
12	-	-	100.00	76.40	67.60



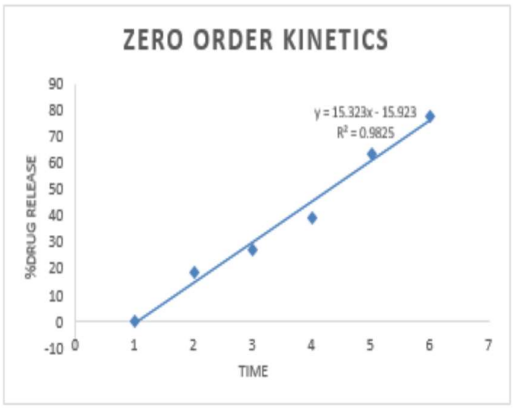


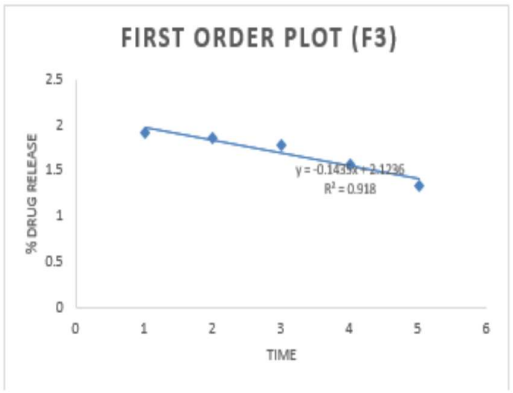
The F3 formulation demonstrated controlled release up to 12 h.

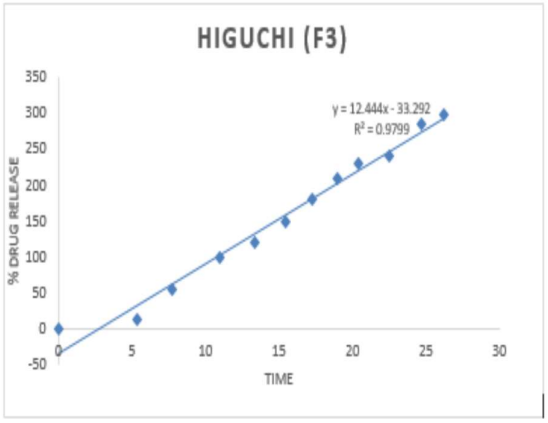
4.4.4. Release Kinetics (F3)

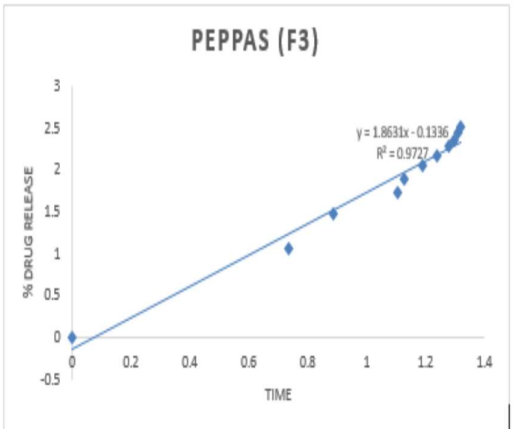
Model	R^2
Zero Order	0.9825
First Order	0.9180
Higuchi	0.9799
Korsmeyer-Peppas	0.9727

The release followed zero-order diffusion-controlled kinetics.







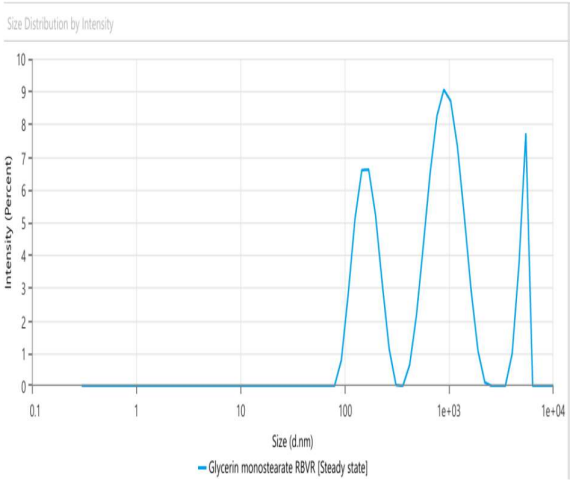


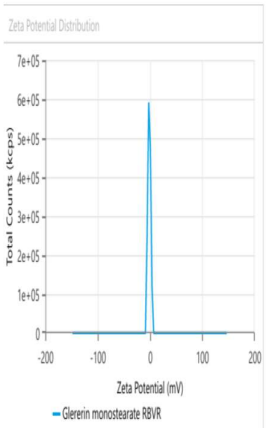
4.4.5 Zeta Potential and Particle Size

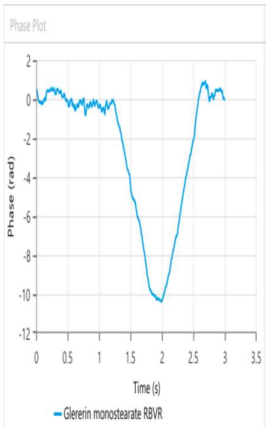
The particle size of the best formulation F3 was done with the help of nanoparticle analyzer HORIBA SZ 100 Z. The formulation contained particles of size of 149-623.6 nm. Thus, it was observed that formulation was found to be in nano range. Optimized F3 formulation exhibited:

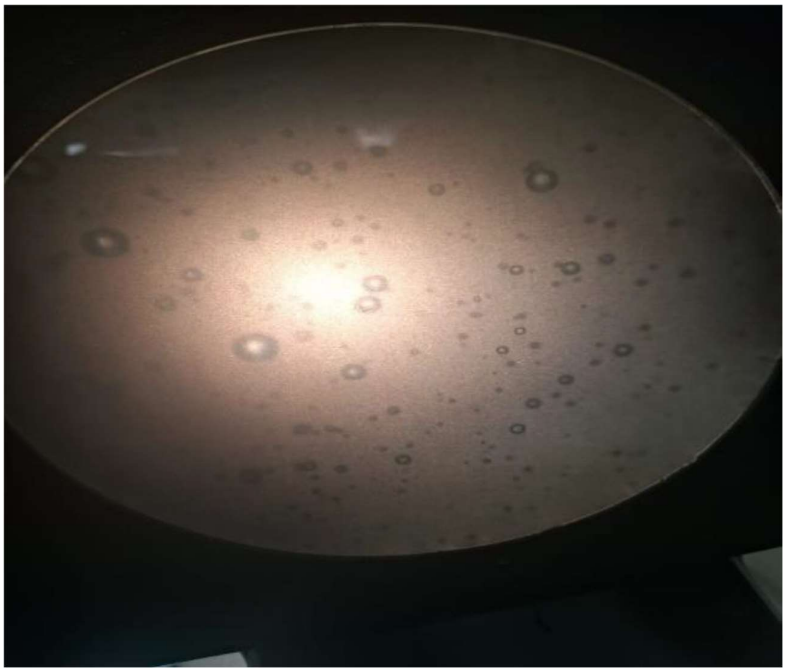
- Particle size: 149–623.6 nm
- Zeta potential: −25.3 to −26.5 mV

These results indicate good nanoparticle stability.









Microscopic Images of SLN using Glyceryl Behanate

4.5 Characterization and Evaluation Of Budesonide Solid Lipid Nanoparticles By Employing Glyceryl Monostearate Using Hot Homogenization.

The six formulations were prepared by using this technique. The prepared formulations were characterized and evaluated for drug content, entrapment efficiency, drug release studies, measurement of particle size, and measurement of zeta potential.

4.5.1 Drug Content of Budesonide Solid Lipid Nanioparticles by Hot Homogenization Lipid Glyceryl Monosterate And Surfactant Soyalechithin.

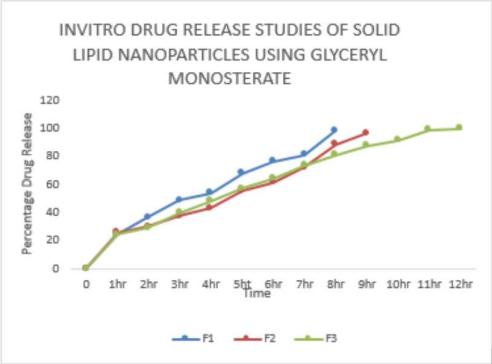
FORMULATION CODE	DRUG CONTENT (%)
S1	45.31±03
S2	59.24±0.5
S3	98.32±04
S4	67.53±0.3
S5	76.20±0.2

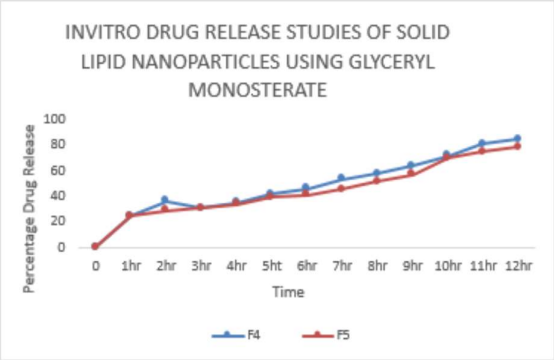
4.5.2 Entrapment Efficiency of Formulations Of Budesonide Solid Lipd Nanoparticles By Using Glyceryl Monosterate And Soyalechthin.

FORMULATION	ENTRAPMENT EFFICIENCY (%)
FI	59.24±0.3
F2	65.36±0.5
F3	98.98±0.2
F4	79.35±0.6
F5	87.49±0.5

4.5.3 In Vitro Drug Release of Glyceryl Monostearate Formulations

Time (h)	**S1**	**S2**	**S3**	**S4**	**S5**
1	24.3	25.9	24.5	24.05	24.41
2	36.7	29.8	29.12	35.66	28.38
3	48.6	37.5	39.6	30.11	30.14
4	54.1	43.3	48.1	34.28	33.38
5	68.11	55.4	57.04	41.43	38.76
6	76.4	61.5	64.2	45.7	40.8
7	81.2	72.2	73.7	52.8	51.2
8	98.2	88.66	81.11	57.3	56.3
9	-	96.7	87.5	63.5	56.3
10	-	-	91.6	71.4	69.2
11	-	-	98.7	80.3	74.5
12	-	-	100	84.2	77.8

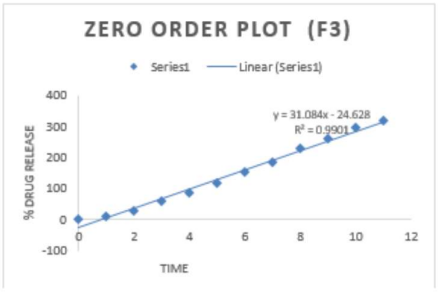


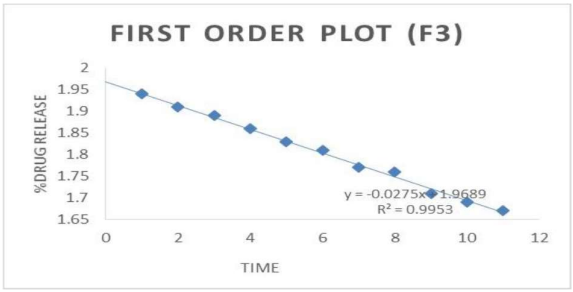


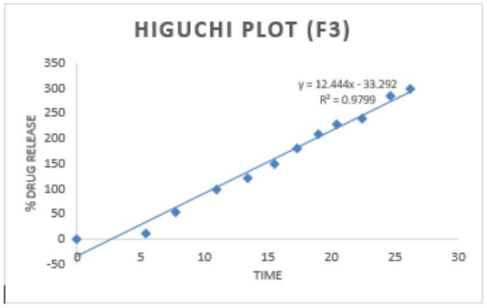
4.5.4 Release Kinetics (S3)

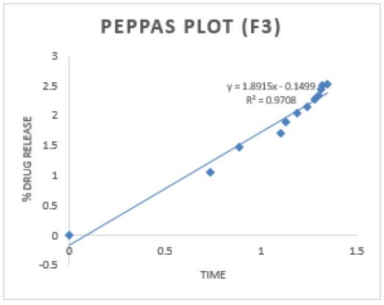
The drug release data was fitted in various kinetic plots (zero order, first order, Higuchi and peppas) in order to determine the order and mode of drug release**.**

Model	**R^2**
Zero Order	0.9901
First Order	0.9953
Higuchi	0.9799
Peppas	0.9708







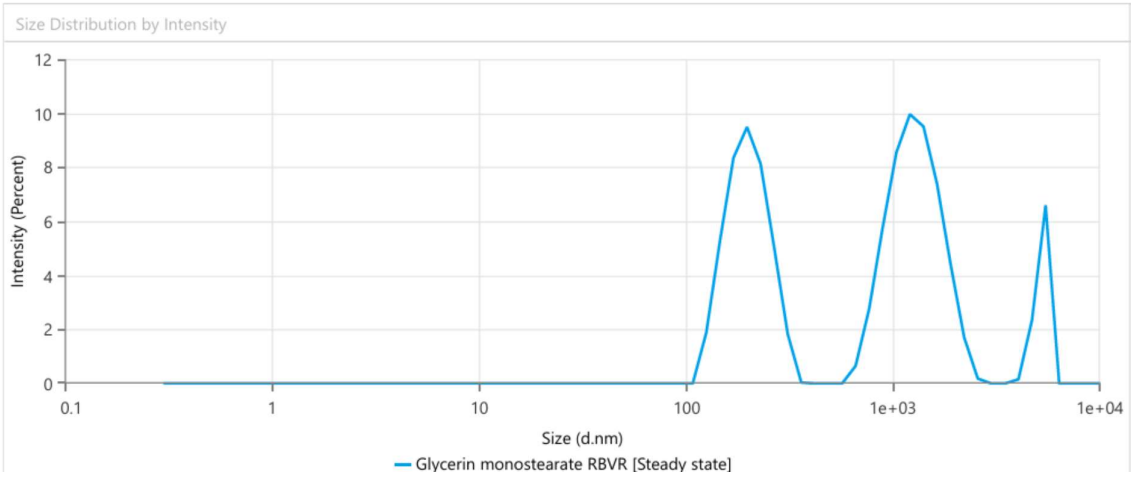


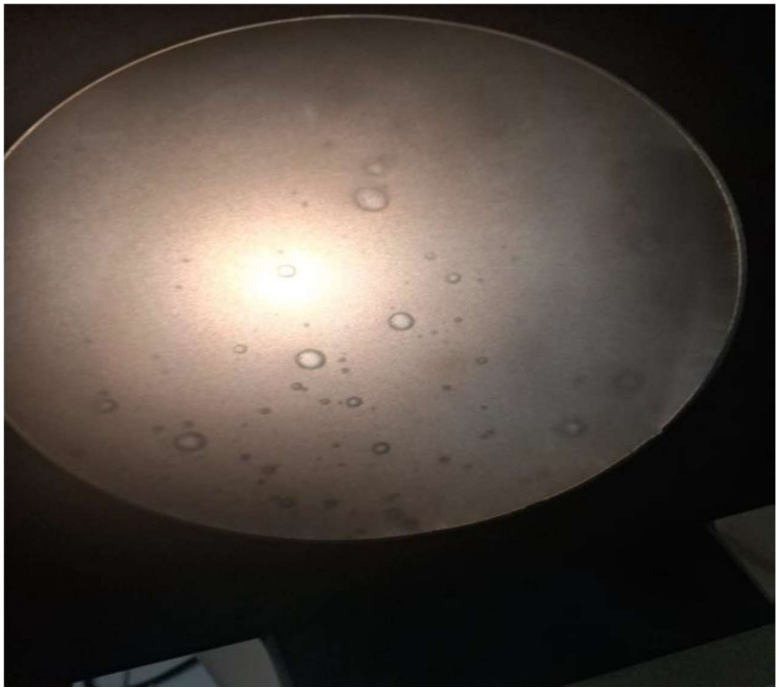
4.5.5 Zeta Potential and Particle Size

The particle size of the best formulation S3 was done with the help of nanoparticle analyzer HORIBA SZ 100 Z. The formulation contained particles of size of 149-623.6 nm. Thus, it was observed that formulation was found to be in nano range. Optimized F3 formulation exhibited:

- Particle size: 148.1 nm
- Zeta potential: −25.3 to −26.5 mV

These results indicate good nanoparticle stability.





Microscopic Images of SLN using Glyceryl Monostearate

5. STABILITY STUDIES

Stability studies showed that the optimised formulation's physical characteristics are identical after a month, as are the particle size and entrapment effectiveness percentage in both cases

6. SUMMARY

The present research work was undertaken with the objective of formulating and optimizing Budesonide-loaded Solid Lipid Nanoparticles (SLNs) using the hot homogenization technique to improve the solubility, bioavailability, and sustained-release characteristics of Budesonide. Budesonide is a potent corticosteroid widely used in the treatment of asthma, chronic obstructive pulmonary disease (COPD), and other inflammatory disorders. However, its therapeutic effectiveness is limited due to its poor aqueous solubility and low bioavailability, as it belongs to the Biopharmaceutical Classification System (BCS) Class II. To overcome these limitations, Budesonide was incorporated into a lipid-based nanocarrier system.

A comprehensive literature review was conducted to understand the significance of lipid-based drug delivery systems, preparation methods, characterization techniques, and pharmaceutical applications of SLNs. The review revealed that SLNs are promising drug delivery carriers due to their biocompatibility, biodegradability, controlled drug release properties, ease of large-scale production, and ability to improve the bioavailability of poorly water-soluble drugs. Based on the literature findings, the hot homogenization technique was selected as the most suitable method for the preparation of Budesonide-loaded SLNs.

Initially, the absorption maximum (λmax) of Budesonide was determined using UV-Visible spectrophotometry and was found to be 248 nm in phosphate buffer pH 7.2. A calibration curve was constructed in the concentration range of 2–10 µg/mL, which exhibited good linearity and compliance with Beer-Lambert's law. Solubility studies were performed in different solvents and buffer systems to assess the solubility behavior of Budesonide and to select appropriate formulation components.

The SLNs were prepared using Glyceryl Behenate and Glyceryl Monostearate as lipid matrices, Soya Lecithin as the surfactant, and PEG-400 as the co-surfactant. The formulations were developed by varying the lipid-to-surfactant ratios of 2:1, 2.5:1, 3.3:1, 5:1, and 10:1. The process parameters such as stirring speed, stirring time, and sonication time were optimized. The optimized preparation conditions were found to be 2700 rpm stirring speed, 3 hours stirring time, and 30 minutes sonication time.

A total of ten formulations were prepared, comprising five formulations using Glyceryl Behenate (F1–F5) and five formulations using Glyceryl Monostearate (S1–S5). The prepared SLNs were evaluated for various physicochemical parameters including drug content, entrapment efficiency, in vitro drug release, particle size, zeta potential, and stability.

The drug content and entrapment efficiency studies demonstrated successful incorporation of Budesonide into the lipid matrix. The in vitro drug release studies showed a sustained-release profile extending up to 12 hours, indicating the suitability of SLNs for prolonged drug delivery. Among all formulations, F3, containing a lipid-to-surfactant ratio of 3.3:1, exhibited the most desirable characteristics, including high drug content, maximum entrapment efficiency, optimum particle size, satisfactory zeta potential, and controlled drug release.

The optimized formulation F3 prepared with Glyceryl Behenate showed particle sizes within the nanometer range (149–623.6 nm) and a zeta potential of approximately −25.3 to −26.5 mV, indicating good colloidal stability. Drug release kinetic analysis revealed that the release pattern followed zero-order and Higuchi diffusion-controlled kinetics, suggesting sustained and controlled release of Budesonide from the lipid matrix.

Similarly, formulations prepared using Glyceryl Monostearate also demonstrated satisfactory performance. Among these, formulation S3 exhibited sustained drug release and favorable particle size characteristics. However, the Glyceryl Behenate-based formulation F3 showed comparatively superior overall performance and was selected as the optimized formulation.

Stability studies carried out under refrigerated and room-temperature conditions revealed no significant changes in the physical appearance, particle size, drug content, entrapment efficiency, or drug release

profile of the optimized formulation, indicating good formulation stability during storage.

Overall, the study successfully demonstrated that Budesonide can be effectively incorporated into solid lipid nanoparticles using the hot homogenization technique. The developed SLNs significantly improved the drug delivery characteristics of Budesonide by enhancing drug encapsulation, maintaining formulation stability, and providing sustained drug release. The results suggest that Budesonide-loaded SLNs have considerable potential as an advanced lipid-based drug delivery system for improving therapeutic efficacy and patient compliance. Furthermore, the developed formulation may serve as a promising platform for future pulmonary and targeted drug delivery applications.

6. CONCLUSION[22]

The results of the present investigation demonstrate that solid lipid nanoparticles are an effective approach for enhancing the delivery of Budesonide. The optimized formulation exhibited desirable physicochemical characteristics, good stability, and a sustained drug release profile, indicating the successful incorporation of the drug within the lipid matrix. The study confirms that the selected lipid and surfactant combination was capable of producing stable nanoparticles with suitable release characteristics, thereby offering a potential strategy to improve the therapeutic performance of Budesonide. The findings highlight the applicability of solid lipid nanoparticles as a versatile lipid-based drug delivery system for poorly water-soluble drugs and support their further development for advanced pulmonary and controlled-release pharmaceutical applications.

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