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Research Article

Biosynthesis and Characterization of Dapagliflozin and Saroglitazar Encapsulated Solid Lipid Nanoparticles

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ABSTRACT

Background: Solid lipid nanoparticles, which have a spherical shape and an average diameter of 1 to 1000 nm, are a fast-emerging area of nanotechnology with numerous potentials uses in drug delivery. Because of Solid lipid nanoparticles have demonstrated encouraging promise as drug delivery vehicles due to their size and characteristics. Saroglitazar & Dapagliflozin are drugs with Neuroprotective activity also possesses diverse Therapeutic effects.
Method: Using lipids (Stearic acid, Compritol 888ATO and Glyceryl monostearate) and stabilizers (Poloxamer 407 and Tween 80), solid lipid nanoparticles of Saroglitazar & Dapagliflozin are created. The prepared formulation was evaluated by different confirmatory test like particle size analysis, entrapment efficiency, scanning electron spectroscopy, Fourier transform-infrared, UV spectral investigations.
Result: EE increased as surfactant content increased and had an inverse relationship with particle size. The medication and excipients do not interact, according to FTIR. According to the SEM study, the particles have a spherical form.
Conclusion: In comparison to other formulations with various surfactants and lipids, the formulation including Compritol 888 ATO and P-407 (03%) demonstrated reduced particle size and a narrow particle size distribution.

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Introduction:

Solid lipid Nanoparticles (NPs) are extremely small particles with sizes ranging from 50 to 1000 nm (Patel et al, 2020). They can be categorized into a number of classes based on their characteristics, dimensions, or forms. Among the various groupings are fullerenes, metal nanoparticles, ceramic nanoparticles, and polymeric nanoparticles. NPs have unique physical and chemical properties due to their enormous surface area and nanoscale size. (Khan et al, 2017) Large quantities of nanoparticles produce a large number of surface atoms, which increases their surface energy and improves their catalytic activity. Because of these characteristics, the nanoparticles are an excellent choice for a variety of catalytic applications (Arshad et al., 2023). Targeted drug delivery is achieved by nanomedicine and it is an important for biomedical application that aims to deliver various types of drugs like anti-cancer and neuroprotective medication (McNamara et al., 2016). Saroglitazar (C25H29NO4) & Dapagliflozin (C21H25ClO6) are anti diabetic drugs act by dual PPAR-alpha/gamma agonist & inhibition of sodium-linked glucose transporter (SGLT-2) (Dhararath et al., 2021; Mohandas et al., 2021). Dapagliflozin 400µg/ml were showed anticancer property in oral cancer cell line and reduces oxidative stress and neuroinflammation caused by microglia and have neuroprotective effects (Vinay et al., 2019; Liu et al., 2025). Saroglitazar has been reported for its neuroprotective activity by inhibition of cholinesterase

enzymes, reduce oxidative stress and neuroinflammation (Jakkamsetti et al., 2004)

The objective of this research is to examine how various lipid matrices and surfactant types influence the formulation and characteristic of solid lipid nanoparticles by analyzing SLN for particle size, UV spectra, polydispersity index, zeta potential and encapsulation efficiency.

Stearic acid, glyceryl monostearate (GMS), Compritol 888ATO were utilized as lipids, Tween 80, Polaxomer 407 (PVA), as surfactants. The study revealed that SLNs based on Tween 80 had the smallest particle size, while SLNs utilizing phosphatidylcholine exhibited the most extended drug release time and the highest drug loading capacity. The authors concluded that the combination of phosphatidylcholine and Pluronic F127 was the optimal surfactant for coating the lipid core composed of stearic acid and glyceryl monostearate (Ebrahimi et al., 2015).

Solid lipid nanoparticles prepared by solvent emulsification-diffusion technique

Dapagliflozin & Saroglitazar loaded SLNs were made using a solvent emulsification diffusion technique with stearic acid, polxamer 407, and Tween 80 as surfactants and various lipid matrices (Glyceryl monostearate and Compritol 888ATO). Drugs was dispersed after the lipid was dissolved in two milliliters of a 1:1 ethanol:choloroform mixture. Drop by drop, 5 ml of an aqueous surfactant solution was added to the above solution while being constantly stirred. A high-speed homogenizer (IKA T25 Digital S22 Homogenizer, India) was used to homogenize the dispersion for 10 minutes at 10000 RPM. 50 ml of volume was filled with ice-cold water, and for two hours, the mixture was continuously stirred to allow the organic solvent to diffuse into the aqueous phase.

Evaluation of Prepared Nanoparticles Production yield

The production yield was calculated as the total weight of the final product after drying, with respect to the initial total amount of drug along with ingredients used for the preparations of formulation (Dinarrad et al., 2002). Production yield were calculated by using equation 1.

% Production yield= W1/W2 * 100……..(1)

Where, W2 = Weight of starting materials

Measurement of particle size, zeta potential and Polydispersity index

Zetatrac (Microtrac Inc., USA) was used to measure the nanoparticle's size, zeta potential, and PDI value by using a light scattering technique. De-ionized water was used to re-disperse the nanoparticles. Place the sample in the sample holder to measure the zeta potential, PDI, and particle size.

Measurement of Drug Entrapment Efficiency (%EE)

After centrifugation, supernant was collected and diluted with 10 ml with 7.4 pH buffer solution. This solution was analysed by UV-Visible Spectrophotometer at 288 nm using pH 7.4. It expresses the amount of unentrapped drug in the supernant (Tayade et al., 2004). The Drug Entrapment Efficiency was calculated by following equation 2

% Entrapment efficiency = Da+Ds/Da * 100……..2

Characterization of Nanoparticles

1.Fourier Transform Infrared Spectroscopy

For qualitative analysis, FTIR analyses of Prepared Nano particles, Compritol 888 ATO, Tween 80, physical mixtures, and formulations were performed. The pellet was stored in an Agilent CARY 630 FTIR spectrophotometer sample holder, and it was scanned between 400 and 4000 cm-1 at a resolution of 4 cm^{-1} (Racault et al., 1994).

2.Shape and surface morphology

The shape and surface morphology of the SLN were done by visualized scanning electron microscopy. A dried sample weighing 10 mg was placed into the scanning electron microscopy (SEM XL 30 ESEM) stub. After being secured in a sample holder, the stub was put inside the scanning electron microscope's vacuum chamber. The surface characteristics of the SLNs were observed (Delpozo et al., 2009).

Table 1: Composition of dapagliflozin & Saroglitazar loaded solid lipid nanoparticles containing different lipids and surfactants and its Particle size and entrapment efficiency.

Formulations	Lipid	% w/v	Surfactant	% w/v	Particle Size (nm)	Entrapment Efficiency (%)
F1	Glyceryl monostearate	3	Poloxamer 407	1	662±0.88	59.52±0.55
F2	Glyceryl monostearate	3	Poloxamer 407	2	601±4.21	65.25±1.54
F3	Glyceryl monostearate	3	Poloxamer 407	3	483±0.54	69.52±2.65
F4	Stearic acid	3	Poloxamer 407	1	1144±0.95	58.42±1.15

F5	Stearic acid	3	Poloxamer 407	2	1014±0.15	61.42±1.15
F6	Stearic acid	3	Poloxamer 407	3	1010±0.55	69.42±1.15
F7	Compritol 888ATO	3	Poloxamer 407	1	488±1.87	58.85±1.45
F8	Compritol 888ATO	3	Poloxamer 407	2	465±1.22	65.58±0.87
F9	Compritol 888ATO	3	Poloxamer 407	3	423±1.55	70.25±2.65
F10	Glyceryl monostearate	3	Tween 80	1	991±0.88	68.32±0.77
F11	Glyceryl monostearate	3	Tween 80	2	971±0.88	69.40±1.45
F12	Glyceryl monostearate	3	Tween 80	3	911±0.88	69.42±0.87
F13	Stearic acid	3	Tween 80	1	1154±0.95	52.42±2.25
F14	Stearic acid	3	Tween 80	2	1084±0.15	55.42±2.05
F15	Stearic acid	3	Tween 80	3	1040±0.55	58.42±1.25
F16	Compritol 888ATO	3	Tween 80	1	1150±2.11	62.31±2.32
F17	Compritol 888ATO	3	Tween 80	2	1025±1.34	61.25±2.32
F18	Compritol 888ATO	3	Tween 80	3	995±1.24	59.25±2.32

UV Spectra analysis

The prepared nanoparticles were monitored by measuring the absorbance spectra in wavelength range of 200-400 nm using shimadzu UV 1800 spectrophotometer. The spectrum was recorded and maximum absorbance wavelength was determined.

RESULTS & DISCUSSION

Particle size analysis

Table 1 shows the effect of the lipid and surfactant concentration on the particle size distribution of SLN prepared by using Stearic acid, GMS and Compritol ATO 888 with Poloxamer 407 and Tween 80. The particle size ranged from 423 nm - 1150 nm. There was shown a significant difference in the particle size of SLN, with change in the lipids and surfactants.

Effect of lipids on the particle size

Solid lipid nanoparticles loaded with dapagliflozin and saroglitazar were made using distinct lipid matrices. The SLN made with compritol 888ATO and Glyceryl Monostearate showed larger particle sizes. This effect may be related to the lipid's melting point because both lipids have a higher melting point, which causes the hot homogenized state to cause slower lipid crystallization and an increase in particle size. Because stearic acid SLN does not stabilize with surfactants within two to three days of production, it may exhibit crystallinity during storage on degradation. By increasing the distances between the glyceride fatty acid chains and general crystal defects, the use of spatially specific lipids gives molecules more room to fit and results in larger particle sizes. After 120 minutes of degradation in the lipase solution, SLN are rapidly and totally broken down. The distribution of particle sizes may be impacted by these degradation behaviors (Abdelbary G). Lipid compritol 888 ATO > GMS > Stearic acid is in decreasing order.

Effect of surfactants on the particle size

As the surfactant concentration increased particle size was decreased respect to all surfactants. SLN prepared using Soy lecithin as stabilizer showed larger particle size than the other surfactants irrespective of the lipids studied. Based on all respective results batch containing Compritol ATO 888 along with Poloxamer 407 (3%) shows the less particle size as compare to others. (Figure 1)

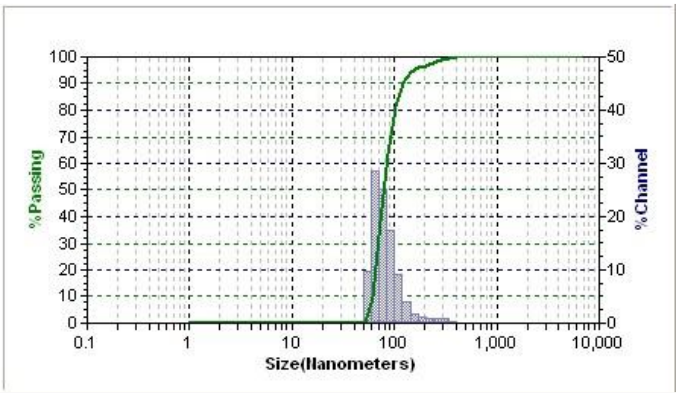

Figure 1: Particle size graph of optimized batch (F9).

Entrapment efficiency

The ability to trap particles is a crucial criterion for describing solid lipid nanoparticles. The type and concentrations of lipids and surfactants were important factors in achieving the best possible encapsulation efficiency. Table 1 displays the entrapment efficiency of every SLN formulation that was prepared. The results showed that the SLN dispersions had an entrapment efficiency between 52.42 % and 70.25%.

Effect of surfactants on entrapment efficiency

The entrapment efficiency of all SLN formulations made with the maximum amount of surfactant, such as 3 percent, was higher. In this case, the entrapment efficiency increased as the surfactant concentration increased. This could be because when the concentration of the surfactant increases, the drug becomes more soluble in the lipid. This outcome concurred with the findings of (Abdelbary et al., 2009). Formulations that used stearic acid as a surfactant demonstrated a lower entrapment efficiency than the other surfactants; this could be because soy lecithin has a lower HLB value. Poloxamer 407 > Tween 80 > Stearic acid is the order in which the entrapment efficiency of different SLNs decreased after stabilizing with different surfactants.

Production Yield

The prepared formulation's production yield was found to be between 47.69 to and 66.14. According to Table 2, the yield percentage was lower in batch 1 (47.69 percent) and higher in batch 18 (66.14 percent). This discrepancy might result from a higher concentration of surfactant or a higher drug to lipid ratio.

Table 2: Production yield, PDI and Zeta potential for all batches of SLNs.

Formulations	Production yield ± SD	PDI ± SD	Zeta Potential ± SD
F1	47.69±0.88	0.47±1.69	36.56±2.58
F2	54.12±1.54	0.42±3.02	24.89±0.65
F3	56.58±2.54	0.37±1.54	22.32±0.87
F4	47.25±0.25	0.91±2.58	26.1±3.02
F5	49.52±1.21	0.67±1.54	27.34±1.58
F6	52.21±0.78	0.44±0.65	22.29±0.88
F7	50.65±1.54	0.55±1.54	25.78±2.32
F8	53.32±1.78	0.42±2.65	29.65±0.88
F9	64.25±2.54	0.38±3.01	33.54±1.45
F10	55.32±1.65	0.75±2.87	28.56±1.05
F11	55.79±2.41	0.54±1.45	30.98±1.25
F12	60.65±0.88	0.55±0.98	31.25±0.98
F13	58.84±3.21	0.69±2.65	30.32±1.54
F14	55.65±0.98	0.64±0.85	30.64±2.54
F15	52.21±1.25	0.24±0.66	23.56±0.74
F16	60.89±2.65	0.35±2.55	29.12±0.87
F17	63.32±1.58	0.29±0.54	31.54±1.65
F18	66.14±0.58	0.20±0.98	33.86±2.54

Polydispersibilty Index

The size distribution of the formulation is displayed by the Polydispersibilty Index (PDI). PDI score. <1 indicate narrow size distribution while in case of > 1 denotes a wide range of sizes distribution. A higher PDI denotes a higher degree of non-uniformity, and the SLNs were classified as monodisperse, homogeneous, and heterogeneous systems based on its value. All formulations' PDIs were shown in Table 2. The PDI in this study was found to be between 0.20 - 0.91.

Zeta potential

The zeta potential is a measure of SLN stability. Expected formulation stability increases with zeta potential. For moderate stability, the ideal range for the zeta potential is between -30 and +30 mV. Table 2 displays the zeta potential of the prepared SLNs. Greater formulation stability is indicated by zeta potentials for all batches that fall between 22.29 and 36.56 mV.

Characterization of Nanoparticles

Fourier Transform Infra-Red Spectroscopy (FTIR)

Fourier Transform Infra-Red Spectroscopy (FTIR) study was performed as per methodology. The FTIR spectra of Compritol 888 ATO, Tween 80, Physical mixture and SLNs formulation spectra shown in Figure 2. FTIR spectrum of dapagliflozin & saroglitazar showed characteristic peaks at 3330.4 & 1638.2 cm-1 (-CH aromatic stretching) & (C=C double bending) were identified. Which were same in SLN formulation. Thus, there was no any interaction between drug and excipients.

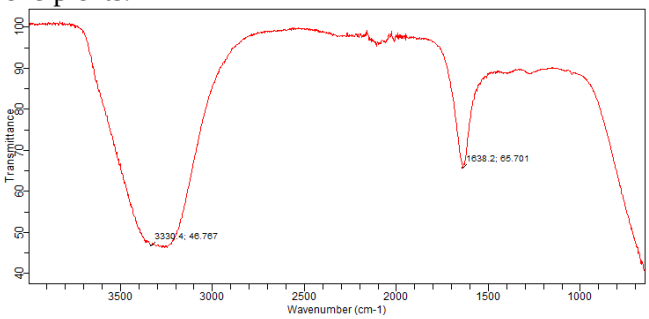

Figure 2: FTIR spectra of Formulation

Scanning electron microscopy (SEM)

SEM was used to examine the morphology of the optimized batch (F9). Figure 3 displays SEM images of the drug-loaded SLN. It is observable that solid lipid nanoparticles are spherical and have a smooth surface.

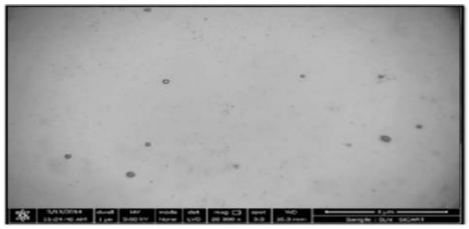

Figure 3: SEM of optimized formulation.

UV visible spectral analysis

The UV absorption spectrum of prepared nanoparticles has shown a peak specific in the rage between 276.00 and 225.80 nm. Peak specific in this region might be due to Mie scattering effect. The UV spectrum of drug loaded nanoparticles shown in figure 4.

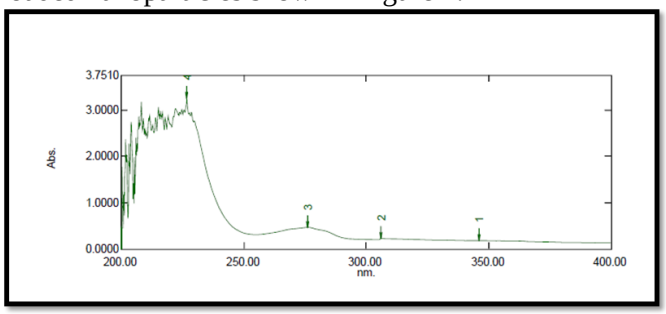

Figure 4: UV visible spectra of formulation.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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