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Research Article

**FORMULATION AND EVALUATION OF
NANOSUSPENSION CONTAINING SOTAGLIFLOZIN****Pravat Ranjan Guru, Suprit Mishra, Biswajit Mohapatra, Satya Ranjan Dalai,
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Vidya- Vihar, Sundargram, Odisha 754002.**Abstract:**

Sotagliflozin is a dual sodium-glucose co-transporter (SGLT-1 and SGLT-2) inhibitor used in the management of diabetes mellitus. However, its poor aqueous solubility may limit its dissolution rate and oral bioavailability. The present study was undertaken to formulate and evaluate a nanosuspension containing Sotagliflozin with the objective of improving its dissolution characteristics and overall pharmaceutical performance.

Sotagliflozin nanosuspensions were prepared using a suitable nanosuspension technique with different concentrations of stabilizers to obtain optimized formulations (F1–F6). The prepared nanosuspensions were evaluated for their physicochemical properties and subsequently compressed into tablets. The powder blends were assessed for pre-compression parameters, including bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio. The compressed tablets were evaluated for post-compression parameters such as weight variation, hardness, thickness, friability, drug content uniformity, disintegration time, and in vitro drug release. All the pre-compression and post-compression parameters were found to be within the acceptable limits prescribed by the Indian Pharmacopoeia (IP), indicating good flow properties, compressibility, and tablet quality. Among all the formulations, F6 was identified as the optimized formulation based on its superior in vitro dissolution performance. The optimized formulation released 97.73% of Sotagliflozin within 60 minutes, which was higher than that of the other formulations, demonstrating the effectiveness of the nanosuspension approach in enhancing drug dissolution. The improved dissolution profile can be attributed to the reduced particle size and increased surface area of the drug in the nanosuspension system.

In conclusion, the developed Sotagliflozin nanosuspension-based formulation exhibited satisfactory pharmaceutical characteristics and complied with all IP quality specifications. The optimized formulation (F6) showed significantly enhanced drug release, suggesting that nanosuspension technology is a promising strategy for improving the dissolution and potential oral bioavailability of poorly water-soluble drugs such as Sotagliflozin.

Keywords: Sotagliflozin nanosuspension**Corresponding author:****Pravat Ranjan Guru,**Department Of Pharmaceutics, Dadhichi College Of Pharmacy,
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INTRODUCTION:

Pharmaceutical industries are always looking for new methods in order to obtain adequate oral bioavailability, as most of the biological properties exhibiting NCEs are poorly Water-soluble. The increasing frequency of poorly water-soluble NCEs exhibiting therapeutic activity is of major concern to the development of new formulations in the pharmaceutical industry, which leads to low turnout in the development of new molecular entities as drug formulations are poor solubility and poor permeability of the lead compounds.¹

Recently, the formulation of such drugs as nanoscale systems (which have a size below 1 μm) has quickly grown as a new and novel drug delivery system. The major distinctive of these systems is the quick dissolution rate, which improves bioavailability after oral administration 1. The present article aims to review the nanosuspensions as an emerging and promising tool for the formulation of poorly soluble drugs.²

Nanotechnology is an emerging field in all areas of science, engineering and technology. It is a novel interdisciplinary area of comprehensive research that combines medicine and other life sciences. It offers a potential for unique and novel approaches with broad spectrum of application in cancer treatment including areas such as diagnostics, therapeutics and prognosis ^{3, 4}. The main advantage of particles in the nano-metric range is its improved physical and chemical properties. The major parameters in drug delivery include particle size, surface area, hydrophobicity, crystallinity and surface charge⁵ More than 40% of new chemical entities being generated through drug discovery programmes are poorly water soluble. The formulation of poorly water soluble drugs has always been a challenging problems faced by pharmaceutical scientists.⁶ There are many conventional methods such as micronization, solubilisation using co-solvents, surfactant dispersions and precipitation technique has been developed for improving solubility of poorly water soluble drugs⁷. But these techniques show limitations to the drugs which are not soluble in both aqueous and organic solvents. Nanosuspension technology can be used to solve the problems associated with various approaches described earlier. Nanosuspension is colloidal dispersion of nano sized drug particles stabilized by surfactants. They can also define as a biphasic system consisting of pure drug particles dispersed in an aqueous vehicle. The diameter of suspended particle is less than 1 μm in size.⁸

Need of Nanosuspension for bioavailability Enhancement:

Nevertheless, pharmacokinetic studies of BCS class-II drugs showed that they have a low oral bioavailability, which may be due to poor water solubility of drug. There are many classical pharmaceutical ways to improve drug dissolution rate such as dissolution in aqueous mixtures with an organic solvent, formation of β -cyclodextrin complexes, solid dispersions and drug salt form. During last 20 years a new technology, reducing drug particle size, has been developed to increase drug dissolution rate.⁹

According to Noyes-Whitney equation, drugs with smaller particle size have enlarged surface areas which lead to increase dissolution velocity. Higher the dissolution rate together with the resulting higher concentration gradient between gastrointestinal lumen and systemic circulation could further increase oral bioavailability of drugs. A nanosuspension is a submicron colloidal dispersion of drug particles which are stabilized by surfactants.¹⁰

A pharmaceutical nanosuspension is defined as very finely dispersed solid drug particles in an aqueous vehicle for oral, topical, parenteral or pulmonary administration. The particle size distribution of the solid particles in nanosuspensions is usually less than one micron with an average particle size ranging between 200 and 600 nm. In nanosuspension technology, the drug is maintained in the required crystalline state with reduced particle size, leading to an increased dissolution rate and therefore improved bioavailability.¹¹⁻¹⁴

Approaches for improvement of bioavailability

Improvement of bioavailability of poorly water-soluble drug remains one of the most challenging aspects of drug development. By many estimates up to 40% of new chemical entities discovered by the pharmaceutical industry today are poorly water compounds.¹⁵

Together with the permeability, the solubility behaviour of a drug is a key determinant of its bioavailability. There have always been certain drugs for which solubility has presented a challenge to the development of a suitable formulation for oral administration. Examples are griseofulvin, digoxin, phenytoin, sulphathiazole etc. With the recent arrival of high throughput screening of potential therapeutic agents, the number of poorly soluble drug candidates has risen sharply and the formulation of poorly soluble compounds for delivery now presents one of the most frequent and greatest challenges to formulation scientists in the pharmaceutical industry.

Consideration of the modified Noyes-Whitney equation provides some hints as to how the dissolution rate of even very poorly soluble compounds might be improved to minimize the limitations on oral availability.¹⁶ The main

possibilities for improving dissolution according to this analysis are:

To increase the surface area available for dissolution by decreasing the particle size Of the solid compound,

- By optimizing the wetting characteristics of the compound surface,
- To decrease the diffusion layer thickness,
- To ensure sink conditions for dissolution and,

- To improve the apparent solubility of the drug under physiologically relevant conditions.¹⁷

A fundamental step in the solubilization of drug compound is the selection of an appropriate salt form, or for liquid drugs, adjustment of pH of the solution. Traditional approaches to drug solubilization include either chemical or mechanical modification of the drug molecule, or physically altering the macromolecular characteristics of aggregated drug particles.

Improvement of bioavailability can be obtained by following measures:

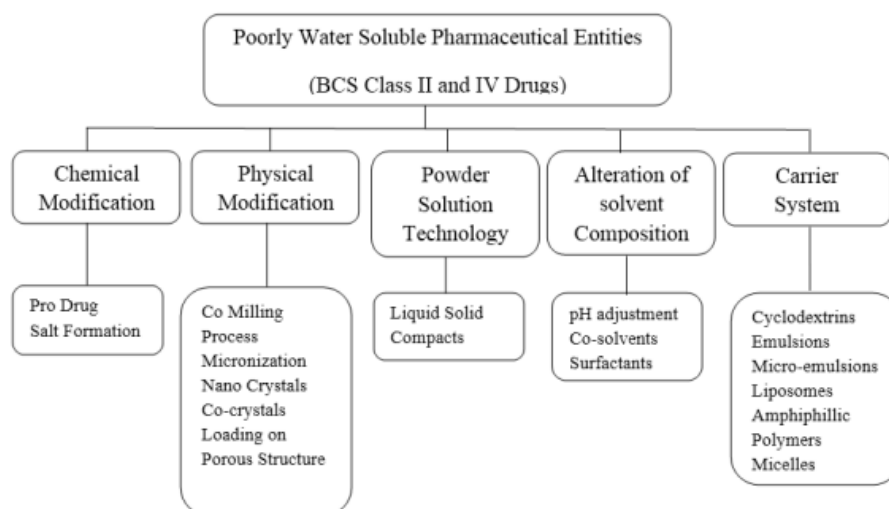


Figure 1.1: Approaches for improvement of bioavailability¹⁸

Nanosuspension

Nevertheless, pharmacokinetic studies of BCS class – II drugs showed that they have a low oral bioavailability, which may be due to the poor water solubility of the drug. There are many classical pharmaceutical ways to improve drug dissolution rates such as dissolution in aqueous mixtures with an organic solvent, the formation of β -cyclodextrin complexes, solid dispersions and drug salt form.¹⁹⁻²¹

During last 20 years a new technology, reducing drug particle size, has been developed to increase drug dissolution rate. According to Noyes–Whitney equation, drugs with smaller particle size have enlarged surface areas which lead to increase dissolution velocity. Higher the dissolution rate together with the resulting higher concentration gradient between the gastrointestinal lumen and systemic circulation could further increase oral bioavailability of drugs²². Nanosuspension is a submicron colloidal dispersion of drug particles which are stabilized by surfactants. A pharmaceutical nanosuspension is defined as very finely dispersed solid drug particles in an aqueous vehicle for oral, topical, parenteral or pulmonary administration. The particle size distribution of the solid particles in nanosuspensions is usually less than one micron with an average particle size

ranging between 200 and 600 nm.²³ In nanosuspension technology, the drug is maintained in the required crystalline state with reduced particle size, leading to an increased dissolution rate and therefore improved bioavailability. An increase in the dissolution rate of micronized particles (particle size < 10 μm) is related to an increase in the surface area and consequently the dissolution velocity. Nanosized particles can increase solution velocity and saturation solubility because of the vapor pressure effect. In addition; the diffusional distance on the surface of drug nanoparticles is decreased, thus leading to an increased concentration gradient. Increase in surface area, as well as concentration gradient, leading to a much more pronounced increase in the dissolution velocity as compared to a micronized product. Another possible explanation for the increased saturation solubility is the creation of high energy surfaces when disrupting the more or less ideal drug microcrystals to nanoparticles. Dissolution experiments can be performed to quantify the increase in the saturation solubility of a drug when formulated into a nanosuspension.²⁴ The stability of the particles obtained in the nanosuspension is attributed to their uniform particle size which is created by various manufacturing processes. The absence of particles with large differences in their size in

nanosuspensions prevents the existence of different saturation solubilities and concentration gradients; consequently preventing the Oswald ripening effect. Ostwald ripening is responsible for crystal growth and subsequently formation of micro-particles. It is caused by a difference in dissolution pressure/saturation solubility between small and large particles. Molecules diffuse from the higher concentration area around small particles which have higher saturation solubility to an area around larger particles possessing a lower drug concentration. This leads to the formation of a supersaturated solution around the large particles and consequently to drug crystallization and growth of the large particles.

Advantages of nanosuspensions

The major advantages of nanosuspension technology are: ²⁵

- ✓ Provides ease of manufacture and scale-up for large-scale production,
- ✓ Long-term physical stability due to the presence of stabilizers,
- ✓ Oral administration of nanosuspensions provide rapid onset, reduced fed/fasted ratio and improved bioavailability,
- ✓ Rapid dissolution and tissue targeting can be achieved by IV route of administration,
- ✓ Reduction in tissue irritation in case of subcutaneous/intramuscular administration,
- ✓ Higher bioavailability in case of ocular administration and inhalation delivery,
- ✓ Drugs with high log P value can be formulated as nanosuspensions to increase the bioavailability of such drugs,
- ✓ Improvement in biological performance due to high dissolution rate and saturation solubility of the drug,
- ✓ Nanosuspensions can be incorporated in tablets, pelle hydrogels, and suppositories are suitable for various routes of administration,
- ✓ The flexibility offered in the modification of surface properties and particle size, and ease of postproduction processing of nanosuspensions enables them to be incorporated in various dosage forms for various routes of administration, thus proving their versatility.

Interesting special features of nanosuspensions ²⁶

- Increase in saturation solubility and consequently an increase in the dissolution rate of the drug.
- Increase in adhesive nature, thus resulting in enhanced bioavailability.
- Increasing the amorphous fraction in the particles, leading to a potential change in the crystalline structure and higher solubility.
- The absence of Ostwald ripening, producing physical long-term stability as an aqueous suspension.
- The possibility of surface-modification of nanosuspensions for site-specific delivery.

Criteria for selection of a drug for nanosuspensions

Nanosuspension can be prepared for the API that is having either of the following characteristics: ²⁷

1. Water-insoluble but which are soluble in oil (high log P) OR API are insoluble in both water and oils
2. Drugs with a reduced tendency of the crystal to dissolve, regardless of the solvent
3. API with a very large dose

Formulation of nanosuspension ²⁸

TABLE 1.1: Formulation consideration for Nanosuspension

Excipients	Function	Examples
Stabilizers	Wet the drug particles thoroughly, prevent Ostwald's ripening and agglomeration of nanosuspensions, providing a steric or ionic barrier	Soya Lecithins, Poloxamers 188/407, Polysorbate 80, HPMC E-15/E-50, PVP K-25/K-30
Co-surfactants	Influence phase behavior when microemulsions are used to formulate nanosuspensions	Bile salts, Dipotassium Glycyrrhizinate, Transcutol, Ethanol, Isopropanol
Organic solvent	Pharmaceutically acceptable less hazardous solvent for preparation of formulation.	Methanol, Ethanol, Chloroform, Isopropanol, Ethyl acetate, Ethyl formate, Butyl lactate, Triacetin, Propylene carbonate, Benzyl alcohol.
Other additives	According to the requirement of the route of administration or the properties of the drug moiety	Buffers, Salts, Polyols, Osmogens, Cryoprotectant etc.

Methods of preparation for nanosuspensions

(A) Milling techniques (Nanocrystals or Nanosystems)

i) Media milling: Media milling is a technique used to prepare nanosuspensions. Nanocrystal is a patent protected technology in which, the drug nanoparticles are obtained by subjecting the drug to media milling. High energy and shear forces generated as a result of impaction of the milling media with the drug provide the necessary energy input to disintegrate the micro-particulate drug into nanosized particles. In the media milling process, the milling chamber is charged with the milling media, water or a suitable buffer, drug and stabilizer. Then the milling media or pearls are rotated at a very high shear rate. The major concern with this method is the residues of milling media remaining in the finished product could be problematic for

administration. Nanosuspensions are produced by using high-shear media mills or pearl mills. The mill consists of a milling chamber, milling shaft, and a recirculation chamber. An aqueous suspension of the drug is then fed into the mill containing small grinding balls/pearls. As these balls rotate at a very high shear rate under controlled temperature, they fly through the grinding jar interior and impact against the sample on the opposite grinding jar wall. The combined forces of friction and impact produce a high degree of particle size reduction. The milling media or balls are made of a ceramic-sintered aluminum oxide or zirconium oxide or highly cross-linked polystyrene resin with high abrasion resistance. Planetary ball mill is one example of the equipment that can be used to achieve a grind size below 0.1 μm .

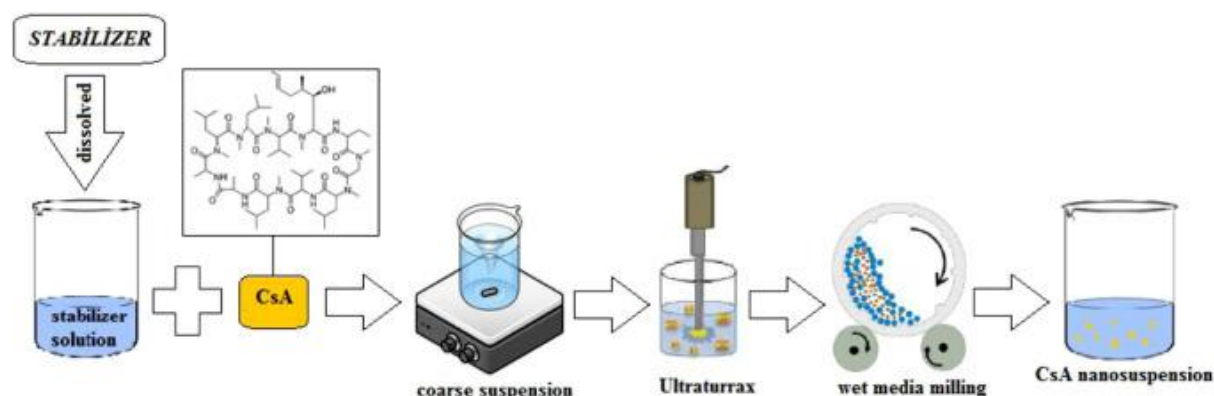


Fig: Milling techniques

ii) Dry co-grinding:

Nanosuspensions prepared by high-pressure homogenization and media milling using pearl-ball mill are wet-grinding processes. Recently, nanosuspensions can be obtained by dry milling techniques. Successful work in preparing stable nanosuspensions using drygrinding of poorly soluble drugs with soluble polymers and copolymers after dispersing in a liquid media has been reported. The colloidal particles formation of many poorly water-soluble drugs; griseofulvin, glibenclamide, and nifedipine were obtained by grinding with polyvinylpyrrolidone (PVP) and sodium dodecyl

sulfate (SDS). Many soluble polymers and copolymers such as PVP, polyethylene glycol (PEG), hydroxypropyl methylcellulose (HPMC) and cyclodextrin derivatives have been used. Physicochemical properties and dissolution of poorly water-soluble drugs were improved by co-grinding because of an improvement in the surface polarity and transformation from a crystalline to an amorphous drug. Dry co-grinding can be carried out easily and economically and can be conducted without organic solvents. The co-grinding technique can reduce particles to the submicron level and a stable amorphous solid can be obtained.

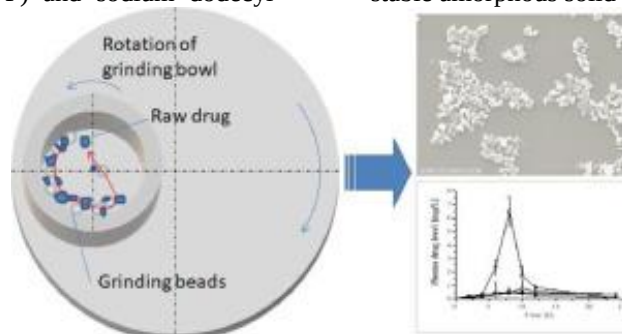


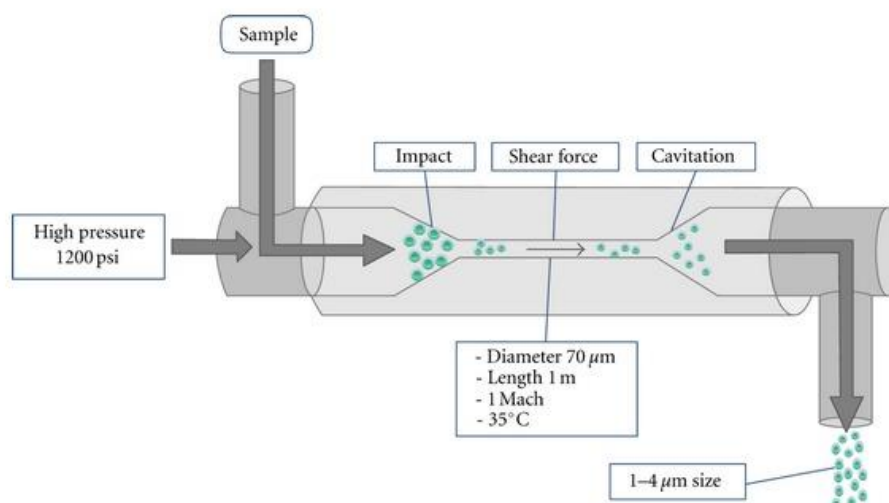
Fig: Dry co-grinding

Advantages

1. Media milling is applicable to the drugs that are poorly soluble in both aqueous and organic media.
2. Very dilute as well as highly concentrated nanosuspensions can be prepared by handling 1 mg/ml to 400 mg/ml drug quantity.
3. Nanosize distribution of final nanosized products.

Disadvantages

1. Nanosuspensions contaminated with materials eroded from balls may be problematic when it is used for long therapy. (Wet milling technique)
2. The media milling technique is time-consuming.
3. Some fractions of particles are in the micrometer range.
4. Scale up is not easy due to mill size and weight.

(B) High-Pressure Homogenization**i) Homogenization in Aqueous media (Dissocubes)****Fig: High-Pressure Homogenization****ii) Homogenization in Non-Aqueous Media (Nanopure)**

Nanopure is the technology in which suspension is homogenized in water-free media or water mixtures. In the Dissocubes technology, the cavitation is the determining factor of the process. But, in contrast to water, oils and oily fatty acids have very low vapor pressure and a high boiling point. Hence, the drop of static pressure will not be sufficient enough to initiate cavitation. Patents covering disintegration of polymeric material by high-pressure homogenization mention that higher temperatures of about 80°C promoted disintegration, which cannot be used for thermolabile compounds. In nanopure technology, the drug suspensions in the non-aqueous media were homogenized at 0°C or even

Homogenization involves the forcing of the suspension under pressure through a valve having a narrow aperture. Dissocube technology was developed by Muller et al. in which, the suspension of the drug is made to pass through a small orifice that results in a reduction of the static pressure below the boiling pressure of water, which leads to boiling of water and formation of gas bubbles. When the suspension leaves the gap and normal air pressure is reached again, the bubbles shrink and the surrounding part containing the drug particles rushes to the center and in the process colloids, causing a reduction in the particle size. Most of the cases require multiple passes or cycles through the homogenizer, which depends on the hardness of drug, the desired mean particle size, and the required homogeneity. Atovaquone nanosuspensions was prepared using Dissocubes technique. To produce a nanosuspension with a higher concentration of solids, it is preferred to start homogenization with very fine drug particles, which can be accomplished by pre-milling.

below the freezing point and hence are called "deep-freeze" homogenization. The results obtained were = comparable to Dissocubes and hence can be used effectively for thermolabile substances at milder conditions.

Advantages

- Drugs that are poorly soluble in both aqueous and organic media can be easily formulated into nanosuspensions.
- Ease of scale-up and little batch-to-batch variation
- Narrow size distribution of the nanoparticulate drug present in the final product

- Allows aseptic production of nanosuspensions for parenteral administration.
- Flexibility in handling the drug quantity, ranging from 1 to 400 mg.ml⁻¹, thus enabling formulation of very dilute as well as highly concentrated nanosuspensions

Disadvantages

- Prerequisite of micronized drug particles.
- Prerequisite of suspension formation using high-speed mixers before subjecting it to homogenization.

(C) Precipitation Method

Using a precipitation technique, the drug is dissolved in an organic solvent and this solution is mixed with a miscible antisolvent. In water-solvent mixture the solubility is low and the drug precipitates. Mixing processes vary considerably. Precipitation has also been coupled with high shear processing. The nanoedge process (is a registered trademark of Baxter International Inc. and its subsidiaries) relies on the precipitation of friable materials for subsequent fragmentation under conditions of high shear and/or thermal energy. Nanoedge The basic principles of Nanoedge are the same as that of precipitation and homogenization. A combination of these techniques results in smaller.

MATERIALS AND METHODOLOGY:

Characterization of Sotagliflozin

Organoleptic properties:

Take a small quantity of sample and spread it on the white paper and examine it visually for color, odour and texture.

Determination of Sotagliflozin Solubility

Determination of solubility of drug by visual observation An excess quantity of Sotagliflozin was taken separately and adds in 10 ml of different solutions. These solutions were shaken well for few minutes. Then the solubility was observed and observations are shown in the Results and discussion.

Pre formulation Studies

Pre formulation involves the application of biopharmaceutical principles to the physicochemical parameters of drug substance are characterized with the goal of designing optimum drug delivery system.

Preparation of 0.1 N HCl:

Dissolve 8.5 ml of concentrated HCl in 1000 ml of distilled water.

Analytical method development for Sotagliflozin:

a) Determination of absorption maxima

A spectrum of the working standards was obtained by scanning from 200-400nm against the reagent blank to fix absorption maxima. The λ_{max} was found to be 271 nm. Hence all further investigation was carried out at the same wavelength.

b) Preparation of Standard graph in 0.1 N HCl

100 mg of Sotagliflozin was dissolved in method 5ml, volumetric flask make up to 100ml of 0.1 N HCl., form primary stock 10ml was transferred to another volumetric flask made up to 100ml with Phosphate buffer of 0.1 N HCl, from this secondary stock was taken separately and made up to 10 ml with Phosphate buffer of 0.1 N HCl, to produce 2, 4, 6, 8 and 10µg/ml respectively. The absorbance was measured at 271 nm by using a UV spectrophotometer.

PREPARATION OF SOTAGLIFLOZIN NANOSUSPENSION BY PRECIPITATION-ULTRASONICATION TECHNIQUE

Sotagliflozin nanoparticles were produced by precipitation-ultrasonication technique. The required amount of drug was completely dissolved in water-miscible solvent. Different concentrations of polymers in solvent (100, 150 and 200 mg/ml) were used. The obtained drug solution was then injected into the water containing the stabilizer under stirring at 1,000 rpm. Precipitation of solid drug particles occurred immediately upon mixing. The suspension was then sonicated for 15 min under cold condition.

INGREDIENTS (MG)	FORMULATION CODES								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Sotagliflozin	200	200	200	200	200	200	200	200	200
Carbopol	100	150	200	-	-	-	-	-	-
Ethyl Cellulose	-	-	-	100	150	200	-	-	-
Na CMC	-	-	-	-	-	-	100	150	200
PVP k-30	25	25	25	25	25	25	25	25	25
Tween-80(mL)	10	10	10	10	10	10	10	10	10
Methanol	50	50	50	50	50	50	50	50	50
Water	100	100	100	100	100	100	100	100	100

EVALUATION OF SOTAGLIFLOZIN NANOSUSPENSION

Particle Size Analysis:

The particle size analysis was carried out using Microtac blue wave particle size analyzer. Before measurement the samples has to be diluted with de-ionized water to obtain a suitable Concentration for measurement. The results obtained for particle size distributions were used to confirm the formation of nano-sized particles.

Scanning Electron Microscopy (SEM):

Surface morphology of the specimen will be determined by using a scanning electron microscope (SEM), Model JSM 84 0A, JEOI, Japan. The samples are dried thoroughly in vacuum desiccator before mounting on brass specimen studies, using double sided adhesive tape. Gold-palladium alloy of 120°A Knees was coated on the sample sputter coating unit (Model E5 100 Polaron U.K) in Argon at ambient of 8-10 with plasma voltage about 20mA. The sputtering was done for nearly 5 minutes to obtain uniform coating on the sample to enable good quality SEM images. The SEM was operated at low accelerating voltage of about 15KV with load current about 80mA. The condenser lens position was maintained between 4.4-5.1. The objective lens aperture has a diameter of 240 microns and working distance WD=39mm.

Particle Size Analysis:

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Saturation Solubility Studies

Saturation solubility of nanosuspensions was carried out in distilled water. A known volume of nanosuspensions (1ml) were added to 10 ml distilled water. The stirred samples were further taken in test tubes and centrifuged at 10,000rpm for 15 minutes. Supernant was then filtered (0.45 µm, Gelman, Mumbai) suitably diluted and analyzed spectrophotometrically at 271 nm. Triplicate determination was performed.

Viscosity measurement

The viscosity of lipid-based formulations of several compositions can be measured at different shear rates at different temperatures using Brookfield type rotatory viscometer.

The sample room of the instrument must be maintained at 37° C by a thermo bath and the samples, for the measurement are to be immersed in it and found viscosity of the formulations.

Zeta potential measurement:

Zeta potential of the suspension is measured by Malvern Zetasizer. The zeta sizer mainly consists of laser which is used to provide a light source to illuminate the particles within the sample. For zeta potential measurements this light splits to provide an incident and reference beam. The incident laser beam passes through the center of the sample cell, and the scattered light at an angle of about 130 is detected. Zetasizer software produces a frequency spectrum from which the electrophoretic mobility hence the zeta potential is calculated.

Drug entrapment efficiency (DEE)

The freshly prepared nanosuspension was centrifuged at 20,000 rpm for 20 min at 5 °C temperature using cool ultracentrifuge. The amount of unincorporated drug was measured by taking the absorbance of the appropriately diluted 25 ml of supernatant solution at 271 nm using UV spectrophotometer against blank/control Nanosuspensions. DEE was calculated by subtracting the amount of free drug in the supernatant from the initial amount of drug taken. The experiment was performed in triplicate for each batch and the average was calculated.

The entrapment efficiency (EE %) could be achieved by the following equation:

$$\text{Entrapment efficiency (\%)} = \frac{W_{\text{initial drug}} - W_{\text{free drug}}}{W_{\text{initial drug}}} \times 100$$

Dissolution study:

In vitro drug release studies were performed in USP apparatus-Type II using paddle method at rotation speed of 50 rpm. Dissolution was carried out in 0.1N HCL as a dissolution medium. The volume and temperature of the dissolution medium were 900 ml and 37.0 ± 0.5°C. 5 ml of sample was withdrawn periodically (after 5minutes) and replaced with an equal volume of fresh 0.1N HCL up to 60min. Samples were suitably diluted and filtered through a filter paper (0.45 µm, Whatman Inc., USA). The filtrate was then subject to the UV analysis against the blank (distilled water). Percent cumulative release of SS was calculated based on the standard UV calibration curve at 271 nm (Systronic 2203, Japan).

Stability Study of Nanosuspension

The stability studies for Nanosuspension have performed storage conditions for 90 days as follows Acceleration stability studies intermediate storage condition has been changed from 30°C ± 2°C and 60% RH ± 5% RH and 40°C ± 2°C and 75% RH ± 5% RH. The optimized batch F6 Nanosuspension was utilized for each condition; the particle size, Drug content, Saturation Solubility, Viscosity and *In-vitro* dissolution are the most vital specification for the activity & physical stability

RESULTS AND DISCUSSION:

The present study was aimed to developing Nanosuspension of Sotagliflozin using various polymers. All the formulations were evaluated for

physicochemical properties and *in vitro* drug release studies.

8.1. Preformulation study:**Identification:****Organoleptic properties****Table 8.1: Organoleptic properties**

S NO.	Properties	Results
1	State	Solid
2	Colour	white
3	Odour	Odorless

Solubility:

Sotagliflozin is sparingly soluble in aqueous buffers. Very soluble in organic solvents such as Methanol, DMSO and Acetonitrile.

8.2. Analytical Method

Graph of Sotagliflozin was taken in 0.1 N HCl (pH 1.2) 271 nm respectively.

Table 8.2: Observations for graph of Sotagliflozin in 0.1N HCl (270)

Concentration ($\mu\text{g/ml}$)	Absorbance
0	0
2	0.126
4	0.234
6	0.356
8	0.452
10	0.567

It was found that the estimation of Sotagliflozin by UV spectrophotometric method at λ_{max} 271 nm in 0.1N Hydrochloric acid had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 2-10 $\mu\text{g/ml}$. The regression equation generated was $y = 0.056x + 0.008$.

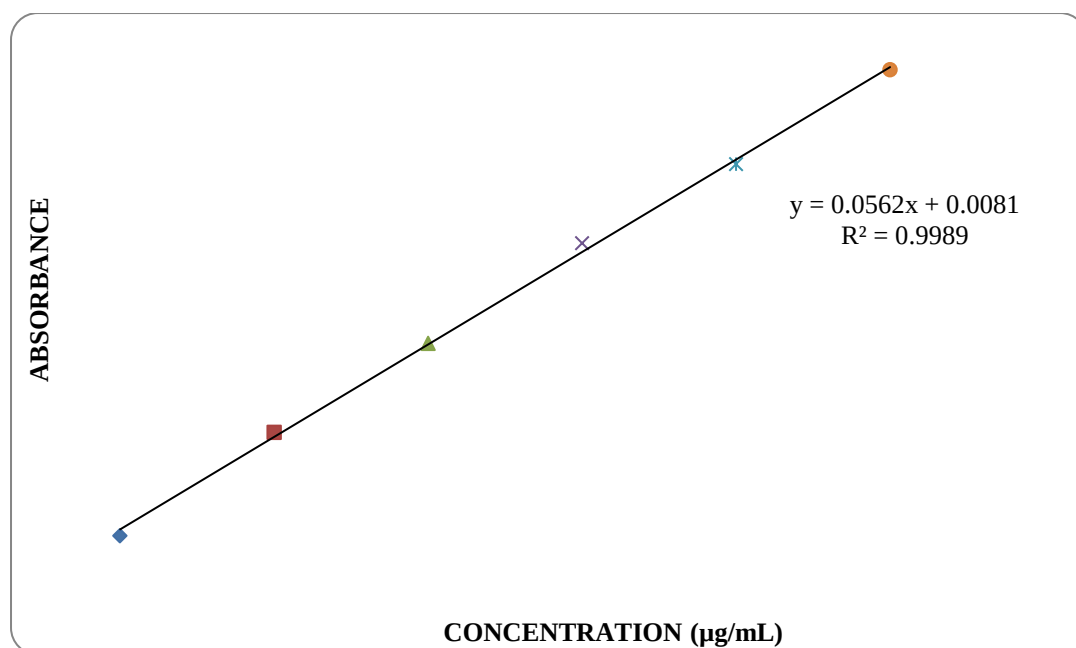


Figure 8.1: Standard graph of Sotagliflozin in 0.1N HCl

8.3. Characterization of Nanosuspension:

Table 8.3: Percentage yield, Drug Content, Entrapment Efficiency of all Nanosuspension formulations

FORMULATION	Entrapment Efficiency (%)	Drug Content (%)	Percentage yield (%)
F1	86.26	90.34	88.01
F2	92.81	92.60	90.65
F3	97.29	96.34	93.23
F4	83.27	85.53	76.94
F5	90.83	90.76	81.76
F6	98.60	97.82	89.34
F7	80.15	79.49	80.08
F8	89.34	85.33	84.65
F9	94.75	89.79	87.91



Figure 8.2: Entrapment efficiency of all Nanosuspension formulations

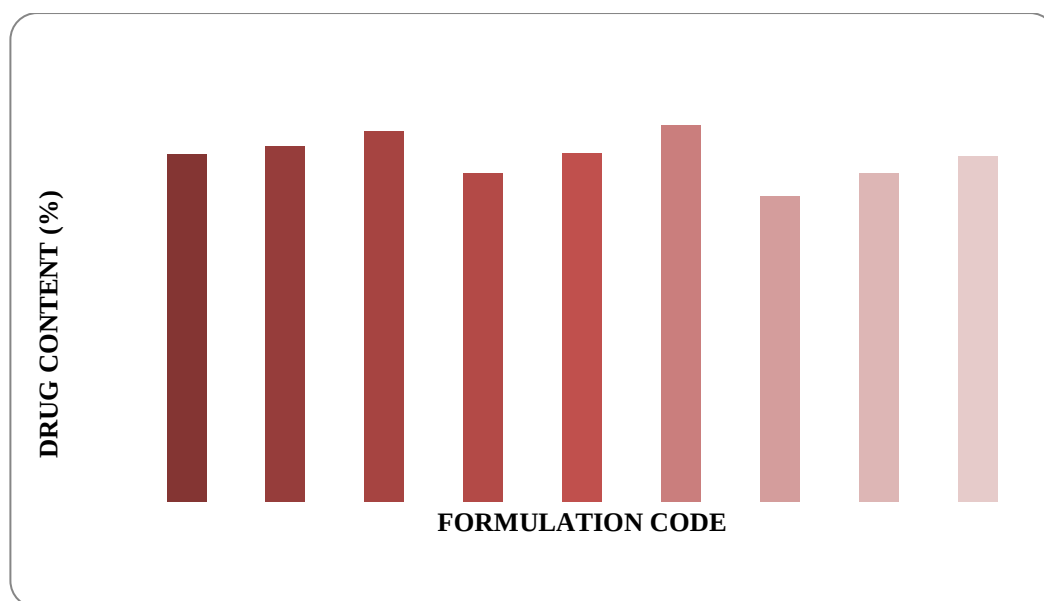


Figure 8.3: Drug content of all Nanosuspension formulations

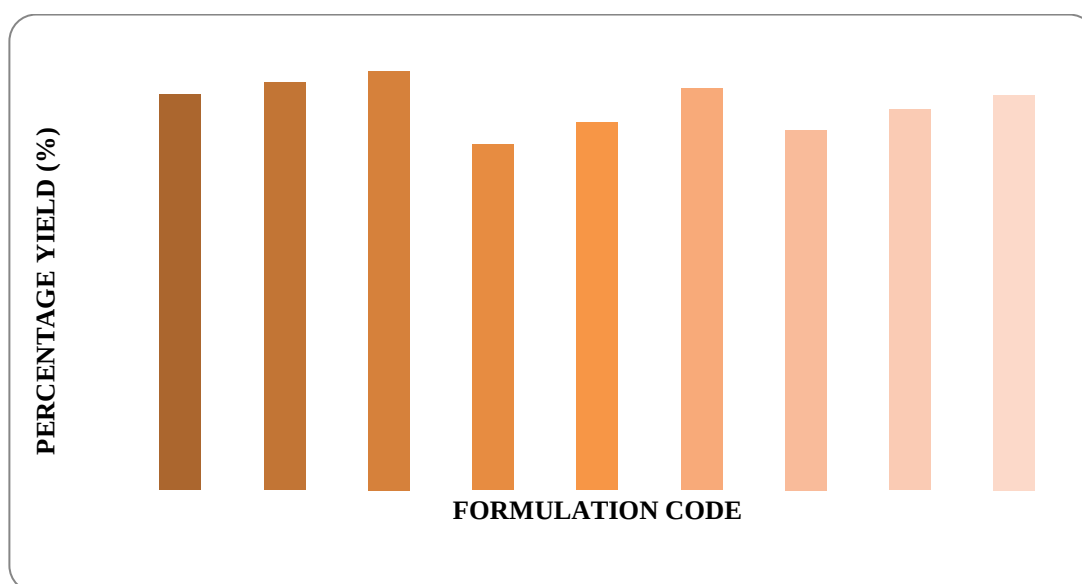


Figure 8.4: Percentage yield of all Nanosuspension formulations

Drug entrapment efficiency:

The formulations showed drug entrapment in the range of 80.157–98.60 %. Formulation (F6) containing polymer ratio 200 mg/ml stabilized with Ethyl Cellulose showed highest entrapment.

Table 8.4: Particle Sizes, PDI, Zeta Potential of all Nanosuspension formulations

FORMULATION	Particle Size (μm)	PDI	Zeta Potential (mV)
F1	5.9	0.81	-28.36
F2	4.6	0.69	-20.52
F3	4.1	0.51	-33.42
F4	4.5	1.56	-15.51
F5	5.8	0.91	-22.19
F6	4.5	0.98	-16.81
F7	6.9	0.46	-28.61
F8	10.5	1.63	-23.28
F9	13.8	1.26	-19.84

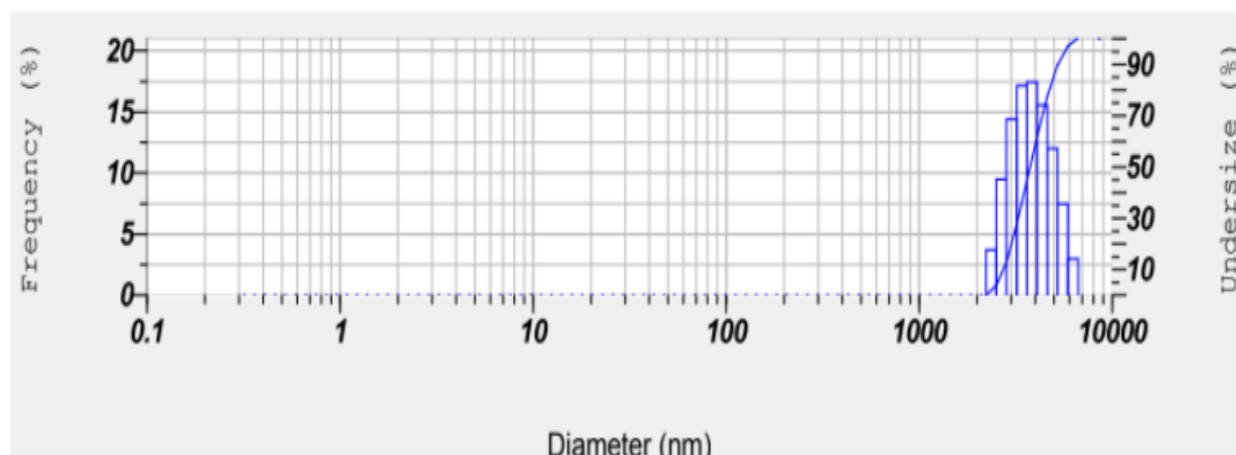


Fig 8.5: Particle Size of F6 Formulation

Particle Size Analysis:

The particle size distribution studies showed that all the formulation particle size was in the range of 4.1-13.8 nm. All the formulations having a particle size in the nanometer range and showing ideal surface morphology.

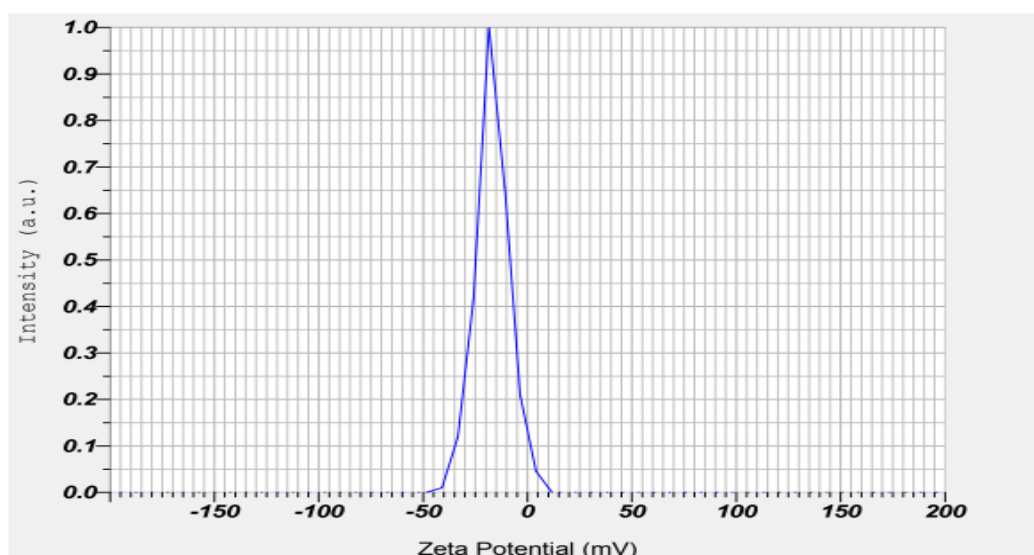


Fig 8.6: Zeta potential of F6 Formulation

Zeta potential is a term related to the stability of samples for molecules and particles that are small enough; high zeta potential will confer stability i.e. it resists aggregation. Here zeta potential of the prepared Nanosuspension was found to be -33.42, which would not allow aggregation.

Saturation Solubility and viscosity Determination

Table 8.5: Saturation Solubility and viscosity of various formulations

Formulations	Saturation solubility in water mg/ml	The viscosity of the dispersion medium
F1	0.781	0.890 mPa-s
F2	0.836	0.892 mPa-s
F3	0.902	0.895 mPa-s
F4	0.681	0.890 mPa-s
F5	0.796	0.879 mPa-s

CONCLUSION:

The present study successfully formulated and evaluated a Sotagliflozin nanosuspension with satisfactory physicochemical characteristics. The optimized formulation demonstrated desirable properties, indicating the effectiveness of the selected formulation method in producing stable nanosized drug particles.

The pre-compression parameters, including bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio, were found to be within the acceptable limits specified by the Indian Pharmacopoeia (IP), indicating good flowability and compressibility of the powder blend. Similarly, the post-compression evaluation parameters such as tablet weight variation, hardness, thickness, friability, drug content uniformity, disintegration time, and dissolution profile complied with the prescribed IP standards, confirming the quality and consistency of the prepared tablets.

Overall, the formulated Sotagliflozin nanosuspension exhibited acceptable pharmaceutical performance and met all the required quality control specifications. The findings suggest that nanosuspension technology is a promising approach to enhance the solubility and dissolution characteristics of Sotagliflozin, potentially leading to improved oral bioavailability and therapeutic efficacy.

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