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Original Article

FORMULATION AND EVALUATION OF SOLID SELF-EMULSIFYING DRUG DELIVERY SYSTEM OF GLICLAZIDE

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ABSTRACT

Objective: Gliclazide (GCZ) is a widely prescribed anti-diabetic drug belongs to class II under BCS and exhibit low and variable oral bioavailability due to its poor aqueous solubility. The present investigations highlight the development of solid self-emulsifying drug delivery system (solid-SEDDS) for improved oral delivery of the poorly water-soluble drug, GCZ.

Methods: Various oils, surfactant and co-surfactant, were screened for their emulsification ability. Ternary phase diagrams were plotted to identify the zone of micro-emulsification. Liquid SEDDS of the drug were formulated using lemon oil as the oil phase, tween 80, as the surfactant, and labrasol, as the co-surfactant. The optimized liquid SEDDS was transformed into free-flowing powder using florite R as the adsorbent.

Results: Self-emulsifying powder retained the self-emulsifying property of the liquid SEDDS. The morphology of solid-SEDDS from scanning electron microscopy studies demonstrated the presence of spherical, granular particles indicating good flowing ability. X-ray powder diffraction studies confirmed solubilization of the drug in the lipid excipients and/or transformation of a crystalline form of the drug to amorphous form. *In vitro* dissolution studies revealed enhanced release of the drug from solid-SEDDS as compared to plain drug and marketed formulation.

Conclusion: Thus it can be concluded that solid-SEDDS, amenable for the development of solid dosage form, can be successfully developed using florite R with the potential of enhancing the solubility, dissolution rate, and bioavailability of the drug.

Keywords: Gliclazide, Self-emulsifying drug delivery system (SEDDS), Solubility, Adsorption, Droplet size, Drug release

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INTRODUCTION

The enhancement of oral bioavailability of poorly soluble drugs remains one of the most challenging aspects of drug development [1].

Poorly water-soluble drug candidates often emerge from contemporary drug discovery programs and present formulators with considerable technical challenges. The absorption of such compounds, when presented in the crystalline state to the gastrointestinal tract, is typically dissolution rate-limited, and the drugs are typically biopharmaceutical classification system (BCS) class II or class IV compounds [2]. To overcome these problems, various strategies are exploited including the use of surfactants, lipids, permeation enhancers, micronization, salt formation, cyclodextrins, nanoparticles and solid dispersions. There are a number of formulation strategies that could be used to improve the bioavailability of class II drugs, either by increasing the dissolution rate or by presenting the drug in solution and maintaining the drug in solution in the intestinal lumen [3].

The interests on lipid-based drug delivery systems (LBDDS) have increased over the past two decades as a function of identification of these pharmaceutically difficult candidates and increased even further after the successful launch of lipid-based oral pharmaceutical products, including in particular cyclosporine A, marketed as Sandimmune TM and Neoral TM [4].

Self-emulsifying drug delivery systems (SEDDS) are isotropic mixtures of drug, lipids and surfactants, usually with one or more hydrophilic co-solvents or co-emulsifiers. Upon mild agitation followed by dilution with aqueous media, these systems can form fine (oil in water) emulsion instantaneously. 'SEDDS' is a broad term, typically producing emulsions with a droplet size ranging from a few nanometers to several microns [5]. Hydrophobic drugs can often be dissolved in SEDDS allowing them to be encapsulated as unit dosage forms for peroral administration [6]. When such a system is released in the lumen of the gastrointestinal tract, it disperses to form a fine emulsion (micro/nano) with the aid of GI fluid. This leads to in situ solubilization of drug that can subsequently be absorbed by lymphatic pathways, bypassing the hepatic first pass effect [7]. SEDDS formulations are viscous liquids and thus marketed usually in the form of soft gelatin capsules, which have some drawbacks in the manufacturing process such as difficulty in process control, leakage of the encapsulated components, high production cost, and lower stability [8]. To address these problems, several attempts have been made to transform liquid SEDDS into solid dosage forms using solid carriers or adsorbents. The solid forms of SEDDS are able to offer the advantages of SEDDS in combination with those of solid dosage forms such as production reproducibility and improved stability when they would lead to the formation of the fine or microemulsion at a similar rate exhibited by liquid SEDDS [9].

Gliclazide (GCZ) is a second generation sulphonylurea oral hypoglycemic agent used in the treatment of non-insulin-dependent diabetes mellitus (NIDDM). It improves defective insulin secretion and may reverse insulin resistance observed in patients with NIDDM. These actions are reflected in a reduction in blood glucose levels which is maintained during both short and long term administration and is comparable with that achieved by other sulphonylurea agents. GCZ is extensively metabolized by the liver. Its metabolites are excreted in both urine (60-70%) and feces (10-20%). GCZ is poorly water soluble, and its bioavailability can be improved by increasing the dissolution rate and/or decreasing the pre-systemic clearance [10]. The objective of the present study was to prepare and evaluate the SEDDS of GCZ using a suitable combination of oil, surfactants and co-surfactants. Further, it was envisaged to convert liquid SEDDS into a solid formulation suitable for capsules/tablets manufacturing by adsorption of liquid self-emulsifying formulations onto porous solid carriers. Solid SEDDS was formulated using florite R as the porous carrier and evaluated for flow properties, solid state characteristics and in vitro dissolution studies.

MATERIALS AND METHODS

GCZ was obtained as a generous gift from Vama Pharmaceuticals Pvt. ltd, Nagpur. Captex 300, capmul MCM were obtained as gift samples from Abitec Corporation, Janesville, USA, while labrasol,

labrafil M 1944, lauroglycol 90, peceol, capryol 90 were gifted by Gattefosse India Pvt. Ltd, Mumbai, India. Florite R was supplied by Tomita Pharmaceuticals, Japan. All other reagents used were of suitable analytical grade and used as supplied.

Solubility studies

Equilibrium solubility of GCZ was measured in various oils, surfactants and co-surfactants [11, 12]. An excess amount of GCZ was added to screw capped vials containing 2 ml of each of the selected vehicles and the mixture was stirred continuously for 72 h at 37±1 °C. After equilibrium was attained, the mixture was centrifuged at 3000 rpm for 10 min, and the obtained supernatant was filtered through a membrane filter. The absorbance of the filtrate was measured using a double beam UV/VIS spectrophotometer (Shimadzu1601, Japan) at λ_{max} of 229.5 nm. The content of GCZ was determined using a previously constructed standard calibration curve

Preliminary screening of surfactant and co-surfactants

The surfactants were screened for emulsification ability as per method reported in the literature [13]. Oil was mixed with a surfactant in 1:1 ratio and vortexed for 5 min to ensure proper mixing. This mixture, 50 mg, was weighed and diluted to 50 ml with double-distilled water to obtain an emulsion. The emulsions were observed for physical appearance, clarity, and phase separation. The emulsions were left undisturbed for 2 h and analyzed for transmittance at 650 nm on UV spectrophotometer (Shimadzu, Japan) using double distilled water as blank. The experiment was performed in triplicate. The same turbidimetric method was used to screen the co-surfactants. During the screening, oil/surfactant/co-surfactant ratio was kept constant as 3: 2: 1. The experiment was performed in triplicate.

Construction of pseudo-ternary phase diagram

Based on the observations of solubility studies, components of emulsion viz, oil phase, surfactants, and co-surfactants, including highest solubility of GCZ were selected. The surfactants and co-surfactants were blended together in 1:1, 2:1, and 1:2 proportions respectively. These blends of surfactants and co-surfactants, (S_{mix}) were mixed with oily phase by adding a small amount with constant stirring. The proportion of oil and S_{mix} were varied as 9:1, 8:2, 7:1, 6:4, 5:5, 4:6, 3:7, 2:8 and 1:9. The resultants blends were titrated with distilled water in 0.5% (w/w) increment ensuring proper stirring of the systems [14]. Systems were then allowed to reach equilibrium and the samples were checked visually for clarity. The pseudo-ternary phase diagrams were constructed for each system of oil, surfactant, co-surfactant by Chemix software. The point indicating the clear and isotopic mixtures were considered to be within the microemulsion region.

Preparation of liquid SEDDS

From the ternary phase diagram, the ratio of surfactants to co-surfactants was optimized. Then, by varying the ratio of oil to optimized ratio of surfactant to co-surfactants, different formulations were prepared with 40 mg of GCZ. The formulations were prepared by dissolving the drug in oil followed by addition of surfactant and co-surfactant in glass vials. The total weight of the formulations was kept as 500 mg. The resulting mixtures were stirred continuously by vortex mixing followed by sonication for few minutes to obtain a homogenous isotropic mixture. The SEDDS formulations were stored at ambient temperatures until further use.

Evaluation of SEDDS

Visual assessment of self-emulsification

A visual test to assess the self-emulsification properties was adopted in the present study. In this method, a unit dose of the formulation was introduced into 250 ml of water in a glass beaker that was maintained at 37±0.5 °C and the contents mixed gently using a magnetic stirrer. The tendency to emulsify spontaneously and progress of emulsion droplets were observed. On the basis of dispensability, appearance and time required to emulsify SEDDS were categorized in “Grade A,” “Grade B” and “Grade C.” All the trials were carried out in triplicate with similar observations being made between repeats [15].

% transmittance

The SEDDS were reconstituted with distilled water and the resulting micro emulsions were observed visually for any turbidity. Thereafter its % transmittance was measured at 650 nm using UV-visible (Vis) spectrophotometer (Jasco V-630, Japan) against distilled water as the blank. The studies were conducted after 100 times dilution.

Cloud point measurement

The cloud point measurement was carried out for the formulations as reported earlier [16]. The formulation was diluted up to 100 folds with distilled water and kept in a water bath which was maintained at a temperature of 25 °C with a gradual increase of temperature at a rate of 5 °C/min and the corresponding cloud point temperatures were read at first sign of turbidity by visual observation.

Drug content estimation

Liquid SEDDS containing GCZ, each equivalent to 40 mg was dispersed in a suitable quantity of methanol. The samples were mixed thoroughly to dissolve the drug in methanol, centrifuged at 3000 rpm for 15 min using 12 ˚C micro-centrifuge (Remi Motors, Mumbai, India) to separate the undissolved excipients. The supernatant was suitably diluted and analyzed spectro-photometrically at 229.5 nm using Shimadzu UV-Vis spectro-photometer.

Emulsion droplet size

The mean droplet size and polydispersity index (PDI) of the formulations were determined by photon correlation spectroscopy using nanosizer (Nanophox NX0088, Sympatec, Germany). Each formulation was diluted with filtered (0.45 µm, Millipore) double distilled water before analysis. Size analysis was carried at 25 °C with an angle of detection of 90°.

Preparation of solid-SEDDS

Solid-SEDDS were prepared by mixing the liquid SEDDS containing GCZ with florite R in the 1:1 Proportion. In brief liquid SEDDS was added dropwise over florite R contained in a broad porcelain dish. After each addition, the mixture was homogenized using a glass rod to ensure uniform distribution of formulation. Resultant mass was passed through sieve no 120 and dried at ambient temperature and stored until further use.

Evaluation of solid-SEDDS

Micromeritic properties of solid-SEDDS

The bulk density tapped density, carr’s compressibility index and hausner ratio were determined for the optimized solid-SEDDS. The angle of repose of self-emulsifying powder was determined by funnel method [17]. Briefly, the sample was poured through a funnel with its tip positioned at a fixed height (h) on a horizontal surface until the apex of pile touches the tip of the funnel. The angle of repose was calculated using the formula $\tan \theta = h/r$ where r is the radius of the pile of powder.

Morphological analysis

The surface morphology of solid SEDDS of GCZ was determined using scanning electron microscope (JEOL JSM-6390 LV, Japan) at 15 keV accelerating voltage. The sample was lightly sprinkled on the double adhesive tape stuck on the aluminum stub. The stubs were then coated with platinum to a thickness of above 10˚ A under an arogon atmosphere using a gold sputter module under a high vacuum evaporator and the stub containing coated sample was placed in scanning electron microscope chamber.

X-Ray powder diffraction studies

X-Ray powder scattering measurements of the GCZ, physical mixture of GCZ with florite R and that of solid self-emulsifying powder were carried out with X-ray diffractometer (X’Pert PRO PAN alytical, U. S.

A.). About 1 g of the sample was required for the analysis. The X-ray powder diffraction patterns were recorded at room temperature using monochromatic CuKα1 radiation (k=1.5406 Å) at 40 mA and at 45 kV over a range of 2θ angles from 3 ° to 50 ° with an angular increment of.02 ° per second.

Emulsion droplet size

The average droplet size and PDI of micro emulsion formed from solid-SEDDS was determined by photon correlation spectroscopy using more nanosize (Nanophox NX0088, Sympatec Germany). The formulation was diluted with filtered (0.45 µm, Millipore) double distilled water before analysis. Size analysis was carried at 25 °C with an angle of detection of 90°.

***In vitro* dissolution studies**

Drug release from solid-SEDDS was performed using USP type II dissolution apparatus (Electrolab, TDT-06 T Mumbai, India). Solid-SEDDS formulation equivalent to 40 mg of GCZ was used for the dissolution studies which were performed in dissolution medium containing 900 ml of pH 1.2 buffer with paddle rotation speed of 100 rpm. An aliquot of 5 ml was withdrawn at predetermined time intervals and filtered through 0.45 µm filter. The concentration of GCZ in the filtrate was analyzed using uv spectrophotometer at 229.5 nm after suitable dilution. Similarly, the dissolution profiles of pure drug and the marketed formulation of GCZ (40 mg tablet) was also carried out.

Stastical analysis

All the results were expressed as mean with standard deviation (mean±SD). The statistical analysis was performed with instant Graph Pad Prism Software (version 4.00; Graph Pad Software San Diago CA, U. S. A)

RESULTS AND DISCUSSION

Solubility studies

Solubility studies were performed to identify suitable excipients with maximum potential to solubilize the drug and having good miscibility with each other which helps in minimizing the final volume of SEDDS and potentiates optimal drug loading [18]. The solubility of GCZ in various oils is shown in fig. 1. The drug displayed poor solubility in castor oil, captex 300 as well as peceol. From the data obtained from the solubility studies lemon oil was selected as oil phase for further studies due to its highest solubilization potential. The surfactant and the co-surfactant were selected based on two parameters, ability to solubilize GCZ and their emulsification ability.

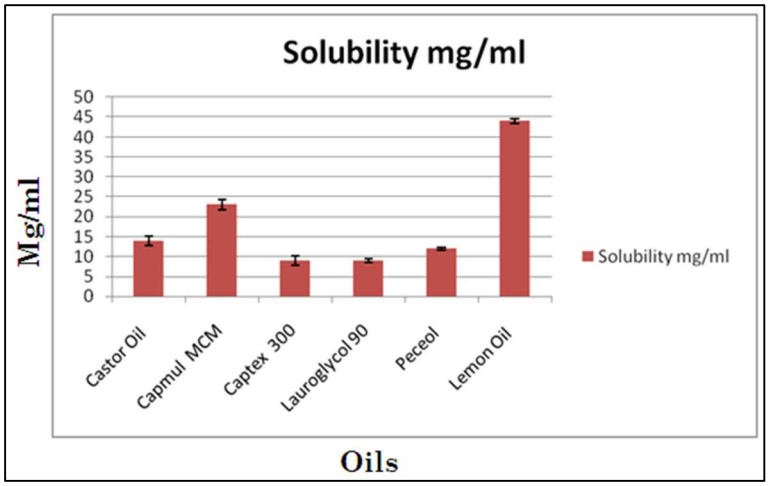

Fig. 1: Solubility of GCZ in various oils

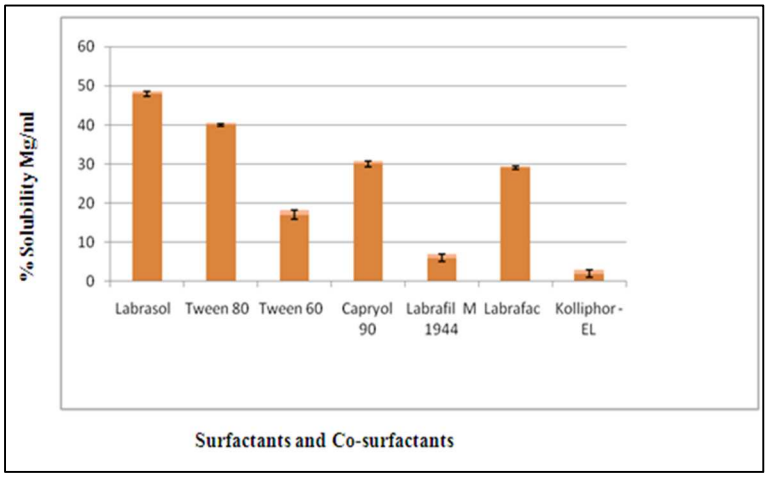

Fig. 2: Solubility of GCZ in various surfactants and co-surfactants

Preliminary screening of surfactant and co-surfactant

Nonionic surfactants are generally considered safer than the ionic surfactants and are usually accepted for oral ingestion. They are also reported to provide better stability to emulsion over a wide range of pH and ionic strength [19]. Thus, various nonionic surfactants were screened to evaluate their ability to emulsify the selected oil phase. For oil-surfactant mixture to be used in SEDDS formulations, it was essential to determine whether it could disperse efficiently to form spontaneous nanoemulsion. Tween 80,

tween 60, labrasol, and capryol 90, labra fac, labrafil M 1944, kolliphor EL were selected for the emulsification study as they showed good solubility potential for GCZ. The % transmittance values of the various dispersions are quoted in table 1. It was observed that the emulsifying ability of tween 80 was highest (98.2±0.29 %) among the surfactants screened as judged by the % transmittance values. labrasol showed highest (96.3±0.56 %) emulsifying ability among co-surfactants.

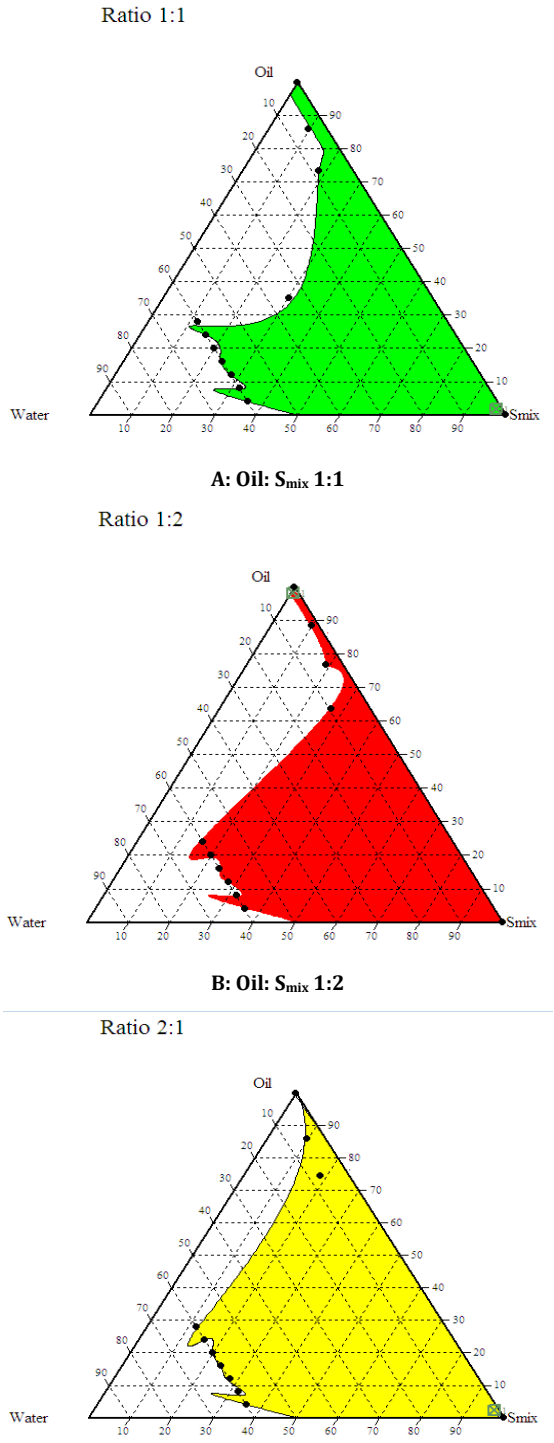

Fig. 3: Pseudo-ternary phase diagram of lemon oil: tween 80: labrasol and water with ratio of surfactant and co-surfactant A) oil and S_{mix} ratio 1:1, B) oil and S_{mix} ratio 1:2, C) oil and S_{mix} ratio 2:1

Table 1: Emulsification ability of various surfactants

Surfactants	% transmittance
Tween 80	98.2±0.29
Capryol 90	85.4±0.34
Labrafil M 1944	72.2±2.3

Data expressed as mean±SD (n=3). SD: standard deviation

Table 2: Emulsification ability of various co-surfactants

Co-surfactants	% transmittance
Labrasol	96.3±0.56
Tween 60	56.4±0.48
Kolliphor EL	73±2.3
Labrafac	77±1.5

Data expressed as mean±SD (n=3). SD: standard deviation

Construction of pseudo-ternary phase diagrams

Pseudo ternary phase diagrams were constructed as depicted in fig. 3 to identify the microemulsion regions and to optimize the concentration of selected vehicles. For the development of SEDDS formulations, optimum ratios of excipients concentrations established by means of phase diagram studies provided the area of the monophasic region. It is important to determine this area in order to ensure successful aqueous dilution without breaking the nanoemulsions [20]. In the present study, the phase diagrams were plotted taking three ratios of surfactant/co-surfactant as 1:1. 2:1 and 1:2. It was observed that the area of microemulsion existence was equally good with all the selected ratios of the surfactant/co-surfactant and thus the same ratios were kept for the formulation of SEDDS.

Preparation of liquid SEDDS

The composition of all the formulation with different ratios of oil to the optimized ratio of surfactant and co-surfactant, with the drug, is shown in table no. 3. In all nine different formulations were prepared.

Evaluation of SEDDS

Visual assessment of self-emulsification

In the study, it was observed that most of the formulations formed microemulsions in less than 2 min and were identified as grade A emulsion. All the formulations except A2 and B2 have shown a spontaneity of emulsification and good stability without any sign of drug or excipients precipitation. Formulation A2 and B3 were not stable and precipitation was seen. Results are shown in table no. 4.

% transmittance

It was revealed from the data that the % transmittance of all the formulations containing 40% of the oil phases were greater than 80% indicating a good clarity of the microemulsions being formed which was confirmed by the resultant average droplet size of the formulations.

Cloud point measurement

The cloud point is a vital parameter in assessing the stability of the SEDDS formulations. The cloud point is the temperature above which the clarity of the formulation turns to cloudiness. This happens due to phase separation and precipitation of the drug from the microemulsions formed from the SEDDS which in turn will obviously hamper the drug release [21].

Thus, the stability of the formulation will get affected as well as the absorption of the drug depending on the cloud point. To avoid this phenomenon, the cloud point for SEDDS should be above body temperature (37 °C). In the present case, the cloud point temperatures of select formulations determined were in the range of 40-72 °C (table 4). This indicates that the formulated SEDDS will be able to form stable microemulsions in a biological environment without any risk of precipitation of the drug. Higher cloud point also infers stability of the formulation during its shelf life.

Table 3: Preparation of liquid SEDDS

Composition (%w/w)		A1	A2	A3	B1	B2	B3	C1	C2	C3
Gliclazide (mg)		40	40	40	40	40	40	40	40	40
OIL (%)		20	20	20	30	30	30	40	40	40
S_{mix}(%)		80	80	80	70	70	70	60	60	60
Ratio		1:1	1:2	2:1	1:1	1:2	2:1	1:1	1:2	2:1
Amount of oil (mg)		100	100	100	150	150	150	200	200	200
Amount S_{mix} (mg)	Surfactant	200	133.33	266.66	175	116.66	233.33	150	100	200
	Co surfactant	200	266.66	133.33	175	233.33	116.66	150	200	100

In all the formulations drug Gliclazide (40 mg) was kept constant, Total formulations made (w/w) was 500 mg

Table 4: Evaluation of SEDDS

Formulation code	Self-emulsification time (Sec)	% transmittance	Cloud point (˚C)	% Drug content
A1	50±0.9	66±0.11	58±2	96.67±0.381
A2	10±0.1	52±0.13	54±1.52	97.28±0.011
A3	66±0.6	74±0.2	68±3.05	96.62±0.332
B1	62±0.2	78±0.4	72±2.51	98.06±0.170
B2	40±0.3	84±0.13	40±1.52	96.05±1.460
B3	90±0.2	86±0.16	72±2.51	97.05±0.890
C1	45±0.2	82±0.9	72±1.52	92.67±2.270
C2	20±0.4	84±0.17	40±2.51	99.71±2.422
C3	56±0.1	96±0.10	74±1.52	99.78±0.106

Data expressed as mean±SD (n=3)

Drug content

From the above study formulation batch C3 of liquid SEDDS has shown highest i.e.; 99.78±0.106 % drug content.

Emulsion droplet size analysis and poly dispersibility index

The droplet size was the main target of the entire formulation of study, where it was postulated that the smaller the droplet size, the larger the interfacial area, thus the greater the partitioning of the drug across the gastrointestinal lining. The droplet size of the emulsion is a crucial factor in self-emulsification performance because it determines the rate and extent of drug release as well as absorption [22]. The droplet size of the formulation was examined at dilution, i.e. 100 times dilution with water and the results are presentable in the table. In the present study, the droplet size of the formulation of C3 batch was found to be 38.09 nm. The poly dispersity index was found to be as shown in the table. The result would show a clear picture regarding the stability behavior of the emulsion within the gastrointestinal tract where the consistency in the emulsion droplet size was observed.

Table 5: Emulsion droplet size analysis and poly dispersibility index

Formulation code	Droplet size (particle size) nm	PDI
B1	393±1.54	0.0942±0.035
B3	206.01±2.05	0.0025±0.003
C1	275.05±0.01	0.255±0.021
C3	38.09±1.0	0.297±0.064

Data expressed as mean**±**SD (n=3)

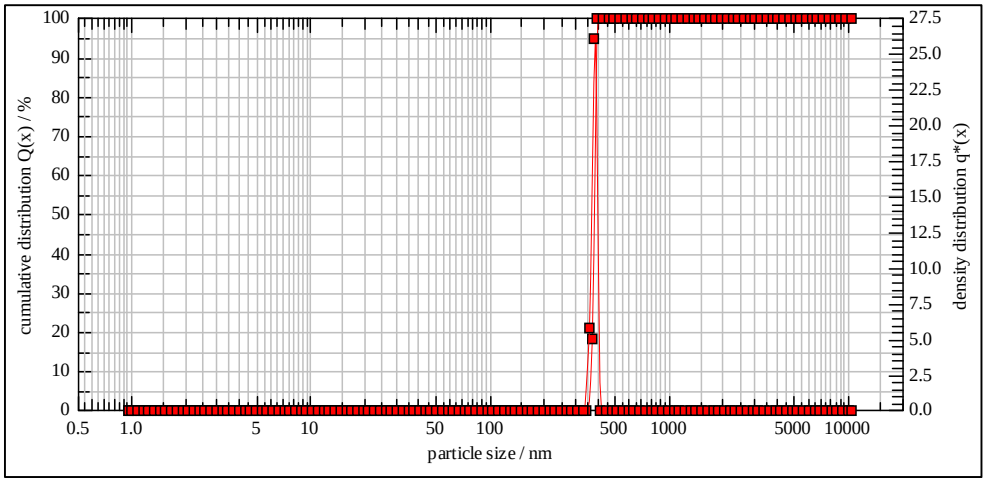

Fig. 4: Graphs of droplet size of formulation C3: 38.09 nm

Optimization of SEDDS

By taking consideration into results of droplet size and poly dispersibility index C3 formulation was chosen for further evaluation.

Evaluations of solid SEDDS

Micromeritics properties of solid SEDDS

Table 6: Micromeretic properties of solid SEDDS

S. No.	Formulation code	Bulk density (g/cc)	Tapped density	Carr's index	Hausner's ratio	Angle of repose
1	C3	0.4043±0.004	0.4624±0.0123	12.56±0.0197	1.14±1.1	26.11˚

Data expressed as mean±SD (n=3) the micromeritic properties of solid-SEDDS prepared with florite R were determined to evaluate the flow properties of the powders (table 6). It was revealed that the bulk and tap densities of powders prepared with fluorite R were found to be 0.4043±0.004 and 0.4624±0.0123, respectively. The solid-SEDDS exhibited good flow characteristics with Carr's index between 11 and 15, Hausner's ratio less than 1.18, and angle of repose (θ)<30. Thus, it can be inferred that the prepared solid-SEDDS with the porous carrier have the ability to be processed into the solid dosage form.

From the results obtained, the C3 batch of solid SEDDS shows good micromeretic properties.

Morphological analysis

The surface morphology of pure GCZ was determined using scanning electron microscope. Pure GCZ appeared under the scanning electron microscope as needle-shaped crystals (fig. 5 A), having smooth surfaces. The SEM of solid SEDDS are shown in (fig. 5 B), The SEM of solid SEDDS showed well-separated particles with no agglomeration (fig. 5 B). The possible reason for this may be the adsorption of liquid SEDDS into the solid carrier florite R.

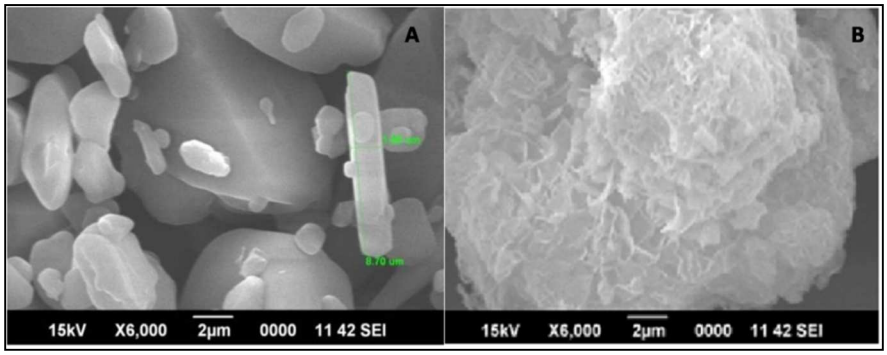

Fig. 5: Scanning electron micrographs of (A) pure drug (B) solid-SEDDS gliclazide and florite R and (C) solid-SEDDS

X ray powder diffraction studies

The x-ray powder diffractograms of GCZ, a physical mixture of GCZ and florite R as well as that of solid SEDDS is shown in fig. 6. The diffraction pattern of GCZ showed characteristics sharp peaks at particular diffraction angle which indicated that the drug was highly crystalline in nature (fig 6A).

All major characteristics peaks of the drug were also observed in the physical mixture shown in fig. 6 B. But this crystalline pattern was not found in the PXRD plot of solid SEDDS which confirmed the molecularly dispersed state of gliclazide in the formulation and effective solubilization of the drug as shown in fig. 6C. This further confirmed that the drug was present in the amorphous form.

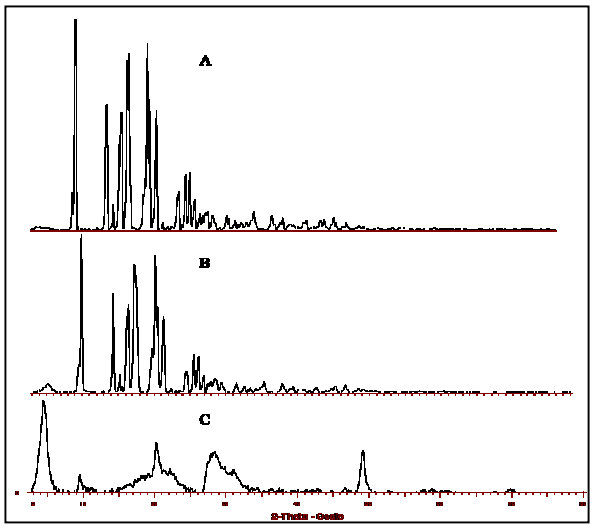

Fig. 6: X-Ray powder diffraction spectra of (A) gliclazide, (B) physical mixture of gliclazide and adsorbent Florite R and (C) solid-SEDDS

Emulsion droplet size determination

Formulation C3 formed a microemulsion in less than 1 min. It has shown spontaneity of emulsification and good stability without any signs of drug and excipients precipitation.

The droplet size of solid SEDDS was found to be 95.76 nm and PDI was found to be 0.298. From this, it is clear that even after conversion of liquid SEDDS into solid one there was no significant alteration in the properties of solid SEDDS. (Fig. 7).

***In vitro* dissolution study**

The effective delivery of a drug from SEDDS is proposed to be governed primarily by small particle size and polarity of the resulting oil droplets, which permits a faster rate of drug release into the aqueous phase. The solubilized drug may not precipitate in the lumen and undergo rapid absorption which is independent of lipid digestion process. *In vitro* dissolution studies were performed to compare the enhancement of solubility of GCZ in SEDDS with respect to marketed product and pure drug.

The solid SEDDS released almost 97.83 % drug within 50 min as compared to marketed formulation i.e.; 53.03% and pure drug 35.05% within 50 min and hence it possessed maximum microemulsion efficiency and maximum release than marketed formulation and pure drug as shown in the fig. 9. The selected formulation C3 indicated considerable enhancement of solubility of GCZ as compared to pure drug.

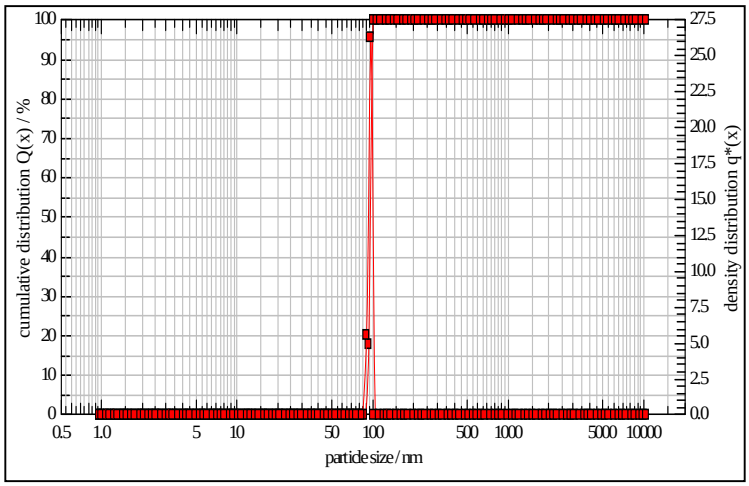

Fig. 7: Emulsion droplet size from solid-SEDDS

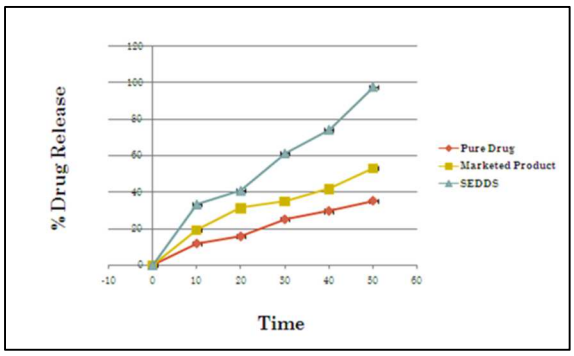

Fig. 9: % Cumulative drug release of solid-SEDDS, pure drug, and marketed preparation in pH 1.2 buffer

CONCLUSION

In the current investigation, SEDDS of GCZ were prepared and evaluated for various parameters. The optimized liquid SEDDS shows desirable percent transmittance, droplet size, PDI, emulsification time and % drug content. Converting the liquid SEDDS to solid dosage has increased stability and ease of handling of SEDDS formulation. The optimized C3 solid SEDDS formulation containing GCZ showed excellent flow properties, drug content, good particle size, polydispersity index (PDI) and cumulative drug release.

Thus, it can be concluded that the problem of efficiently delivering GCZ which is a poorly water soluble drug could be solved by lipid-based drug delivery system that increases its solubility, enhances its bioavailability and hence reduces its dose

Hence, GCZ can be formulated as solid self-emulsifying system which confirmed its potential as an innovative, stable solid dosage form for oral delivery

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CONFLICTS OF INTERESTS

Declared none

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