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Comparative *in vitro* evaluation of glimepiride containing nanosuspension drug delivery system developed by different techniques

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Abstract: The present study was aimed to develop the Glimepiride (GLM) loaded nanosuspension by different methods for increasing the solubility of GLM. Twelve formulations were prepared by combination method (FG), which included antisolvent precipitation method followed by sonication (Method 1) selecting drug and polymer in ratio of 1:10, 1:20 and 1:30. Further 6 formulations were prepared by nanoprecipitation method (Fg) (Method 2) selecting drug and polymer in ratio of 1:10, 1:20 by using different polymers like polyvinyl pyrrolidone (PVP K30), and poly(ethylene glycol) (PEG) such as PEG6000 and PEG400. The GLM nanosuspensions prepared by different techniques were evaluated by optical microscopy, percent entrapment efficiency (%EE), particle size analysis, zeta potential, transmission electron microscopy (TEM) and *in vitro* dissolution. FG1 formulation was found to be better formulation showing 82.04% EE, 129-180 nm particle size range, 30.16 mV zeta potential, 0.253 polydispersity index (PDI) and 86.76% drug release as compared to Fgii formulation having %EE, average particle size, zeta potential, PDI value and drug release as 80.03%, 72-383 nm, -22.19 mV, 0.358 and 74.77%, respectively. On the basis of results obtained from different studies, it can be concluded that GLM nanosuspension prepared by combination technique (FG) shows good solubility and dissolution than those prepared by nanoprecipitation technique (Fg), hence the combination technique is found to be a preferred technique to prepare GLM nanosuspension over nanoprecipitation technique.

Keywords: Diabetes mellitus; Nanosuspension; Antidiabetic; Glimepiride; Polymers; Drug delivery.

1. Introduction

Diabetes mellitus (DM) is chronic, life-long endocrine and metabolic disorder, which occurs due to the defect in insulin secretion and its action [1, 2]. The DM can be classified as type 1 i.e. insulin-dependent, type 2 i.e. non-insulin dependent and gestational diabetes (in pregnant women) [3]. According to International Diabetes Federation (IDF), people with diabetes in India will reach 80 million by the year 2025. One survey has stated that 4% of adults in India are suffering from diabetes in the year 2000 and it is expected to increase up to 6% from the year 2025 [4, 5].

Since 1995 Food and Drug Administration (FDA) approved various anti-diabetic medications for the management of type-2 DM. Several types of oral anti-hyperglycaemic agents are used as monotherapy or combination therapy to treat DM [6]. These include meglitinides, biguanides, sulphonylurea, and α -glucosidase inhibitors [7]. In oral hypoglycemic therapy, the sulphonylureas are class first anti-diabetic drugs generally used in the treatment of type-2 DM. They increase the insulin secretion by acting on β -cells of pancreas [8].

Biopharmaceutics Classification System (BCS) is fundamentally a classification system based on 2 major parameters e.g. solubility and permeability, which determine the fraction of drug dose absorbed and consequently its chances to be bioavailable. On the basis of these parameters, drugs can be categorized into four main classes- (i) BCS Class I (high soluble/high permeable drugs), (ii) BCS Class II (low soluble/high permeable drugs), (iii) BCS Class III (high soluble/low permeable drugs) and (iv) BCS Class IV (low soluble/low permeable drugs) [9, 10]. The BCS is based on the tube model of the intestinal lumen. This model considers constant drug permeability along the intestines, a plug flow fluid with the suspended drug particles moving with the fluid, and dissolution in the small particle limit [11]. The major advances associated with the BCS concern the extensive work on dissolution

of poorly absorbed BCS class II drugs in nutritional liquids and biorelevant media for the accurate prediction of the rate and the extent of oral absorption [12].

Glimepiride (GLM), an anti-diabetic drug of class sulphonylurea belonging to BCS class-II is mostly used for the treatment of type-2 DM [13]. The reported solubility of GLM in aqueous media with pH 7.0 and pH 6.8 is 1.2 $\mu\text{g/mL}$ and 0.87 $\mu\text{g/mL}$, respectively, which shows pH-dependent solubility behavior. Poor solubility, a major problem of GLM results in poor dissolution and bioavailability. Due to limited aqueous solubility of class II drugs, dissolution in gastric media acts as rate-limiting step for absorption [14]. The GLM in tablet form has some problems like poor solubility, incomplete dissolution, and low efficacy [15]. Marketed formulations of GLM provide an immediate release with peak serum concentrations achieved 2-3 h after oral administration, resulting into a fluctuating release profile. Such fluctuations can be minimized by preparing its sustained and prolonged delivery systems, which will be able to maintain steady state drug level in plasma. Such drugs necessitate the preparation of suitable dosage forms which can improve solubility as well as therapeutic efficacy [14,16]. Nanotechnology based promising approaches of nanosuspension formulation not only solve the problem of solubility and bioavailability but also can alter the pharmacokinetics and help in improving the safety and efficacy of the drug [15].

Nanosuspension is the novel approach to overcome the problem of low dissolution rate and compromised oral bioavailability and reduce the delivery issues by maintaining the drug in preferred crystalline state [17]. Nanosuspension signifies sufficient safety and efficacy [18]. Nanosuspension is a biphasic system composed of the finely divided insoluble solid drug of size range 10^{-9} m in a liquid medium which is stabilised by surfactants. Because of reduced size of the drug, there is an increase in solubility. So by the fabrication of nanosuspension, the solubility of a poorly soluble drug can be increased [19,20].

Nanosuspensions offer potential advantages such as reduction of dose as well as cost of therapy, avoiding dose dumping in the body, minimizing fast/fed state plasma level

fluctuation and intersubject variability. These advantages have driven towards faster development of nanosuspension technology during last few decades [21]. Various methods are utilized for the formation of nanosuspension [22-27], including cosolvency [28], solid dispersion [29], inclusion complexation [30], cryogenic technique [31], salt formation [32], solvent-antisolvent method [33,34], supercritical fluid process [35], emulsification-solvent evaporation technique [36] and media milling techniques [37].

The aim of the present work was to compare the *in vitro* profile of GLM containing nanosuspensions prepared by different techniques giving emphasis on the particle size control during the preparation of nanosuspensions. From pre-screening study, two techniques were selected such as combination technique, which includes antisolvent evaporation followed by sonication and nanoprecipitation technique. The characterization and evaluation were done by optical microscopy, drug entrapment efficiency, particle size analysis, zeta potential, *in vitro* dissolution and transmission electron microscopy (TEM).

2. Materials and Methods

2.1 Materials

Glimepiride was kindly provided by Swiss Garnier Life Sciences (Mehatpur, Una, Himachal Pradesh, India) as a gift sample. Acetone, dichloromethane, polyethylene glycol (PEG400, PEG6000), Span 80, Tween 80, polyvinyl pyrrolidone (PVP K30), microcrystalline cellulose and sodium dodecyl sulphate were purchased from Loba Chemie Pvt. Ltd. (Mumbai, India). All other chemicals and reagents were of analytical grade.

2.2. Methods

2.2.1. Screening of method for fabrication of nanosuspension

2.2.1.1. Combination technique (Method 1)

In this method nanosuspension formulation (FG) was prepared by anti-solvent evaporation followed by sonication technique. Briefly, appropriate amount of drug was taken and dissolved in water immiscible anti-solvent. Then, 1 mL of GLM solution was injected in

to deionized water with or without polymers or surfactants at 4 ± 0.5 °C with rapid stirring at 1200 rpm followed by intense sonication [38]. The drug:polymer ratio and formulations for different batches prepared by combination technique were represented in **Table 1A** and **Table 1B**, respectively.

Table 1A Screening the ratio of components for formulation prepared by combination technique

Batch code	Components	Ratio
FG1	Glimepiride: PEG 6000	1:10
FG2	Glimepiride: PEG 6000	1:20
FG3	Glimepiride: PEG 6000	1:30
FG4	Glimepiride: PVP K30	1:10
FG5	Glimepiride: PVP K30	1:20
FG6	Glimepiride: PVP K30	1:30
FG7	Glimepiride: PEG 400	1:10
FG8	Glimepiride: PEG 400	1:20
FG9	Glimepiride: PEG 400	1:30
FG10	Glimepiride:PEG6000:PVPK30	1:05:05
FG11	Glimepiride:PEG6000:PEG400	1:10:10
FG12	Glimepiride:PEG400: PVPK30	1:15:15

Table 1B Formulation details of batches (FG1-FG12) prepared by combination technique

Batch code	Glimepiride (mg)	PEG 6000 (mg)	PEG 400 (mg)	PVP K30 (mg)	Water (mL)	Homogenization speed (rpm)
FG1	1	10	-	-	40	1200
FG2	1	20	-	-	40	1200

FG3	1	30	-	-	40	1200
FG4	1	-	-	10	40	1200
FG5	1	-	-	20	40	1200
FG6	1	-	-	30	40	1200
FG7	1	-	10	-	40	1200
FG8	1	-	20	-	40	1200
FG9	1	-	30	-	40	1200
FG10	1	05	-	05	40	1200
FG11	1	10	10	-	40	1200
FG12	1	-	15	15	40	1200

2.2.1.2. Nanoprecipitation technique (Method 2)

In this method, the drug GLM was dissolved in methanol (organic phase). The polymer PVPK30, PEG6000 and PEG400 were added to 40 mL of distilled water (aqueous phase). The organic phase was drop wise added to the aqueous phase with syringe at room temperature and stirred at 1200 rpm for 1 h on magnetic stirrer [39]. The drug:polymer ratio and formulations for different batches prepared by nanoprecipitation technique (Fg) were represented in **Table 2A** and **Table 2B**, respectively.

Table 2A Screening the ratio of components for formulations prepared by nanoprecipitation technique

Batch code	Components	Ratio
Fgi	Glimepiride: PEG 6000	1:10
Fgii	Glimepiride: PEG 6000	1:20
Fgiii	Glimepiride: PVP K30	1:10
Fgiv	Glimepiride: PVP K30	1:20

Fgv	Glimepiride: PEG 400	1:10
Fgvi	Glimepiride: PEG 400	1:20

Table 2B Formulation details of batches (Fgi-Fgvi) prepared by nanoprecipitation technique

Batch code	Glimepiride (mg)	PEG 6000 (mg)	PEG 400 (mg)	PVP K30 (mg)	Water (mL)	Homogenization speed (rpm)
Fgi	1	10	-	-	40	1200
Fgii	1	20	-	-	40	1200
Fgiii	1	-	-	10	40	1200
Fgiv	1	-	-	20	40	1200
Fgv	1	-	10	-	40	1200
Fgvi	1	-	20	-	40	1200

2.2.2. Determination of drug entrapment efficiency

The entrapment efficiency of GLM loaded nanosuspensions was evaluated indirectly by estimating the untrapped GLM. Briefly, the amount of untrapped drug was first separated from nanosuspension by centrifugation at 20000 rpm for 30 min at 4±0.5 °C using cool ultracentrifuge and was analyzed from supernatant spectrophotometrically (1601 UV–vis spectrophotometer, Shimadzu, Kyoto, Japan) at $\lambda_{\max}$ 228 nm (n=3) [40-42]. The percent entrapment efficiency (%EE) was determined by applying following equation:

$$\% \text{ Entrapment efficiency (\%EE)} = \frac{(\text{Total drug taken} - \text{Drug in supernatant liquid})}{\text{Total drug taken}} \times 100$$

2.2.3. Particle size and zeta potential

The nanosuspensions prepared by combination technique and nanoprecipitation technique were subjected to particle size analysis using Beckman Coulter (RQ-121 D, Beckman Coulter India Pvt. Ltd., Mumbai, India) [43,44].

2.2.4. Transmission electron microscopy

Another technique, transmission electron microscopy (TEM) was employed for the characterization of the developed nanosuspensions after drying a drop of a sample on carbon grid and negatively stained with phosphotungstic acid (1%) by the metal shadowing techniques (Philips CM-10 TEM, Eindhoven, The Netherlands). The microphotographs were captured at different magnifications of 19000-50000 X.

2.2.5. In vitro drug release studies

Drug release profiles of nanosuspensions prepared by different techniques were observed using USP type II dissolution apparatus at a rate of 50 rpm employing phosphate buffer saline (PBS) pH 6.8 as dissolution medium at 37 ± 0.5 °C. A sample (5 mL) was withdrawn at different time intervals ranging from 5-60 min. The same volume was replenished with fresh dissolution medium. The amount of released GLM was analyzed spectrophotometrically (1601 UV-Vis Spectrophotometer, Shimadzu, Kyoto, Japan) at $\lambda_{\max}$ 228 nm (n=3) [45,46].

2.2.6. Statistical analysis

Results were depicted as mean $\pm$ SD from at least three measurements (n=3). A P-value < 0.05 was considered statistically significant.

3. Results and Discussion

3.1. Formulation development trials

Drug-excipient compatibility study was carried out using drug and different excipients mixture in 1:1 ratio by placing the mixtures in glass containers stored at 40 ± 1 °C. Observations were made on predetermined day interval physically for any change in color, appearance, state and lump formation (**Table S1**).

Drug-polymer compatibility study is an important parameter in the development of stable dosage form. Compatibility of GLM with other excipients of nanosuspension was analyzed on 15th day by using Fourier-transform infrared spectroscopy (FTIR, Shimadzu, Model 8400, Japan) with pressed pellet technique using potassium bromide. Samples were scanned in the region of 4000-400 cm⁻¹. The effect of the excipients on the major peaks of GLM was observed to find the compatibility of the drug and excipients. The undisturbed peak of drug signifies compatibility of the drug with the excipients [14] (**Fig. S1**).

3.1.1. Optimization of nanosuspension formulation prepared by combination technique and by nanoprecipitation technique

The design of optimization for combination technique contained two independent variables (X1, X2) and one dependent variable (Y1). The X1 and X2 variables represented drug (% w/w) and polymer (% w/w), respectively, whereas, the Y1 variable was %EE. Accordingly, 12 formulations were formulated and analyzed for EE (**Table 3**). Similarly, the design of optimization for nanoprecipitation technique contained two independent variables (Xi, Xii) and one dependent variable (Yi). The Xi and Xii variables represented drug (% w/w) and polymer (% w/w) respectively, whereas, the Yi variable was %EE. Accordingly, 6 formulations were formulated and analyzed for EE (**Table 4**).

Table 3. Factor combination and responses for combination technique

Batch code	Amount of drug (mg) (X1)	Amount of polymer (mg) (X2)	Homogenization speed (rpm)	Entrapment efficiency (%)
FG1	1 mg Glimepiride	10 mg (PEG6000)	1200	82.04
FG2	1 mg Glimepiride	20 mg (PEG6000)	1200	43.63
FG3	1 mg Glimepiride	30 mg (PEG6000)	1200	32.42
FG4	1 mg Glimepiride	10 mg (PVPK30)	1200	78.44
FG5	1 mg Glimepiride	20 mg (PVPK30)	1200	74.02

FG6	1 mg Glimepiride	30 mg (PVPK30)	1200	61.23
FG7	1 mg Glimepiride	10 mg (PEG400)	1200	55.61
FG8	1 mg Glimepiride	20 mg (PEG400)	1200	33.65
FG9	1 mg Glimepiride	30 mg (PEG400)	1200	46.41
FG10	1 mg Glimepiride	10 mg (PEG6000:PVPK30)	1200	38.42
FG11	1 mg Glimepiride	20 mg (PEG6000:PEG400)	1200	72.42
FG12	1 mg Glimepiride	30 mg (PEG400: PVPK30)	1200	77.24

Table 4. Factor combination and responses for nanoprecipitation technique

Batch code	Amount of drug (mg) (Xi)	Amount of polymer (mg)(Xii)	Homogenization speed (rpm)	Entrapment efficiency (%)
Fgi	1 mg Glimepiride	10 mg PEG 6000	1200	62.82
Fgii	1 mg Glimepiride	20 mg PEG 6000	1200	80.03
Fgiii	1 mg Glimepiride	10 mg PVP K30	1200	49.24
Fgiv	1 mg Glimepiride	20 mg PVP K30	1200	76.01
Fgv	1 mg Glimepiride	10 mg PEG 400	1200	25.26
Fgvi	1 mg Glimepiride	20 mg PEG 400	1200	63.64

For GLM nanosuspension prepared by combination technique, the appropriate processing was found at 1 mg GLM, 10 mg polymer (PEG6000) and homogenization speed 1200 rpm. However, for nanoprecipitation technique the appropriate processing was found at 1 mg GLM, 20 mg polymer (PEG6000) and homogenization speed 1200 rpm. The actual drug

content found in FG1 and Fgii was $82.04 \pm 4.11\%$ and $80.03 \pm 2.35\%$, respectively. The optical photomicrographs of formulation FG1 and Fgii at 450X magnification represented the abundance/aggregates of nanoparticles in formulations (**Fig. S2**).

3.2. Drug entrapment efficiency

The drug entrapment efficiency of formulations prepared by combination technique and nanoprecipitation technique is represented in **Fig. 1** and **Fig. 2**. These figures depicted that among all formulations, FG1 and Fgii showed highest %EE *i.e.* 82.04% and 80.03% prepared by Method 1 and Method 2, respectively.

Fig. 1. Percent drug entrapment of different nanosuspension formulations (FG1-FG12) prepared by Combination technique

Fig. 2. Percent drug entrapment of different nanosuspension formulations (Fgi-Fgvi) prepared by Nanoprecipitation technique

It is visible in **Table 3** (Combination technique) that on keeping amount of drug and homogenization speed constant and by selecting minimum amount (10 mg) of polymers PEG6000, PVPK30 and PEG400, the highest %EE *i.e.* 82.04%, 78.44% and 55.61%, respectively was observed. As the amount of these polymers were increased to 20 mg and 30 mg then decrease in %EE was observed. However, in case of combination of polymers (PEG400:PVPK30), the highest %EE (77.24%) was observed on 30 mg of polymers and on decreasing the amount of combination of different polymers, lower %EE was seen. Under Nanoprecipitation technique (**Table 4**), by selecting 20 mg of polymers PEG6000, PVPK30 and PEG400, the highest %EE *i.e.* 80.03%, 76.01% and 63.64%, respectively was obtained. The increased drug entrapment efficiency was due to formation of polymeric matrix [22].

3.2. Analysis of particle size and polydispersity index

The effects of formulation variables like drug/polymer ratios on the physical characteristics of the prepared nanosuspensions and the *in vitro* drug release characteristics

were studied. Nanosuspensions were analyzed for particle size and polydispersity index (PDI). The differences in the particle size of nanosuspension formulations prepared with variable ratios of polymer and drug were utilized to find out the optimized formulation. The particle sizes for FG1 nanosuspension were falling in the range of 129-180 nm with PDI of 0.253 while particle size for Fgii nanosuspension was found to be 72-383 nm with PDI 0.358 (Fig. 3A and B).

Fig. 3. Size distribution of optimized nanosuspension (A) Formulation FG1 and (B) Formulation Fgii

In general, drug delivery systems with PDI value higher than 0.5 shows large size distributions and have the tendency to aggregate. Closer the value of PDI to zero, more will be the homogeneous nanosuspension formed [47]. The results projected the FG1 formulation prepared by combination technique as optimized formulation having average particle size 180 nm and PDI 0.253. The values of particle size and PDI revealed that the optimized nanosuspension formulation was found to be homogeneous with uniform distribution.

3.3. Determination of zeta potential

It is well known that particle size and zeta potential are significant characteristics, which suggest the physiochemical behaviors of the formulation, involving dissolution velocity, saturation solubility and physical stability. Zeta potential indicates the stability of the nanoparticles to be stably dispersed in suspension [48,49].

Zeta potential was determined by measuring the electrophoretic mobility of particles in the electrical field using same instrument. The value of zeta potential is a judgment of the electrical charge at the surface of particles that ensures the physical stability of fabricated nanosuspensions [16]. A minimum zeta potential of ± 30 mv is required where as in case of combined electrostatic or for steric stabilizer, a zeta potential of ± 20 mv would be sufficient [14,50]. At 25 °C zeta value for formulation FG1 and Fgii was found to be 30.16 mV and -22.19 mV, respectively. So it concludes that FG1 formulation having more stability as compared to Fgii formulation. The high value of zeta potential (more than ± 30 mV) shows electrostatic repulsion between particles. Electrostatic repulsion causes the particles to repel each other and avoids aggregation, which shows good stability. Zeta potentials of formulations FG1 and Fgii were shown in **Fig. 4A** and **4B**, respectively.

Fig. 4. Zeta potential of optimized nanosuspension (A) Formulation FG1 and (B) Formulation Fgii

3.4. Transmission electron microscopy

The TEM photomicrographs of GLM nanosuspensions (FG1 and Fgii) are shown in **Fig. 5A and B**. The size of nanoparticles was found to be within the range of 20-100 nm.

Fig. 5. TEM images of optimized nanosuspension (A) Formulation FG1 and (B) Formulation Fgii

3.5. *In vitro* drug release studies

The dissolution profiles of formulations FG1 and Fgii were observed. The comparative *in vitro* drug release profile of formulations FG1 and Fgii was shown in **Fig. 6**.

Fig. 6. Comparative drug release from nanosuspension formulation FG1 and formulation Fgii

In 30 min more than 60% drug release was observed from FG1 formulation. The release was, however, sustained thereafter for the whole period of the study. The enhanced burst release can be attributed to leaching of drug from the polymer and increase in free drug content during. Another probable reason for enhanced burst release may be the erosion of nanoparticles [14,51]. The *in vitro* dissolution data revealed that formulation FG1 exhibited better drug release (86.76%) as compared to that of formulation Fgii (74.77%) after 60 min in PBS pH 6.8.

4. Conclusion

Glimepiride was selected as a model drug for treatment of diabetes. Two techniques such as combination technique, which included antisolvent evaporation followed by sonication and nanoprecipitation were selected for the preparation of nanosuspension by prescreening study. From literature review, the drug-polymer ratio was selected to use in preparation of nanosuspension formulations by both of the techniques. In combination technique 12 formulations and in nanoprecipitation method 6 formulations were prepared by varying the ratio of polymers like PEG6000, PEG400 and PVPK30 in 1:10, 1:20 and 1:30.

The optimized GLM containing nanosuspension formulations FG1 (combination technique) and Fgii (nanoprecipitation technique) demonstrated highest %EE *i.e.* 82.04% and 80.03%, respectively. The average particle size, zeta potential and PDI values for formulations FG1 and Fgii were found in the range of 129-180 nm, 30.16 mV and 0.253, and 72-383 nm, -22.19 mV and 0.358, respectively. On the basis of these data, FG1 and Fgii formulations were selected for *in vitro* dissolution study.

The *in vitro* dissolution study revealed that FG1 formulation showed greater drug release *i.e.* 86.76% in comparison to Fgii formulation (74.77%) after 60 min in PBS pH 6.8. The formulation FG1 was studied for morphology by TEM, which ensured the formation of round nanoparticles.

From the different studies carried out on nanosuspensions FG1 and Fgii prepared by two different techniques, it can be concluded that the formulation FG1 prepared by combination technique showed good solubility, dissolution and drug release as compared to formulation Fgii, prepared by nanoprecipitation technique. So, the present study concludes that the combination technique is found to be better technique to fabricate GLM nanosuspension as compared to nanoprecipitation technique.

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Research involving human participation and/or animals: None

Informed consent: None

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Highlights

- Sulphonylureas are class first oral hypoglycemic drugs.
- Glimepiride of BCS class-II is mostly used in treatment of type-2 diabetes mellitus
- Nanosuspensions improve the solubility of the drugs.
- Comparison of glimepiride nanosuspensions prepared by different techniques.

Supporting Information

Table S1 Compatibility studies of drug-excipient in 1:1 ratio at different time intervals

Features	1 st Day	2 nd Day	3 rd Day	10 th Day	15 th Day
Glimepiride:PEG6000					
Color	White	√	√	√	√
Appearance	Crystalline	√	√	√	√
State	Solid	√	√	√	√
Lumps	Not present	√	√	√	√
Glimepiride:PVPK30					
Color	White	√	√	√	√
Appearance	Crystalline	√	√	√	√
State	Solid	√	√	√	√
Lumps	Not present	√	√	√	√
Glimepiride:SLS					
Color	White	√	√	√	√
Appearance	Crystalline	√	√	√	√
State	Solid	√	√	√	√
Lumps	Not present	√	√	√	√
Glimepiride:PEG6000:PVPK30					
Color	White	√	√	√	√
Appearance	Crystalline	√	√	√	√
State	Solid	√	√	√	√
Lumps	Not present	√	√	√	√
Glimepiride:PEG6000:SLS					

Color	White	√	√	√	√
Appearance	Crystalline	√	√	√	√
State	Solid	√	√	√	√
Lumps	Not present	√	√	√	√
Glimepiride:PVPK30:SLS					
Color	White	√	√	√	√
Appearance	Crystalline	√	√	√	√
State	Solid	√	√	√	√
Lumps	Not present	√	√	√	√
Glimepiride:SLS:PVPK30:PEG6000					
Color	White	√	√	√	√
Appearance	Crystalline	√	√	√	√
State	Solid	√	√	√	√
Lumps	Not present	√	√	√	√

Where √ represents No change from initial observation

Drug-polymer compatibility study

Fourier transform infrared (FTIR) spectrum of pure glimepiride exhibited characteristic sharp peaks at 3369 cm^{-1} and 3288 cm^{-1} of N-H stretching, 1707 cm^{-1} and 1674 cm^{-1} of carbonyl group, 1345 cm^{-1} of C-N stretching vibration, and 1153 cm^{-1} of S=O stretching vibration.

Fig. S1 FTIR spectrum of glimepiride

Fig. S2. Optical photomicrographs of nanosuspension (A) Formulation FG1 and (B) Formulation Fgii at 450X magnification

Credit author statement

Sujit Bose: Conceptualization, Writing - original draft; Pooja Sharma: Data curation; Vijay Mishra: Formal analysis, Writing - review & editing, Supervision; Swati Patial: Methodology; Gaurav K. Saraogi: Writing - review & editing; Murtaza M. Tambuwala: Writing - review & editing; Kamal Dua: Writing - review & editing

Declaration of interests

✓ ☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: