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Formulation And Evaluation of Glimepiride Nanosuspension by Various Methods

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A B S T R A C T :

The main purpose of glimepiride is to treat type-2 diabetes. It belongs to the family of sulphonylureas. Glimepiride belongs to Class-I of the Biopharmaceutics Classification System (BCS) because of its poor solubility and high permeability. Gill, B., et al. (2010). One major problem that leads to glimepiride's poor bioavailability and dissolution is its solubility. Glimepiride tablets have several problems, such as inadequate solubility, insufficient dissolving, and limited efficacy. Glimepiride was selected to serve as the model drug. To characterise glimepiride, FTIR and melting point measurements were employed. By examining the partition coefficients and solubility, the type of the medication was determined.

Analytical method validation for glimepiride in methanol was carried out in order to provide a simple, reproducible analytical procedure for glimepiride determination utilising a UV spectrophotometer. The formulation known as nanosuspension is an interesting way to address these problems. The nanosuspension formulation method can alter the drug's pharmacokinetics and improve its safety and efficacy in addition to resolving the problems of solubility and bioavailability. Furthermore, it increases glimepiride's pharmacological action when given parenterally.

Glimepiride is only given orally in tablet form; however, it can be given both orally and parenterally in nanosuspension dose form.

Keywords: Nanosuspension, Glimepiride, Diabetes, BCS class I medicine,

1. Introduction

A chronic, lifelong endocrine and metabolic condition, diabetes mellitus (DM) is brought on by a malfunction in the production and action of insulin. A specialised cell called β-cells found on the pancreatic organ produces the hormone insulin. Our bodies normally break down sugars and carbs to produce glucose molecules, which serve as fuel for our bodies. However, insulin is necessary for the hormones to use glucose. A lack of insulin causes the body's blood glucose levels to rise and interferes with the metabolism of proteins, lipids, and carbs. Serious diabetic consequences, such as retinopathy, neuropathy, and other cardiovascular issues, develop if diabetes is not managed. By 2010, diabetes was the most prevalent illness, affecting over 200 million individuals.

Type -1
It is diabeties is insulin dependend diabeties.

Type II
In this kind, the pancreas ordinarily generates some insulin, but either not enough or insulin-resistant body cells are created. Obese patients are more likely to have this kind of diabetes.

2. Material and Methods

Apparatus and chemicals: Glimipride by Cilpa Indore., Acetone by Dr. Reddy's Laboratories, Hyderabad, PEG400, Span 80, Isopropyl Alcohol by Ranchem Ltd.., India, Mineral oil by Loba Chemie, Mumbai.

Methods: Preparation of Nanoemulsion.
Formulations of nanosuspensions made by sonication and antisolvent precipitation respectively. Glimepiride was accurately weighed, and then 1

millilitre of the solution was added to deionised water at 4 degrees Celsius while being vigorously sonicated and continuously stirred at 1200 rpm. Some of the solvents that were assessed included methanol, ethanol, isopropyl alcohol, and di-chloromethane. They selected polymers and surfactants from PVP K30, PEG 400, and PEG 6000. Processing parameters were assessed to determine their capacity to create nanosuspension.

3. Experimental work

3.1 Preformulation Studies

The study of a medical ingredient's physical and chemical properties, both alone and in conjunction with excipients, is known as preformulation. Preformulation studies aim to identify the physicochemical properties and excipients that may affect the manufacturing process, formulation design, and pharmacokinetic-biopharmaceutical aspects of the final product.

3.2 Determination of Solubility

Solubility was tested in various media including ethanol, methanol, absolute ethanol, acetone, chloroform, ether, water, 10% v/v HCl and 10% w/v sodium hydroxide.

3.3 UV and FTIR Spectroscopy

Glimepiride was scanned in the 200–400 nm range, as indicated in Fig.6.3, and its λ max in methanol was found to be 228.50 nm.Result and discussion The reference standard FT-IR spectra of piperine and the acquired FT-IR spectrum of piperine were compared.

4. Result and discussion

4.1 Preformulation Study

4.1.1 Description

Glimipride is white crystalline solid

4.1.2 Result of Solubility

Glimepiride's solubility was assessed in methanol, 0.1 N Hcl, DCM (di-chloromethane), pH 7.8 phosphate buffer, and 6.8 phosphate buffer. A 50 ml conical flask was filled with an excess of the medication, and it was shaken for 72 hours (using a rotating shaker). The prepared solution's absorbance was then estimated using the amount of medication that was dissolved, as indicated in the table..

4.2 Result of Melting Point

The medicine's melting point was determined to be comparable to the stated value, confirming that the drug samples that were received met the stated specifications. The melting point of a particular pharmacological ingredient will vary depending on any impurities that may be present. Glimipride has a reported melting point of 207°C. When the capillary technique was used to determine the medication's melting point, the substance began to melt at 203°C and melted fully at 205°C.

4.3 UV Spectroscopy

Glimepiride was scanned in the 200–400 nm range, as indicated in Fig.6.3, and its λ max in methanol was found to be 228.50 nm.

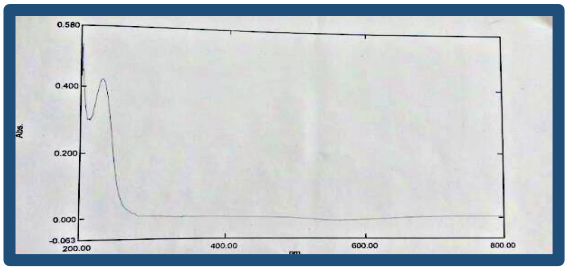

Fig 2. Lambda max determination of Glimipride

4.3.1 FT-IR Spectroscopy

The existence of several functional groups was ascertained by recording the sample's infrared spectra. A distinctive strong peak was seen in the pure glimipride shows reading of FTIR at 3369 cm-1

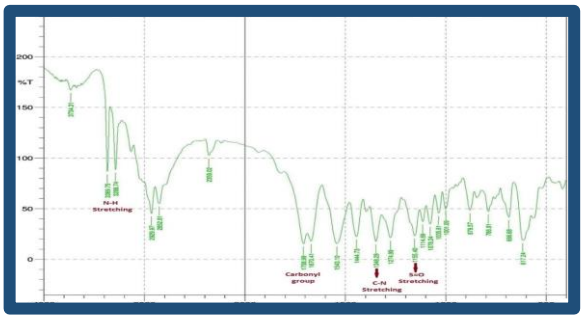

Fig 3. FT-IR of Glimipride

4.4 Optimization of nanosuspension formulation prepared by nanoprecipitation technique

Two independent variables (X i and X ii) and one dependent variable (Y i) were included in the optimisation design. The Yi variable was percentage entrapment efficiency, while the X variables were drug (% w/w) and polymer (% w/w), respectively. Six formulations were proposed based on the literature, and each one was created and examined for entrapment efficiency, as indicated in below table .

Table 1 Factor combination and responses for nanoprecipitation technique technique

Run no.	drug (mg) (Xi)	Amount of polymer	Homogenization speed (rpm)	efficiency (%)
G_i	Glimepiride 1mg	10mg PEG 6000	1000-1200	62.82
G_{ii}	Glimepiride 1mg	20mg PEG 6000	1000-1200	80.03
G_{iii}	Glimepiride 1mg	10mg PVP K30	1000-1200	49.24
G_{iv}	Glimepiride 1mg	20mg PVP K30	1000-1200	76.01
G_v	Glimepiride 1mg	10mg PEG 400	1000-1200	25.26
G_{vi}	Glimepiride 1mg	20mg PEG 400	1000-1200	63.64

4.5. Evaluation of nanosuspension

4.5.1 Optical microscopy

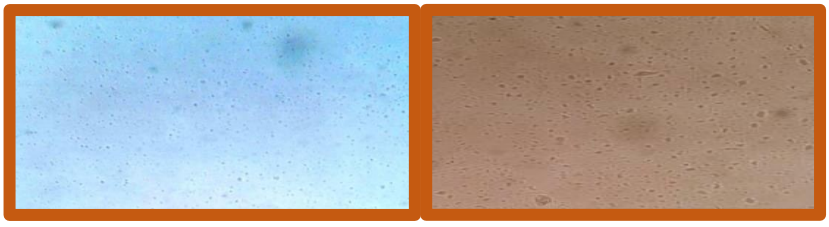

Fig. 2 Optical photomicrographs of some representative nanosuspension formulations

4.5.2 Particle size analysis

In the following table the values of polydispersity index and particle size of the nanosuspension helps in identify best formulation. With different sizes of nanosuspension formulation with various polymer and drug ratio used. The range of particle size seen between 129 to 180 nm and PI was 0.253 for first formulation G1 nanosuspension. The second formulation of nanosuspension G2 shows particle size in the range of 72 and 383nm and PI was 0.358 for another nanosuspension G2.

Table 2 Results of particle size analysis

Cumulants Results		
Parameters	**G1**	**Gii**
Diameter (d)	180.01 nm	383nm

Polydispersity Index (PI)	0.253	0.358
Diffusion Const. (D)	1.014e-008 cm^2/sec	1.222e-008 cm^2/sec
Measurement Condition		
Temperature	25.1 ^0C	25.0^0C
Diluent Name	Water	Water
Refractive Index	1.3328	1.3328
Viscosity	0.8878 (cP)	0.8878 (cP)
Scattering Intensity	6928 (cps)	3244(cps)

4.5.3 Zeta potential

With the help of Zeta potential we can know the stability of the nanosuspension. For the normal value needed is 20mv for a combined effect of electrostatic stabiliser. With a higher zeta value on the positive side at 24.9˚, the G1 formulation's value was found to be 30.16 mV,

4.5.4 In-vitro release of study

Utilising a USP type II dissolving device, the glimipride nanosuspensions formulations G1 and G2 at the rate of rpm 50 with buffer 6.8. the dissolution medium. A constant temperature of 37 ± 0.5^o C was maintained. Samples were taken out on a regular basis, and new dissolving media was added in the same volume. The necessary dilutions were prepared, and a UV-visible spectrophotometer was used to examine the samples at 214 nm. (Yadav and others, 2012)

Table 3 In vitro drug release

Drug release in percentage		
G1and G2 time	G1	G2
5	6.66	3.52
10	18.99	13.22
20	37.6	22.64
30	62.56	47.99
40	76.80	61.88
50	84.1	70.11
60	86.72	73.56

4.5.5 Transmission electron microscopy (TEM)

The sample were placed and analyse by using TEM microscome.120 kV accelerating voltage and a magnification of between 19,000 and 50,000 times. It was discovered that the diameter fell between 20 and 100 nm.

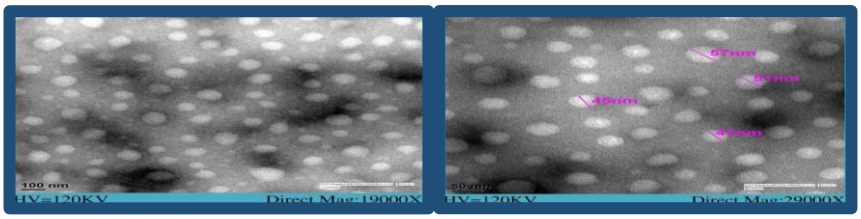

Fig.3 .Transmission electron microscopy images of (G1) glimepiride nanosuspension with magnification of 19000X and 29000X

Conclusion

Particle size and zeta potential were investigated, and the results showed that the G1 formulation had an average particle size of 129 – 180 nm, a zeta potential of 30.16 mV, and a PI of 0.253. The zeta and PI values for the G ii formulation were -22.19 mV and 0.358, respectively, and the particle size range was 72 – 383 nm. Following that, the formulations G1 and G ii were selected for the in-vitro dissolution analysis. The in-vitro dissolving investigation's findings indicate that the G1 formulation has a greater rate of drug release (87%). than the G ii formulation, which, after 60 minutes in a pH 6.8 phosphate buffer, exhibits a rate of 74.77%. The TEM analysis of the G1 formulation's shape based on the in-vitro dissolving data guaranteed the development of round nanoparticles in the nanosuspension.

Glimepiride was chosen as the model medication. FTIR and melting point measurements were used to characterise glimepiride. The drug's nature was ascertained by analysing the partition coefficients and solubility. In order to develop a straightforward, repeatable analytical technique for glimepiride estimation using a UV spectrophotometer, analytical method validation for glimepiride in methanol was conducted. Two methods were chosen from the prescreening study: the combinatiossn method, which involves evaporating an antisolvent and then sonicating it, and the nanoprecipitation method, which creates a nanosuspension. The ratio of medication to polymers was chosen from the literature study to be used in the creation of nanosuspension formulations using both methods.

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