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Formulation Development and Evaluation of Self Emulsifying Drug Delivery System of Poorly Soluble Drugs

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ABSTRACT

Gliclazide has an oral bioavailability of 40-60% and is marketed as a medication in the Class II category of the Biopharmaceutical categorisation system (BCS). An important component of its efficacy is its small absorption window, which is confined to the gastrointestinal system. From the stomach, food is propelled down the GI tract and into the small and large intestines, where it is absorbed and expelled along with water. The study aims to develop a self-emulsifying drug delivery system (SEDDS) for Gliclazide to improve oral bioavailability and membrane permeability. The goal is to achieve immediate drug release with increased solubility and bioavailability, as Gliclazide has poor solubility and low oral bioavailability. The resulting tablets were evaluated for different quality-control parameters at pre- and postcompression levels. Gliclazide showed better solubility in a mixture of oils and Tween 60 (10:1). All the developed formulations showed lower self-emulsification time (<200 seconds) and higher cloud point (>60°C). They were free of physical defects and had drug content within the acceptable range (98.5%–101%). The crushing strength of all formulations was in the range of 58–96 N, and the results of the friability test were within the range of USP (≤1). Disintegration time was within the official limits (NMT 15 min), and complete drug release was achieved within 30 min.

Keywords: Gliclazide; self-emulsifying drug delivery system (SEDDS); oral bioavailability; Biopharmaceutical Categorization System.

I. INTRODUCTION

Gliclazide is a drug that attaches to the sulfonyl urea receptor (SUR1) on β cells, blocking ATP-sensitive potassium channels and causing a drop in potassium efflux. This leads to β cells depolarizing, activating voltage-dependent calcium channels, activating calmodulin, and triggering insulin exocytosis (1, 2). Gliclazide is absorbed orally in comparable amounts by both patients and healthy volunteers, but there is intersubject heterogeneity in peak plasma concentrations (tmax) and age-related variations. The drug's strong protein binding affinity results in a modest volume of distribution in both patients and healthy individuals. The elimination half-life (t1/2) in healthy individuals is between 8.1 and 20.5 hours, resulting in low bioavailability of conventional dosage forms. Solubilizing agents like PEG 400 can increase the bioavailability of gliclazide in oral dosage forms (3, 4). The recommended starting dosage is 40 mg per day, with the option to increase to 320 mg if needed. A divided dose should be taken in the morning and evening for dosages over 160 mg. Gliclazide should not be used for patients with a history of recurrent ketoacidosis or coma, severe renal or hepatic impairment, compromised liver or kidney function, or those sensitive to sulphonylurea medications (5). The study aims to develop a self-emulsifying drug delivery system (SEDDS) for Gliclazide to improve oral bioavailability and membrane permeability. The goal is to achieve immediate drug release with increased solubility and bioavailability, as Gliclazide has poor solubility and low oral bioavailability. Quality by design is used to select excipients for a more scientific method, resulting in a robust product.

II. MATERIALS AND METHODS

2.1 Preformulation Studies

The drug samples were examined for appearance, color, and odor. The melting point of drug was determined using the capillary method, where a fine powder of the drug was filled in a glass capillary tube and dipped in liquid paraffin. Solubility was also determined in various buffers of different pH values, with the drug being dissolved in different beakers containing solvents and shaken for 24 hours at regular intervals (6-10).

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2.3 Pre-compression evaluation of powdered blend

Key parameters evaluated during pre-compression include bulk density, tapped density, Hausner's ratio, and Carr's index, which provide insights into the flow properties and compressibility of the powder blend. Moisture content and particle size distribution also play a significant role in determining the stability and release profile of omeprazole within floating matrices (11, 12).

2.4 Formulation of Self Emulsifying Tablets containing Gliclazide

2.4.1 Selection of Oil Phase

The criterion for selection of the oil phase was drug solubility. Drug solubility in oil was determined by the standard flask-shake method. Oil was taken in a flask (capacity 50 mL) and excess drug mixed by water bath sonication for 10 min. The flask was continuously shaken for 8 h by a mechanical flask shaker at ambient temperature (26°±3°C). Following shaking, the drug solution was kept undisturbed for 1 h to reach equilibrium, filtered, and then Gliclazide content was determined. The solubility of Gliclazide was checked in castor and olive oils, alone and in combination with different concentrations of Tween 60 (13).

2.4.2 Preparation of Liquid SEDDS

Several SEDDS formulations were developed using different ratios of the selected oils, keeping the ratio of drug to surfactant constant (Table 1). The surfactant was mixed with the oil by gentle heating in a water bath. A weighed quantity of drug was added to this mixture and subsequently mixed with the help of a high-speed homogenizer for 15 min (14).

Table 1: Preparation of Liquid SEDDS

Formulation	Drug	Castor oil	Tween 60	Total Quantity
F1	80	10	2.0	92
F2	80	10	2.5	92.5
F3	80	10	3.0	93
F4	80	10	3.5	93.5
F5	80	10	4.0	94

2.4.3 Preparation of Solid SEDDS

The liquid SEDDS preparations were converted to S-SEDDSs by adsorption on microcrystalline cellulose. Microcrystalline cellulose was taken in a benchtop cone mixer (Morgan Instruments, Lahore, Pakistan) and liquid SEDDS formulations added in portions with proper mixing. Colloidal silicon dioxide (1% w/w) was added to enhance adsorption and get a free-flowing powder (Table 2) (15).

Table 2: Preparation of Solid SEDDS

Formulation	Liquid SEDDS	Microcrystalline cellulose	Colloidal silicon dioxide (1% w/w)	Total Quantity
F1	92	10	2.5	104.5
F2	92.5	10	2.5	105
F3	93	10	2.5	105.5
F4	93.5	10	2.5	106
F5	94	10	2.5	106.5

2.4.3 Preparation of Tablets Containing Self-Emulsifying Formulations

S-SEDDS preparations were blended with other excipients (Table 3) for 30 min in a laboratory scale double-cone mixer at 25 rpm. The compression weight of the tablets was set at 350 mg/tablet, and at least 300 tablets were compressed from each formulation (16).

Table 3: Preparation of Tablets Containing Self-Emulsifying Formulations

Formulation	F1	F2	F3	F4	F5
Solid SEDDS	104.5	105	105.5	106	106.5
Crospovidone	3.5	3.5	3.5	3.5	3.5
Magnesium stearate	1.5	1.5	1.5	1.5	1.5
Talc	1.5	1.5	1.5	1.5	1.5
Tablettose 80	9	8.5	8	7.5	7
Total Weight (mg)	120	120	120	120	120

2.5 Postcompression Evaluation of Tablet Formulation

The study focuses on factors such as hardness, friability, disintegration time, and drug release kinetics. Understanding these characteristics is crucial for optimizing tablet performance and ensuring effective therapeutic outcomes. Factors like particle size distribution and moisture content also impact these evaluations. Comprehensive postcompression evaluations are essential for developing effective floating tablets that meet pharmacological standards (17-19).

III. RESULTS AND DISCUSSION

3.1 Preformulation Studies

Preformulation is a crucial process in determining the physical and chemical properties of a drug, which are crucial for its stability and effectiveness in dosage form formulation. A systematic preformulation study was conducted using the standard procedures of Indian Pharmacopoeia and British Pharmacopoeia, involving drug identification, melting point analysis, and compatibility studies with selected polymers. The melting point range of a solid substance can be found by measuring its temperature, and its identity can be verified by comparing the resultant value with known values. Gliclazide is a crystalline solid that exhibits a melting point of about 168.95±0.969°C, also The partition coefficient of Gliclazide is found to be 2.10, indicating that gliclazide is moderately lipophilic and has good permeability across membranes; this value suggests a relatively high ability to distribute between an oily phase (octanol) and water. This information is essential for validating formulation design and determining molecular alteration needs (Table 4).

Table 4: Observed organoleptic properties of drug sample

Organoleptic properties	
Parameter	**Observation**
Colour	White to off-white
Texture	Crystalline powder
Taste	Tasteless
Odour	Odourless

3.2 Precompression Evaluation of Powder Blended Characteristics

The ideal drug release kinetics in tablet formulations are affected by parameters like particle size distribution, flow characteristics, mix consistency, and compressibility. A tight particle size distribution guarantees homogeneous mixing and inhibits segregation during compression, leading to a more consistent drug release profile. Suboptimal flow characteristics may result in heterogeneous dispersion of active compounds, leading to inconsistencies in medication release rates (Table 5).

Table 5: Physical properties of powder blends of single unit tablet formulations

Formulation	Angle of repose	Bulked Density	Compressibility index	Hausner's Ratio	Tapped Density
F1	30.6 ± 0.540	0.399 ± 0.545	17.3 ± 0.142	1.03 ± 2.056	0.494 ± 0.541
F2	29.6 ± 0.055	0.399 ± 0.056	16.5 ± 0.256	1.07 ± 0.020	0.498 ± 0.011
F3	29.5 ± 0.452	0.398 ± 0.056	17.7 ± 0.044	1.02 ± 0.856	0.491 ± 0.216
F4	30.5 ± 0.245	0.403 ± 1.556	18.9 ± 0.140	1.04 ± 0.044	0.495 ± 2.123
F5	29.2 ± 0.542	0.401 ± 0.185	20.9 ± 0.141	1.26 ± 0.056	0.499 ± 1.056

3.2.2 Postcompression Evaluation of Tablet Formulation

Postcompression assessment is an essential procedure for assessing the quality and efficacy of tablet formulations. The evaluation encompasses factors such as hardness, friability, disintegration time, and drug release profile to ascertain the tablet's efficacy. Hardness quantifies the mechanical strength of a tablet, whereas friability assesses its propensity to fracture or chip under stress. A low friability score signifies excellent tablet integrity. The disintegration time influences the pace and degree of drug release, hence directly affecting the therapeutic efficacy of a tablet formulation. The drug release profile is the key characteristic in post-compression assessment, since it directly influences the therapeutic effectiveness of a tablet formulation (Table 6).

Table 6: Postcompression Evaluation of Tablet Formulation

Formulations	Drug Content Assay (%)	Disintegration Time (sec)	Hardness (kg/cm^2)	Friability (%)	Thickness (mm)	Weight Variation (mg)
F1	99.45 ± 0.076	42 ± 0.106	5.98 ± 0.056	0.32 ± 0.666	3.015 ± 0.46	120.24 ± 1.254
F2	99.65 ± 0.056	45 ± 0.486	6.15 ± 0.156	0.32 ± 0.106	2.214 ± 0.116	119.23 ± 1.256
F3	99.55 ± 0.996	47 ± 0.886	6.01 ± 0.106	0.33 ± 0.666	2.145 ± 0.416	120.54 ± 1.056
F4	99.55 ± 0.006	44 ± 0.926	5.98 ± 0.046	0.33 ± 0.126	3.152 ± 0.106	120.48 ± 2.551
F5	99.45 ± 0.106	38 ± 0.916	6.01 ± 0.116	0.29 ± 0.116	2.153 ± 0.456	118.69 ± 1.554

IV. CONCLUSIONS

This study aimed at formulating a SEDDS for Gliclazide. Different formulations of Gliclazide were prepared (n=5). Drug solutions were adsorbed in MCC, and the formulations were compressed and tested at pre- and postcompression levels for different quality-control parameters. All the formulations, particularly F5, showed short emulsification time and high cloud point and dissolution rate. In conclusion, using commonly available excipients and machinery, self-emulsified tablets with better dissolution profiles can be prepared by direct compression. Enhanced dissolution rate, along with drug presence in emulsion form, will improve the bioavailability of Gliclazide.

Conflict of Interest
None

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