Uttar Pradesh Journal of Zoology

Volume 44, Issue 22, Page 207-217, 2023; Article no.UPJOZ.2910
ISSN: 0256-971X (P)

Solubility and Bioavailability Enhancement of a Novel Liquisolid Compact of Gliclazide

Bimal Debbarma [a++*], Peter De Roux Sumer [a++], Loushambam Samananda Singh [a++], Kmensiful Binan [a++] and Waibiangki Lyngdoh [a++]

[a] Institute of Pharmacy, Assam Don Bosco University, Tapesia, Assam-782402, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.56557/UPJOZ/2023/v44i223735

Editor(s):
(1) Dr. Takashi Ikeno, Clinical Research Support Office, Japan.
Reviewers:
(1) Burhanuddin Madriwala, M S Ramaiah University of Applied Sciences, India.
(2) Ajeet Kumar, Rama University, India.

Original research Article

Received: 12/08/2023
Accepted: 16/10/2023
Published: 04/11/2023

ABSTRACT

The study investigates the use of liquisolid compacts, a revolutionary pharmaceutical formulation technique, to improve the dissolution rate of weakly water-soluble medicines, with gliclazide as a case study. Nonvolatile solvents such as polyethylene glycol (PEG) 400, tween 80, and propylene glycol were used to make liquidsolid tablets, together with carrier ingredients such as Avicel PH102, starch, or HPMC, and Aerosil 200 as a coating material. The drug-excipient interaction was studied utilizing techniques such as differential scanning calorimetry (DSC) and Fourier transform infrared spectroscopy (FTIR). The produced tablets were tested for appearance, weight fluctuation,

---

[++] *Assistant Professor;*
**Corresponding author: Email: bimald32@gmail.com;*

hardness, friability, drug content, and in-vitro drug release before being compared to traditional tablets (control) to determine the improvement in dissolution rate. The optimum formulation was subjected to stability tests. FTIR and DSC investigations revealed no significant drug-excipient interactions. All pill formulations met the requirements. Liquisolid tablets significantly increased gliclazide dissolving when compared to conventional tablets, which was ascribed to improved wetting qualities and particle effective surface area. According to the study, the liquisolid technique is a potential approach for increasing the dissolving rate of poorly soluble pharmaceuticals. The tablets remained stable at accelerated settings for three months, demonstrating the efficacy and feasibility of the liquisolid approach in increasing gliclazide dissolving rates.

Keywords: Gliclazide; liquisolid compact; carrier material; coating material.

1. INTRODUCTION

The major issue for pharmaceutical scientists over the last three decades has been to improve the dissolving profile, absorption efficiency, and bioavailability of water-insoluble medicines [1]. When it comes to oral administration, drug release from its pharmaceutical form and dissolution into gastrointestinal fluids generally come first, followed by absorption and systemic availability. Because an increasing number of newly developed drug candidates in pre-clinical development stages have poor water solubility characteristics, there is a great need for formulation approaches to overcome this factor [2]. According to Venkateswarlu et al. [3], 40% of all newly produced medications are poorly soluble or insoluble in water. Furthermore, up to 50% of orally taken therapeutic compounds have formulation issues due to low solubility and excessive lipophilicity [4]. Micronization, Lyophilisation, Solid dispersions, use of complexing agents, co solvency, chemical modification, pH adjustment, solubilisation by surfactants, solid solutions, inclusion of liquid drug into soft gelatin capsules, salt formation, liquisolid technique, and other techniques are available to increase the solubility of poorly water soluble drugs [5]. These strategies have been developed to enhance the rate of dissolution, and thereby absorption and bioavailability [6]. However, there are certain practical constraints. Because fine particles tend to form aggregates (or) agglomerates due to increased surface energy and Vander Waals attraction, the desired dissolution and absorption rates may not be attained during the micronization process. Solid dispersions are significant for increasing drug solubility, wettability, dissolution rate, and bioavailability. However, due to their poor physical properties for dosage form manufacturing, only a few items are commercially accessible. Solid dispersions created using the melting process may have stability issues. Salt production generates hygroscopicity, which can lead to stability issues. Precipitation may occur during dilution when co solvents are used [7]. The technique of 'liquisolid compacts' is a fresh and promising complement to such an ambitious goal. The active ingredient in a solid dose form must dissolve before it may be absorbed from the gastrointestinal tract. Water-insoluble medicines' poor dissolving characteristics provide a significant problem to pharmaceutical formulation experts. The dissolution rate in the fluid present at the absorption site controls the absorption rate of a poorly water-soluble drug designed as an orally administered solid dosage form, i.e. the dissolution rate is frequently the rate-determining step in drug absorption. Several studies have demonstrated that the liquisolid technique is the most promising strategy for increasing the dissolution rate of pharmaceuticals that are poorly water-soluble [8]. Liquisolid system is a newly developed technique that involves converting liquid lipophilic drugs or water insoluble solid drugs dissolved in non-volatile solvent into free-flowing, non-adherent, dry-looking, and readily compressible powders using carrier and coating materials. Sustained release of water-soluble medicines is possible [9].

2. MATERIALS AND METHODS

2.1 Drugs and Ingredients

Gliclazide is manufactured by Yarrow ChemProducts Ltd in Mumbai. Sd Fine Chem Ltd. in Mumbai provides Avicel pH 102, Aerosil 200, Kyron-T 314, PEG 400, PG, Starch, HPMC, and Tween 80 [10].

2.2 Methods

2.2.1 Preparation of vonventional tablet

Gliclazide conventional tablets were made by combining the medicine for 10 minutes with

microcrystalline cellulose and the other component. For 10 minutes, the mixture was combined with 5% disintegration agent (Cross povidone). A rotary tableting machine (Shakti, India) was used to crush the mixture on a 6-mm punch and die. To create tablets with the hardness, a sufficient compression load was used. Each direct compression tablet (DCT) contains 40 mg gliclazide [11].

2.3 Preparation of Liquisolid Tablets

The liquisolid compacts in this investigation were created using the approach described by "Spireas et al." To make the medication solution, gliclazide was dissolved in a nonvolatile solvent (PEG-400 or propylene glycol ortween-80). Avicel PH102 or Starch or HPMC or PEG 4000 or PEG 6000 as the carrier powder and Aerosil 200 as the coating material were added to the liquid medication and blended in a porcelain mortar to avoid excessive trituration and particle size reduction [12]. The mixing was done in three steps. The substance was slowly combined in the first stage to ensure consistent distribution of the liquid treatment. In the second stage, the mixture was applied in a uniform coating on the surface of the mortar and allowed to set for a few minutes. In the final stage, 5% disintegration agent (Kyron T 314) was added to the powder and carefully mixed. The finished combination was compacted into a tablet [1].

2.4 Evaluation of Liquisolid Systems

2.4.1 Bulk density

A known amount of sample (3g) was poured into a 10ml graduated cylinder using a funnel. The cylinder was then softly tapped twice to collect all of the powder that had adhered to the cylinder's wall. The volume was then immediately read from the cylinder and utilized to determine the bulk density using the formula shown below. It is measured in grams per milliliter.

Formula : Db = M/V

Where,

M= Mass of powder
Vo = Bulk volume of the powder

2.4.2 Tapped Density

A known amount of sample (3g) was poured into a 10ml graduated cylinder using a funnel. The cylinder was then softly tapped twice to gather all of the powder that had adhered to its walls. To determine the tapped volume, the cylinder was tapped 100 times from a height of 2.5cm on the wooden bench top to acquire the constant volume. The tapped density was then estimated using the procedure below. It is measured in grams per milliliter.

Formula Dt = M/Vt

Where,

M = Mass of powder
Vt = Tapped volume of powder

2.4.3 Car's compressibility index

The bulk and tapped densities were determined according to procedure described above. Car's compressibility index expressed in percentage.

$I=D_b-D_t/D_t x100$

Where,

D_b = Bulk density of powder
D_t = Tapped density of powder

2.4.4 Friability

The produced tablets' friability was assessed using a Roche friabilator (TAR 200 Eureka, Germany), and the % loss in weights was determined and used as a measure of friability.

F = W initial - W final/W initial x 100

2.4.5 Hardness

The Monsanto hardness tester was used to determine the hardness of the tablets. It is measured in kilograms per square centimeter. The hardness of six tablets from each formulation was determined.

2.4.6 Weight variation

Individual weights of 10 liquisolid compact pills were measured using an electronic weighing balance, and the average weight and percentage weight variation were computed.

% Deviation = (Individual weight – Average weight / Average weight) × 100

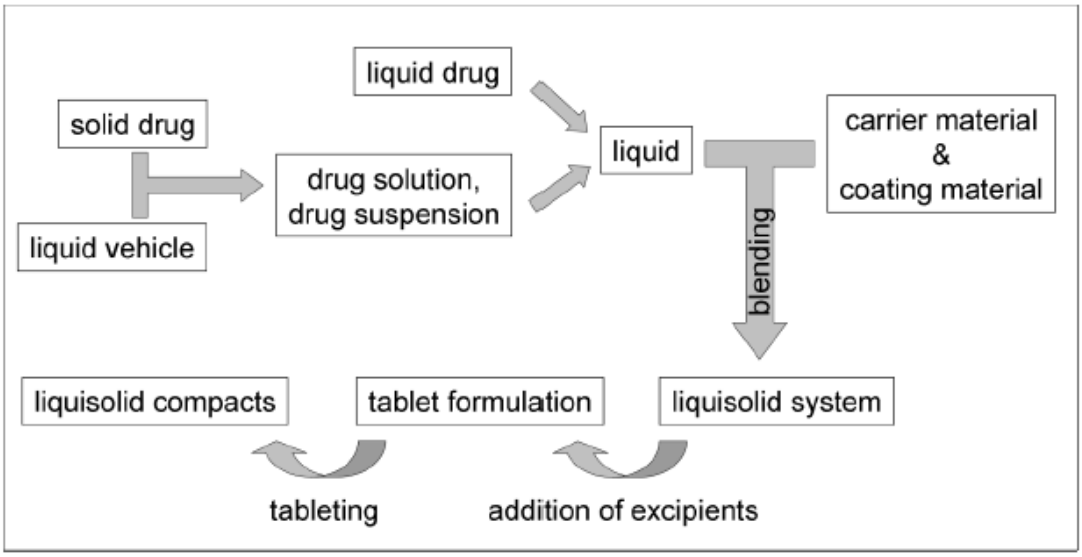

Fig. 1. General method of preparation of liquisolid Systems

2.5 *In-Vitro* Disintegration Time

The disintegration time of the tablets was determined in distilled water (37 2°C) using a disintegration test instrument with disk (Electro lab, India). For the disintegration time calculations, five tablets from each formulation were tested [13].

2.6 Drug Content Uniformity

Five tablets were crushed, and 40 mg of powder were transferred to a 100 ml volumetric flask containing a little amount of methanol. To obtain stock solution, the flask was shaken to dissolve the medication and the volume was adjusted with pH 7.4 phosphate buffer solution. The volumetric flask solution was filtered, diluted appropriately, and spectrophotometrically examined using a UV-visible double-beam spectrophotometer (UV1800, Shimadzu, Japan) [14].

2.7 *In-vitro* Drug Release Study

The dissolving test was conducted to compare the dissolution of liquisolid compact tablets and CT. The tablets were tested for in-vitro drug release using a USP type II equipment paddle (Electrolab) at 37°C 0.5°C with phosphate buffer pH 7.4 (900 ml) as a dissolution medium at 50 rpm. 5 ml samples were extracted and replaced with fresh dissolution medium at predefined time intervals. The samples were drawn, filtered through a 0.45m membrane filter, diluted, and analyzed with a Shimadzu UV-1800 double-beam spectrophotometer. An algorithm derived from a calibration curve was used to compute cumulative percentage medication release [15].

2.8 Stability Studies

Optimized formulation of liquisolid compacts and compressed tablets of the agglomerates were packed in butter paper. The initial drug content was evaluated then the formulations were subjected for the accelerated stability studies in accordance with the ICH guidelines. As per the ICH guidelines it falls into 3 zones, and as per the recommendation the accelerated stability studies were to be carried out at 40±2˚C temperature and 75±5% relative humidity for a period of 3 months. Sample were withdrawn at predetermined time intervals i.e., 30, 60, 90 days and evaluated for the drug content of the liquisolid compacts and compressed tablets [16, 17].

3. RESULTS

The melting point of gliclazide was discovered to be between 180 and 182°C. The melting point of gliclazide has been reported to be 181°C. As a result, experimental values agreed well with official values. FT-IR spectrophotometer was used for drug excipient compatibility studies such as Fourier Transform Infrared Spectroscopy. The FTIR spectrum of a pure drug and a physical mixture of drug and several polymers were investigated. All physical mixtures' FT-IR spectrums exhibit no discernible change in the

position of assigned bands. It can be concluded that the medicine and the polymer have no significant chemical interactions and are hence compatible. . Scanning calorimetry to confirm the interaction between drug and excipients in prepared liquisolid formulation. A prominent endothermic peak at 161.03°C, which corresponds to its melting temperature (Tm), was visible in the DSC thermograms of pure gliclazide and the final liquisolid formulation system. This demonstrates that the gliclazide utilized was in its purest form. The resultant liquisolid system's melting peak was barely different from the pure drug's peak, which was 153.27°C. These findings demonstrated that the medicine and excipients are not incompatible. This demonstrates that the medication was molecularly disseminated in the liquisolid system and guarantees the creation of a drug solution in the formulation.

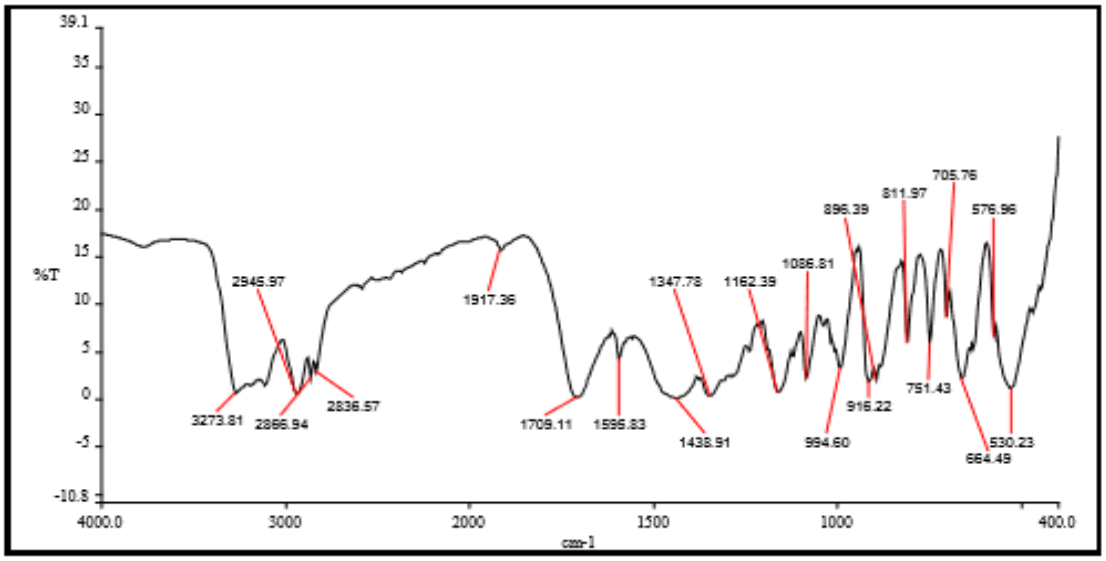

Fig. 2. FTIR Spectra of pure gliclazide

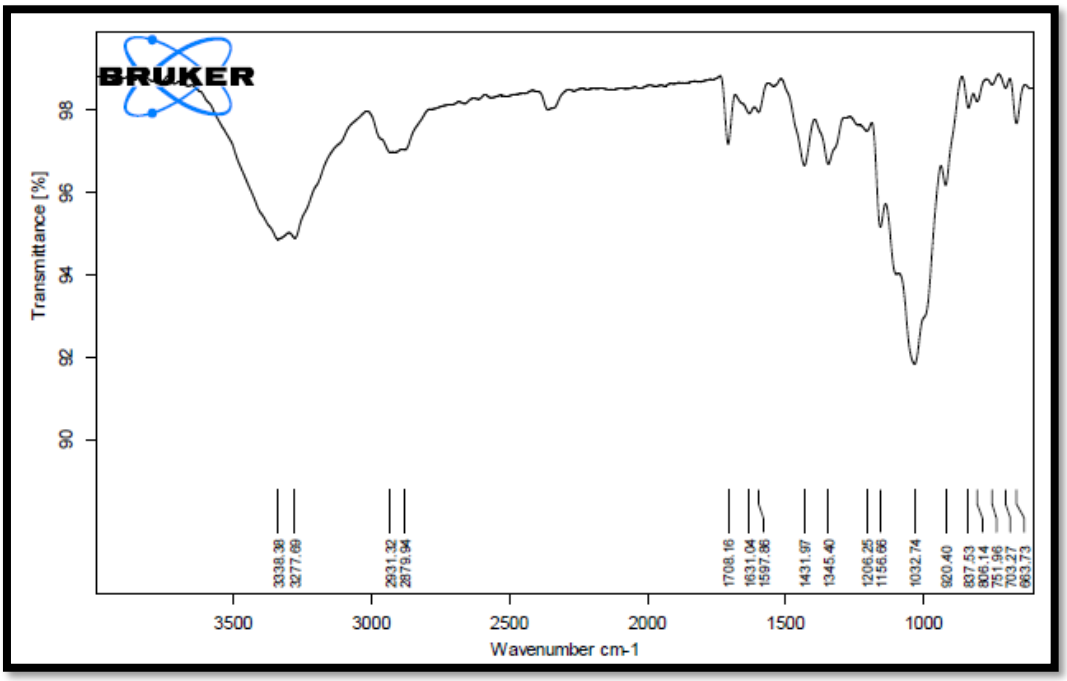

Fig. 3. FTIR spectra of physical mixture of gliclazide and avicel PH 200

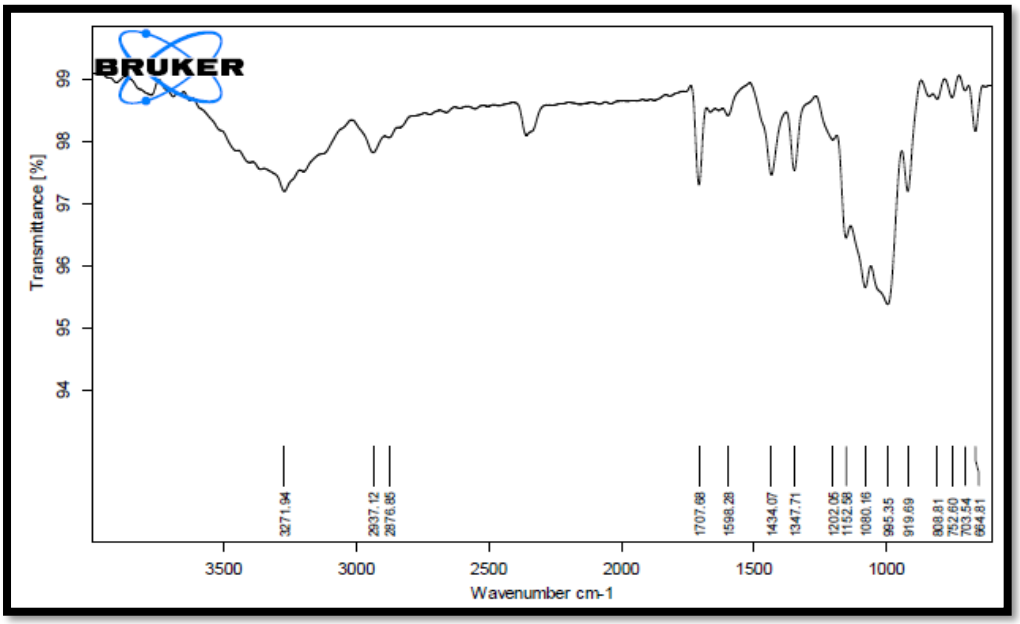

Fig. 4. FTIR Spectra of physical mixture of gliclazide and starch

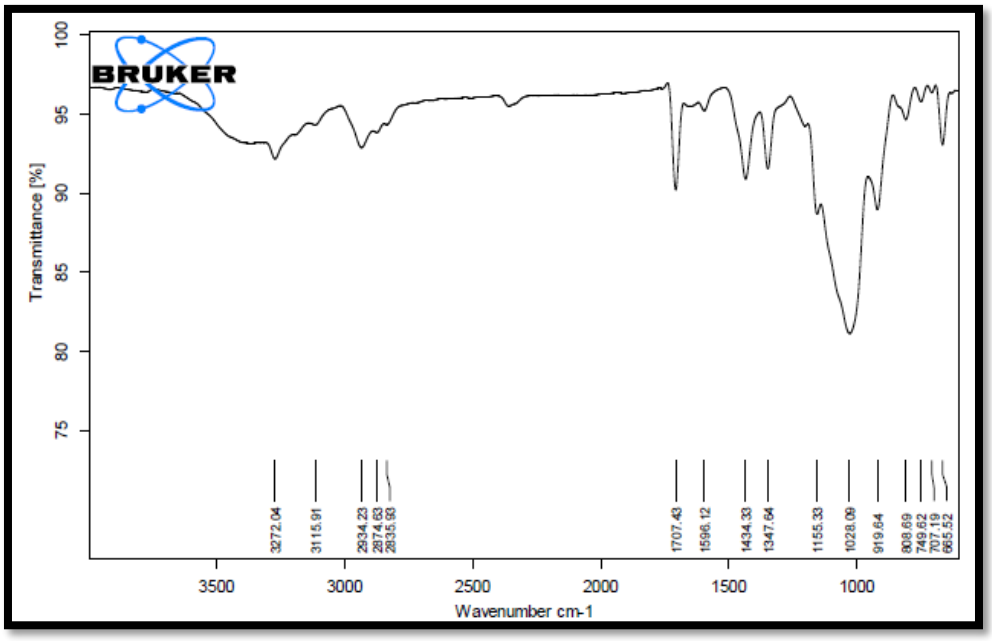

Fig. 5. FTIR Spectra of physical mixture of gliclazide and HPMC

A suitable analytical procedure for gliclazide was created utilizing a UV spectrophotometer. Gliclazide was found to have a maximum analytical wavelength of 228 nm in 7.4 phosphate buffer solution. The most crucial factor in liquisolid systems is drug solubility in a non-volatile carrier. The drug's solubility aids in molecular dispersion in a non-volatile solvent, increasing the rate of dissolution. PEG 400, PG, and Tween-80 were chosen as the vehicle for gliclazide based on the solubility data. Gliclazide's saturation solubility rises in the following order: PEG > Tween 80 > PG > pure water. There are no significant discrepancies between bulk density and tapped density, and the value obtained is within the permitted range. These findings aid in determining the powder's percent compressibility. The Carr's consolidation index values for each formulation clearly demonstrated that each formulation had good

flow and compressibility properties. The Angle of Repose () values were established to be within the range. The angle of repose for every formulation was below 30 degrees, which denotes smooth flow with the lowest standard deviation. The visual appeal of every batch of gliclazide liquisolid pills was assessed. Each tablet's macroscopic examination revealed that it was circular and free of pinholes or fissures. All tablets were kept between 3 and 4 kg/cm2 hard. Using a Monsanto hardness tester, the mean hardness values were calculated for each formulation. Table No. 2 contains the results in tabular form. The hardness value ranges from 3.3 to 3.86 kg/cm2, and it has a low standard deviation, meaning that all formulations' hardnesses were essentially uniform when made using a particular process. It also has a high mechanical strength. The percentage of friability for all formulations was under 1%, suggesting that the friability was within the allowed ranges and that the tablet has a strong mechanical structure based on the findings of the friability test. Since the average weight variation was under 5%, all of the tablets passed the weight variation test. All of the tablets' weights were determined to be uniform and had minimal standard deviation values. The micrometer (mm) unit of measurement for tablet thickness was used. The tablet's thickness suggests that the die fill was consistent. The thickness varies according on the punches' size and the 300 mg weight of each tablet. The thickness measurement ranges from 4.34 to 4.8 mm. The drug content percentage figures are between 85.8 and 98.06%. The results within the range suggested that the mixing was uniform.

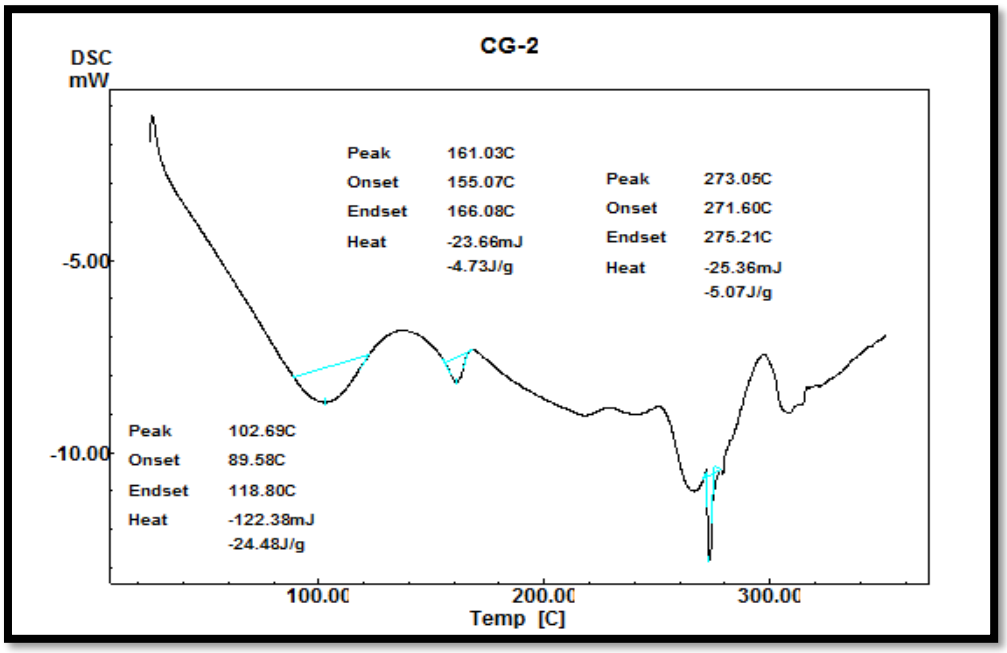

Fig. 6. DSC of pure gliclazide

Table 1. Precompressional parameters of all the formulations

Formulation code	Bulk density (gm/ml)	Tapped density(gm/ml)	Carr's index (%)	Angle of repose(°)
F1	0.179±.0036	0.20±0.0040	10.23±0.25	22.7±0.25
F2	0.21±0.005	0.262±0.0058	17.9±0.36	29.1±1.542
F3	0.218±0.006	0.247±0.0040	16.33±0.28	26.5.9±0.59
F4	0.199±0.0051	0.22±0.0068	14.53±0.45	21.1±1.997
F5	0.18±0.0045	0.21±0.001	16.23±0.25	30.7±1.609
F6	0.172±0.0020	0.19±0.0055	10.6±0.36	21.8±0.40
F7	0.165±0.0045	0.193±0.0028	17.3±0.28	30.3±0.173
F8	0.176±0.0028	0.20±0.0051	20.4±0.52	27.6±0.23
F9	0.177±0.0055	0.20±0.0005	15.3±0.173	28.1±0.71

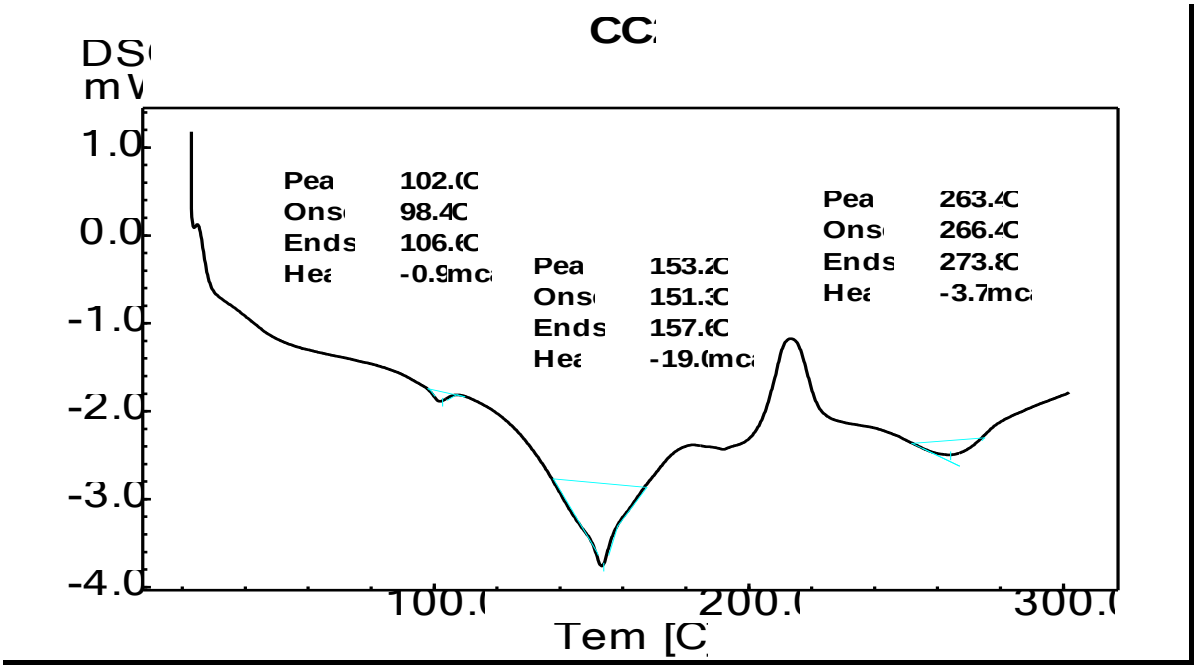

Fig. 7. DSC of liquisolid compact(F4)

Table 2. Postcompressional parameters of all the formulations

Formulation code	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Weight variation (mg)	Disintegration time (sec)	Drug content (%)
F1	3.33±0.2	4.51±0.05	0.42±0.023	294±3.64	46.6±2.88	94.8±1.04
F2	3.7±0.17	4.8±0.05	0.25±0.05	296±2.88	155±5	91.6±1.5
F3	3.6±0.17	4.86±0.11	0.283±0.02	298±1.34	245±5	85.8±2.27
F4	3.5±0.01	4.34±0.07	0.67±0.025	297.4±2.6	63.3±2.88	98.06±0.8
F5	3.6±0.2	4.45±0.05	0.95±0.05	297.2±0.8	153.3±7.63	92.02±1.0
F6	3.56±0.11	4.73±0.05	0.383±0.07	297±1.87	268±7.21	87.2±1.3
F7	3.8±0.21	4.56±0.11	0.68±0.076	298.2±1.3	72.3±2.51	95.2±1.21
F8	3.4±0.05	4.63±0.11	0.063±0.02	296±2.88	163.6±3.21	91.6±1.21
F9	3.86±0.05	4.8±0.1	0.51±0.028	299.4±2.7	253.6±3.21	87.7±1.80

3.1 *In vitro* dissolution studies

To find the most effective formulation, the drug's dissolving rates were compared between all LS compact and CT. The increased dissolution rate was discovered, which may be related to the highest solubility of gliclazide, as well as to the increased wettability of the drug molecules, and may also be related to the carrier coating material ratio (20:1) as they adsorb the drug molecules and thereby make the drug exposed to the dissolution media. Fig. 8 shows the comparative drug release of all LS compact and CT. According to in-vitro drug release trials, formulation F4 was found to be the most effective at producing gliclazide's rapid release when compared to other formulations. The medication is likely presented in a solubilized state, which adds to greater wetting qualities and improves the dissolve rate, explaining the improvement in the liquisolid tablets' dissolution rate. According to the aforementioned findings, PEG 400 is the best solvent in terms of solubility and flow characteristics when compared to PG and tween 80. Avicel is the ideal carrier when compared to other materials because of its hydrophilic nature and suitable physical characteristics for tablet use. The presence of the medication in a solubilized state in the formulation may be the cause of the increased dissolution from liquisolid formulations. This may improve the in-vitro dissolution rate by increasing the formulation's

wetting qualities. Accordingly, the drug will be delivered in a condition of molecular dispersion as the tablet formulation dissolves in the dissolving medium, increasing the effective surface area of the particles that are available for disintegration. PEG400 > PG > Tween-80 was determined to be the order of non-volatile solvents that improved the dissolving rate.

3.2 Stability Studies

The promising formulation F4 underwent a 90-day short-term accelerated stability trial by being kept at 40 °C and 75% RH. At monthly intervals, the samples were examined for any alterations in their physical appearance and drug content. The findings of stability examinations on the physical attributes and drug content did not reveal any appreciable change. Accelerated stability studies showed the improved formulation to be stable at the necessary standard conditions.

4. DISCUSSION

It was discovered that the melting point was between 180 and 182 °C. Gliclazide's reported melting point was 181°C. Therefore, there was good agreement between experimental and official value. All physical mixtures' FT-IR spectra reveal no discernible change in the designated bands' positions. Gliclazide and physical mixes' FTIR spectra are discovered to fall within the acceptable range. The gliclazide peak, which corresponds to its melting temperature of 161.03°C, was clearly visible in the thermogram produced by the DSC analysis of the compound. This demonstrates that the gliclazide utilized was in its purest form. There are no significant differences between the bulk density and the tapped density for any of the formulation values that were obtained for the untapped bulk density and tapped density. The Carr's consolidation index results for each formulation clearly demonstrated that each formulation had good flow and compressibility properties. The angle of repose for every formulation was below 30 degrees, which denotes smooth flow with the lowest standard deviation. Each tablet's macroscopic examination revealed that it was circular and free of pinholes or fissures. All tablets were kept between 3 and 4 kg/cm2 hard. All of the formulas' friability percentages were under 1%, which shows that they were all within the permitted ranges.

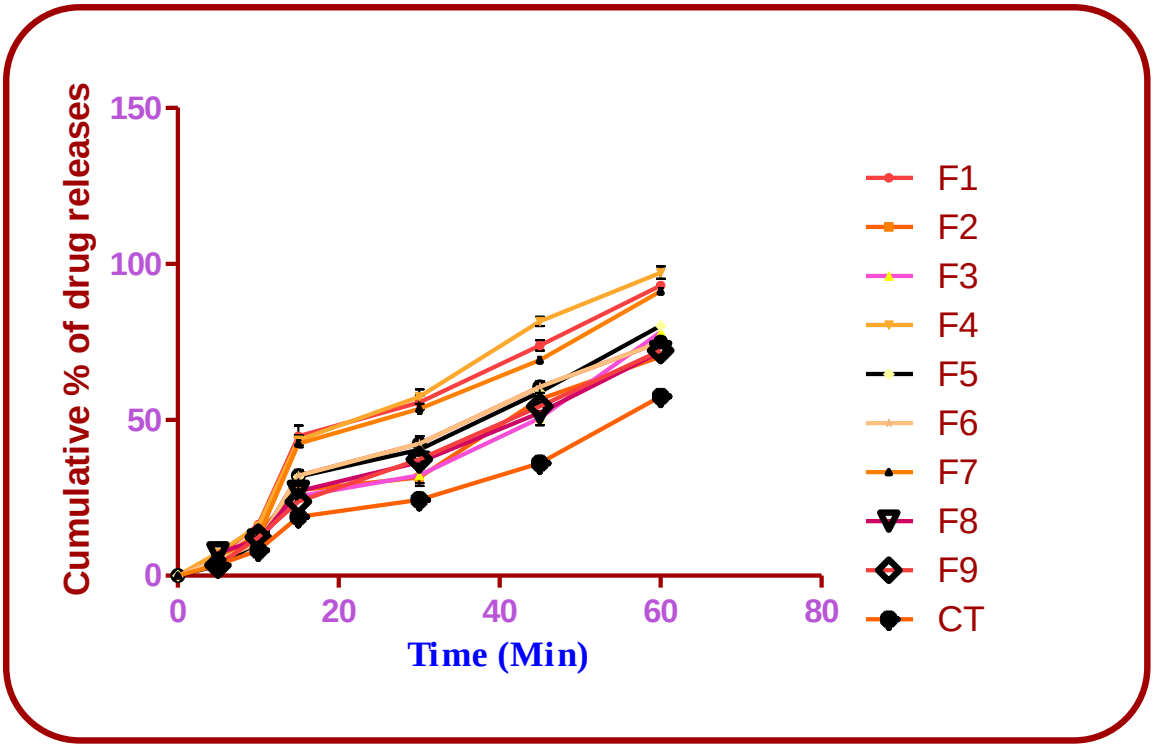

Fig. 8. *In-vitro* dissolution study of gliclazide liquisolid compacts and CT

5. CONCLUSION

It was discovered that the liquisolid technique was a potential method for enhancing the dissolving of medications that weren't very soluble. It was decided to apply the liquisolid approach to improve the solubility and dissolving characteristics of gliclazide. The polyethylene glycol (PEG) 400, tween 80, and propylene glycol used as non-solvents, Avicel PH102 or starch or HPMC as carrier materials, and Aerosil 200 utilized as coating material were employed to create the gliclazide liquisolid compacts. A investigation using FT-IR and DSC verified that there was no interaction between the medicine and the excipients used to make gliclazide liquisolid compacts. Gliclazide was studied for saturation solubility in a variety of solvents, and the results showed that it was more soluble in PEG 400. The results of the tests for hardness, friability, weight variation, and disintegration were acceptable. The in vitro dissolution investigation showed that liquisolid compacts release drugs more effectively than directly crushed tablets. It was found that the medication content and dissolving profile of the liquisolid compacts were not significantly affected by age. All of the tablets' weights were determined to be uniform and had minimal standard deviation values. The thickness measurement ranges from 4.34 to 4.8 mm. The drug content percentage figures are between 85.8 and 98.06%. The results within the range suggested that the mixing was uniform.According to in-vitro drug release trials, formulation F4 was found to be the most effective at producing gliclazide's rapid release when compared to other formulations.

ACKNOWLEDGEMENT

The authors want to thank Institute of Pharmacy, Assam Don Bosco University, Tapesia, Assam, India, for proving necessary requirement during the experiment.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Shi Q, Li F, Yeh S, Moinuddin SM, Xin J, Xu J, Chen H, Ling B. Recent advances in enhancement of dissolution and super saturation of poorly water-soluble drug in amorphous pharmaceutical solids: A Review. AAPS PharmSciTech, 2022;23(1):16.
Available:https://doi.org/10.1208/s12249-021-02137-0
2. Hadinugroho W, Martodihardjo S, Fudholi A, Riyanto S. Preparation of Citric Acid-Locust Bean Gum (CA-LBG) for the Disintegrating Agent of Tablet Dosage Forms. Journal of Pharmaceutical Innovation. 2022;17(4):1160–1175.
Available:https://doi.org/10.1007/s12247-021-09591-0
3. Venkateswarlu K, Preethi JK, Chandrasekhar KB. Enhancement of loperamide dissolution rate by liquisolid compact technique. Advanced Pharmaceutical Bulletin. 2016;6(3):385–390.
Available:https://doi.org/10.15171/apb.2016.050
4. Chella N, Narra N, Rama Rao T. Preparation and characterization of liquisolid compacts for improved dissolution of telmisartan. Journal of Drug Delivery. 2014:1–10.
Available:https://doi.org/10.1155/2014/692793
5. Spireas SS, Jarowski CI, Rohera BD. Powdered solution technology: Principles and Mechanism. Pharmaceutical Research. 1992;09(10):1351–1358.
Available:https://doi.org/10.1023/A:1015877905988
6. Prajapati ST, Bulchandani HH, Patel DM, Dumaniya SK, Patel CN. Formulation and evaluation of liquisolid compacts for olmesartan medoxomil. Journal of Drug Delivery. 2013: 1–9.
Available:https://doi.org/10.1155/2013/870579
7. Albayrak C, Barım G, Dag Ö. Effect of hygroscopicity of the metal salt on the formation and air stability of lyotropic liquid crystalline mesophases in hydrated salt–surfactant systems. Journal of Colloid and Interface Science. 2014;433:26–33.
Available:https://doi.org/10.1016/j.jcis.2014.07.008
8. Kumar R, Thakur AK, Chaudhari P, Banerjee N. Particle size reduction techniques of pharmaceutical compounds for the enhancement of their dissolution rate and bioavailability. Journal of Pharmaceutical Innovation. 2022;17(2):333–352.
Available:https://doi.org/10.1007/s12247-020-09530-5

9. Savjani KT, Gajjar AK, Savjani JK. Drug Solubility: Importance and Enhancement Techniques. ISRN Pharmaceutics. 2012:1–10.
Available:https://doi.org/10.5402/2012/195727
10. Wong SM, Kellaway IW, Murdan S. Enhancement of the dissolution rate and oral absorption of a poorly water soluble drug by formation of surfactant-containing microparticles. International Journal of Pharmaceutics. 2006;317(1):61–68.
Available:https://doi.org/10.1016/j.ijpharm.2006.03.001
11. Kalepu S, Nekkanti V. Insoluble drug delivery strategies: review of recent advances and business prospects. Acta Pharmaceutica Sinica B. 20155(5):442–453.
Available:https://doi.org/10.1016/j.apsb.2015.07.003
12. Bhalani DV, Nutan B, Kumar A, Singh Chandel AK. Bioavailability enhancement techniques for poorly aqueous soluble drugs and therapeutics. Biomedicines. 202210(9):2055.
Available:https://doi.org/10.3390/biomedicines10092055
13. Gupta A, Hunt RL, Shah RB, Sayeed VA, Khan MA. Disintegration of highly soluble immediate release tablets: A Surrogate for Dissolution. *AAPS* PharmSciTech, 2009;10(2):495–499.
Available:https://doi.org/10.1208/s12249-009-9227-0
14. Semalty A, Semalty M, Nautiyal U. Formulation and evaluation of mucoadhesive buccal films of enalapril maleate. Indian Journal of Pharmaceutical Sciences. 2010;72(5):571.
Available:https://doi.org/10.4103/0250-474X.78522
15. Cheng X, Gao J, Li J, Cheng G, Zou M, Piao H. In Vitro-In Vivo correlation for solid dispersion of a poorly water-soluble drug efonidipine hydrochloride. AAPS PharmSciTech. 2020;21(5), 160.
Available:https://doi.org/10.1208/s12249-020-01685-1
16. Gunawardhana LN, Al-Rawas GA, Kazama S. An alternative method for predicting relative humidity for climate change studies. Meteorological Applications. 2017;24(4):551–559.
https://doi.org/10.1002/met.1641
17. Patel S, Kaushal AM, Bansal AK. Compression physics in the formulation development of tablets. Critical Reviews™ in Therapeutic Drug Carrier Systems. 2006;23(1):1–66.
Available:https://doi.org/10.1615/CritRevTherDrugCarrierSyst.v23.i1.10