www.ijarp.com ISSN 2456-9992 Page: 01-24

International Journal Advanced Research Publications

Research Article

Volume: 02
Issue: 05

"SOLUBILITY ENHANCEMENT OF TORSEMIDE BY SOLID DISPERSION TECHNIQUE"

***Tanmay Jagtap, Prathamesh Jathar, Rutik Jare, Dr. Gautam Palshikar**

Principal Dr. Tushar T. Shelke

Genba Sopanrao Moze College of Pharmacy.

Article Received: 06 April 2026, Article Revised: 26 April 2026, Published on: 16 May 2026

***Corresponding Author: Tanmay Jagtap**

Genba Sopanrao Moze College of Pharmacy.

DOI: https://doi-doi.org/101555/ijarp.8911

1. ABSTRACT

TORSEMIDE belongs to pyridine-sulfonyl class of drugs. It works by which acts by inhibiting sodium and chloride reabsorption in the kidneys' loop of Henle, increasing urine production.. It has been classified as a Biopharmaceutics Classification System (BCS) class II drug, which typically exhibits high permeability and poor solubility. TORSEMIDE has a slow dissolution rate, impacting its bioavailability. The objective of the work was to enhance the solubility prior to formulation. Solid dispersion as a dosage form has been established as a superior option for the drugs having poor aqueous solubility. The solid dispersion of TORSEMIDE was prepared with the polymer PEG 4000 using kneading method. The solid dispersion formulations were characterized by saturation solubility, melting point and evaluated for in vitro dissolution studies. The formulation prepared with TORSEMIDE and PEG 4000 in the ratio of 1:4 gives better solubility results when compared to the other ratios of 1:1, 1:2, 1:3, and 1:4. The optimized batch exhibited a cumulative drug release of 74.47% within 60 minutes, which was significantly higher than that of the pure drug.

KEYWORDS: TORSEMIDE, Solubility, Solid dispersion, Dissolution, Bioavailability.

2. INTRODUCTION

SOLUBILITY:

The solubility of a drug is a crucial physicochemical characteristic, particularly in relation to its aqueous solubility. This is because water serves as the exclusive solvent in biological systems. It is evident that for a drug to effectively reach its receptors within the body, it must

traverse both aqueous and non-aqueous environments. However, the likelihood of a drug with low water solubility successfully entering the market is exceedingly low.

The term 'solubility' is defined as maximum amount of solute that can be dissolved in a given amount of solvent. It can also be defined quantitatively as well as qualitatively. Quantitatively it is defined as the concentration of the solute in a saturated solution at a certain temperature. In qualitative terms, solubility may be defined as the spontaneous interaction of two or more substances to form a homogenous molecular dispersion. A saturated solution is one in which the solute is in equilibrium with the solvent. Over 90% of medications are typically administered orally.

Drug absorption, sufficient and reproducible bioavailability, pharmacokinetic profile of orally administered drug substances is highly dependent on Solubility of that compound in aqueous medium. More than 90% of drugs are approved since 1995 have poor solubility. It is estimated that 40% of active new chemical entities (NCEs) identified in combinatorial screening programs employed by many pharmaceutical companies are poorly water soluble Drug absorption, sufficient and reproducible bioavailability and pharmacokinetic profile in humans are recognized today as one of the major challenges in oral delivery of new drug substances. Orally administered drugs on the Model list of Essential Medicines of the World Health Organization (WHO) are assigned BCS classifications on the basis of data available in the public domain. The 130 orally administered drugs on the WHO list, 61 could be classified with certainty. 84% of these belong to class I (highly soluble, highly permeable), 17% to class II (poorly soluble, highly permeable), 39% to class III (highly soluble, poorly permeable) and 10% to class IV (poorly soluble, poorly permeable). The rate and extent of absorption of class II and class IV compounds is highly dependent on the bioavailability which ultimately depends on solubility. Due to this major reason Solubility enhancement is one of the important parameters which should be considered in formulation development of orally administered drug with poor aqueous solubility.

Table 1 Different Solubility terms used in USP.

Descriptive Term (Solubility Definition)	Parts of Solvent Required for One Part of Solute	Solubility Range (mg/mL)	Solubility Assigned (mg/mL)
Very soluble (vs)	<1	>1000	1000
Freely soluble (fs)	from 1 to 10	100–1000	100
Soluble (s)	from 10 to 30	33–100	33
Sparingly soluble (sps)	from 30 to 100	10–33	10
Slightly soluble (ss)	from 100 to 1000	1–10	1
Very slightly soluble (vss)	from 1000 to 10000	0.1–1	0.1
Practically insoluble (pi)	>10000	<0.1	0.01

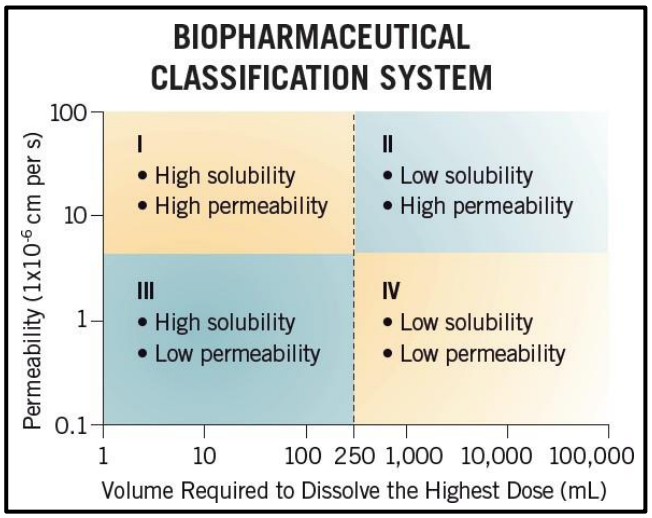


Figure 1 Biopharmaceutical Classification System.

In above figure 1 X-axis shows the volume (ml) required to dissolve the highest dose strength of the parent drug at the lowest solubility over the pH 1-7.5. A parent drug is considered highly soluble" when the highest dose strength is soluble in <250 ml water over a pH range of 1-7.5, in which 250 ml reflects the so-called FDA glass of water. The Y-axis shows the permeability, which is defined by various in vivo or in vitro assays, and a permeable drug is the one associated with 90% oral bioavailability or 90% absorption as assessed by urinary excretion data.

TECHNIQUES TO OVERCOME POOR SOLUBILITY

I. Physical Modifications

A. Particle size reduction

a. Micronization

b. Nanosuspension

B. Modification of the crystal habit

a. Polymorphs

b. Pseudo polymorphs

C. Drug dispersion in carriers

a. Eutectic mixtures

b. Solid dispersions

c. Solid solutions

D. Complexation

a. Use of Complexing agents

E. Solubilization by surfactants:

a. Microemulsions

b. Self microemulsifying drug delivery systems

II. Chemical Modifications

1. Salt Formation
2. Co-crystallisation
3. Co-solvent
4. Hydrotropic

SOLID DISPERSION:

The term solid dispersion refers to the dispersion of one or more active ingredients in a hydrophilic inert carrier matrix at molecular level. It is a vital concept in pharmaceutical formulation, offering a versatile approach to enhance the solubility and bioavailability of poorly water-soluble drugs. It involves dispersing drug molecules within a solid matrix, typically a polymer, to overcome solubility limitations. This technique has gained prominence due to its effectiveness in improving drug dissolution rates and overall therapeutic outcomes.

The basic principle involved in enhancing the poor solubility of drug with solid dispersion includes complete removal of the drug crystalline structure and its conversion into a amorphous molecular dispersion in a hydrophilic polymeric carrier. When the solid dispersion is exposed to a aqueous media, the carrier dissolves and the drug releases as fine colloidal particles. This increases surface area of dissolution rate and hence the bioavailability of poorly water soluble drugs. Drug in soluble hydrophilic carrier improves the dissolution rate by reducing particle size and increasing the particle porosity. The enhancement of drug release is achieved using the drug in its amorphous state, because no energy is required to break up the crystal lattice during the dissolution process. In solid dispersions, drugs are presented as supersaturated solutions after system dissolution, and it is speculated that, if drugs precipitate, it is as a metastable polymorphic form with higher solubility than the most stable crystal form.

Advantages of Solid Dispersion:

- Enhancement of the active agent bioavailability to a desirable extent.
- Avoiding polymorphic changes and the consequent bioavailability problems.
- Transformation of liquid or gaseous form of the drug into solid form is possible.
- Homogeneous distribution of small amount of drug at solid state is possible

CLASSIFICATION OF SOLID DISPERSION:

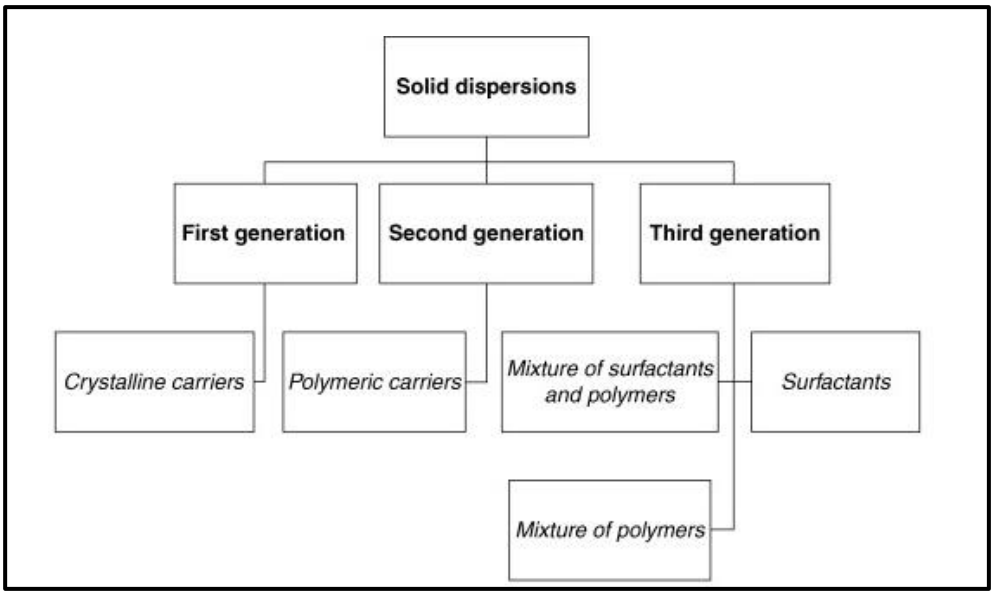


Figure 2 Classification of Solid Dispersion.

❖ Classification of solid dispersion on the basis of recent advancement:

1. First generation solid dispersion: These solid dispersions are prepared by using crystalline carriers. Urea and sugars were the first crystalline carriers that were used in the preparation of solid dispersions. These have a disadvantage of being thermodynamically unstable and they do not release drug at a faster rate.

2. Second generation solid dispersion: These solid dispersions are prepared using amorphous carriers instead of crystalline carriers. The drug is molecularly dispersed in the polymeric carrier. The polymeric carriers are divided into two groups: a. Synthetic polymer– povidone, polyethylene glycols and polymethacrylates. b. Natural polymers – hydroxypropyl methylcellulose, ethyl cellulose, starch derivatives like cyclodextrin.

3. Third generation solid dispersion: These solid dispersions contain a surfactant carrier, or a mixture of amorphous polymers and surfactants as carriers. These achieve the highest degree of bioavailability for the drugs that are having poor solubility. The surfactants being used in the third generation solid dispersion are such as inulin, poloxamer 407 etc.

❖ Classification of solid dispersions depending on the molecular arrangement, solid dispersions can be of the following types:

- **Eutectic mixtures:** Solid eutectic mixtures are usually prepared by rapidly cooling the co-melt of the two components in order to obtain a physical mixture of very fine crystals of the two components.

- **Solid solutions:** Depending on the miscibility, the two types of solid solutions are:

1. Continuous solid solutions: In continuous solid solutions, the components are miscible in all proportions i.e. the bonding strength between the components is stronger than the bonding between the individual component.
2. Discontinuous solid solutions: In discontinuous solid solutions, the solubility of each of the component in the other component is limited in nature.

Solid solutions Depending on the distribution of the solvates in the solvent, solid solutions can be of two types:

1. Substitution crystalline solution: These are those solid solutions which have a crystalline structure, the solute molecules substitute for the solvent molecules in the crystal lattice.
2. Interstitial crystalline solid solution: These are those solid solutions in which the dissolved molecules occupy the interstitial spaces between the solvent molecules in the crystal lattice.

- **Amorphous solid solutions:** In amorphous solid solutions, the solute molecules are dispersed molecularly but irregularly within the amorphous solvent.
- **Glass solutions and glass suspension:** A glass solution is a homogenous system in which the solute dissolves in the glassy solvent. The glassy state is characterized by transparency and brittleness below the glass transition temperature. The term glass refers to a pure chemical or a mixture of pure chemicals in the glassy state.

METHODS FOR PREPARING SOLID DISPERSIONS

1. Kneading Technique:

The drug and carrier are kneaded together with a small amount of solvent or a melting aid, such as a plasticizer or a surfactant. The mixture is then dried to remove the solvent or melting aid, leaving behind a solid dispersion.

2. Solvent Evaporation method:

This method involves dissolving both the drug and the carrier in a common solvent, followed by evaporation of the solvent to obtain a solid dispersion. The choice of solvent depends on the solubility of the drug and carrier. Common solvents include ethanol, methanol, and dichloromethane.

3. Co-precipitation method:

In this technique, the drug and carrier are dissolved in a common solvent, and then a non-solvent is added to precipitate the solid dispersion. The precipitate is then collected and dried to obtain the final product.

4. Melting method:

In this technique, the drug and the carrier (such as a polymer) are melted together at an elevated temperature, mixed thoroughly, and then cooled to form a solid dispersion. Common carriers include PEG (polyethylene glycol), PVP (polyvinylpyrrolidone), and various polymethacrylates.

5. Co-grinding method:

Co-grinding is a method for preparing solid dispersions of poorly water-soluble drugs by grinding the drug and a carrier together using high-energy milling equipment. This process increases the surface area of the drug particles, leading to improved solubility and dissolution rates. It's a simple, cost-effective, and scalable technique suitable for a wide range of drugs and carriers.

6. Gel Entrapment technique:

Gel entrapment is a method where drugs or bioactive compounds are encapsulated within a gel matrix formed by cross-linked polymer chains. The active ingredient is mixed with a gel-forming polymer solution, and gelation occurs to trap the drug within the gel.

7. Spray-Drying Method:

In spray drying, a solution of the drug and carrier is atomized into fine droplets using a spray nozzle. The droplets are then dried in a stream of hot air to yield solid particles. This technique is suitable for heat-sensitive drugs

8. Lyophilization Technique:

This method involves freezing a solution of the drug and carrier followed by sublimation of the solvent under reduced pressure. Freeze-drying is particularly useful for thermolabile drugs and produces solid dispersions with excellent dispersibility.

9. Electrospinning Method:

Electrospinning for solid dispersion involves dissolving the drug and carrier in a polymer solution, then electrospinning it into nanofibers. The process creates a high surface area-to-volume ratio, enhancing drug dissolution and bioavailability in drug delivery applications.

10. Dropping Method Solution:

In the dropping method for solid dispersion, a solution containing the drug and carrier is dropped into a non-solvent, causing precipitation of solid dispersion particles. This technique

enables controlled particle size and drug release properties, enhancing solubility and bioavailability of the drug.

11.Melt Extrusion Method:

Melt extrusion involves heating a physical mixture of the drug and carrier above the melting point of the carrier, followed by forcing the molten mass through a die to form solid extrudates. This method is widely used for industrial-scale production of solid dispersions.

12.Melt Agglomeration Process:

Melt agglomeration involves melting the drug and carrier together, followed by controlled cooling to form agglomerates. This process enhances drug dispersion, leading to improved solubility and dissolution rates in solid dispersion formulations.

DRUG- TORSEMIDE:

TORSEMIDE is a potent loop diuretic belonging to the BCS Class II category, primarily used for the treatment of edema associated with congestive heart failure, renal disease, and hepatic cirrhosis, as well as hypertension. It is generally administered in oral dosage forms and is known for its poor aqueous solubility, which can influence its dissolution rate.TORSEMIDE exerts its diuretic activity by inhibiting the **$Na^+/K^+/2Cl^-$ co-transporter** in the thick ascending limb of the loop of Henle. This inhibition reduces the reabsorption of sodium and chloride ions, leading to increased excretion of water, electrolytes, and subsequent reduction in fluid overload.Its absorption is relatively consistent compared to other loop diuretics, with an oral bioavailability of approximately 80–90%, though it may still be influenced by physiological factors. Due to its low solubility characteristics, the aim of the present study is to enhance the dissolution rate and solubility of TORSEMIDE by preparing a solid dispersion formulation, thereby improving its therapeutic efficiency.

POLYMER- PEG (4000):

PEGs, ranging from MW 200 to 300,000, are commonly used in solid dispersions and solutions. Different MWs exhibit varying viscosities and physical states, with lower MWs being fluid and higher MWs forming hard, brittle crystals. Their solubility in water decreases as MW increases, but they remain soluble in various organic solvents. PEG 4000 is a polyethylene glycol polymer with a molecular weight of approximately 4000, commonly used in the formulation of solid dispersions and pharmaceutical solutions. It exists as a waxy solid at room temperature and exhibits intermediate viscosity compared to lower and higher

molecular weight PEGs. PEG 4000 has a melting point in the range of 50–58°C, which makes it suitable for processing under mild thermal conditions. It is moderately soluble in water and highly soluble in various organic solvents. Due to its ability to improve drug wettability, solubilize poorly soluble compounds, and enhance the dissolution rate, PEG 4000 is widely employed as a carrier in solid dispersion systems. It has been shown to enhance the dissolution performance of drugs with limited solubility, thereby improving their bioavailability.

Problems with PEGs

In general, there are few toxicity concerns associated with the PEGs and they are approved for many purposes as excipients. The low molecular weights PEGs do, however, tend to show slightly greater toxicity than those of higher molecular weight (Price *et al*., 1994).

3. LITERATURE REVIEW

Sr. No.	Authors & Year	Title of Study	Key Focus / Findings
1	Ladan Akbarpour Nikghalb, Gurinder Singh, Gaurav Singh, Kimia Fazeli Kehkashan (2012)	*Solid Dispersion: Methods and Polymers to Increase the Solubility of Poorly Soluble Drugs*	Discusses various preparation methods such as melting method, solvent evaporation method, fusion method, kneading method, and highlights different carriers used in solid dispersions.
2	Satish K. Patil, Kalpesh S. Wagh, Venkatesh B. Parikh, Anup M. Akarte, Dheeraj T. Baviskar (2011)	*Strategies for Solubility Enhancement of Poorly Soluble Drugs*	Describes techniques to overcome poor solubility categorized into: (I) Physical Modifications (II) Chemical Modifications.
3	Teresa Vasconcelos, Bruno Sarmento, Paulo Costa (2007)	*Solid Dispersions as Strategy to Improve Oral Bioavailability of Poor Water-Soluble Drugs*	Explores solid dispersion as an effective approach to enhance oral bioavailability of poorly water-soluble drugs.
4	National Library of Medicine	*Potential of Solid Dispersions to Enhance Solubility, Bioavailability, and Therapeutic Efficacy of Poorly Water-Soluble Drugs*	Covers newer formulation techniques, current marketed products, and patents related to solid dispersions.
5	K. Rajbhar et al. (2023)	*Comparative Assessment of Solubility Enhancement of Torsemide by Solid Dispersion and Co-Crystallization Technique*	Compares solid dispersion and co-crystallization techniques for Torsemide, including the effect of media composition on drug dissolution.

7 . AIM AND OBJECTIVES

1. AIM:

To enhance solubility of TORSEMIDE by Solid Dispersion technique.

2. OBJECTIVE:

The objectives of present work are-

1. To study solubility profile of TORSEMIDE.
2. Preparation of solid dispersion of TORSEMIDE.
3. To enhance solubility and dissolution rate of poorly water-soluble TORSEMIDE.
4. To assess the physical characteristics of the solid dispersion formulations.
5. To compare the dissolution profiles of TORSEMIDE solid dispersion formulations with the pure drug.

1. HYPOTHESIS:

Solid Dispersion modification may be achieved by the solid dispersion technique by kneading method which may improve the physicochemical properties of drug like solubility, dissolution and also the bioavailability.

4. RATIONALE

TORSEMIDE is a loop diuretic that inhibits the $Na^+/K^+/2Cl^-$ co-transporter in the thick ascending limb of the loop of Henle, thereby promoting the excretion of sodium, chloride, and water. It is widely used in the management of edema associated with congestive heart failure, chronic kidney disease, and hepatic cirrhosis, as well as in the treatment of hypertension. TORSEMIDE offers advantages over other loop diuretics, including a longer duration of action and more predictable pharmacokinetics.

A single oral dose of TORSEMIDE (10–20 mg) typically produces peak plasma concentrations (Cmax) within 1–2 hours (Tmax). The drug exhibits relatively high permeability but limited aqueous solubility, which can influence its dissolution rate and absorption under certain physiological conditions. Although TORSEMIDE shows better and more consistent bioavailability compared to some other loop diuretics, its solubility remains a limiting factor for optimal drug release.

TORSEMIDE has a moderate volume of distribution and is highly bound to plasma proteins (>95%). It undergoes hepatic metabolism primarily via cytochrome P450 enzymes (mainly CYP2C9), forming inactive metabolites. The drug has an elimination half-life of approximately 3–4 hours and is excreted through both renal and fecal routes.

Due to its **poor aqueous solubility and high permeability**, TORSEMIDE is classified as a **BCS Class II drug**. Enhancement of its solubility and dissolution rate is therefore essential to ensure rapid onset of action and consistent therapeutic performance. Various formulation strategies, including solid dispersions, micronization, and lipid-based systems, have been explored to address these limitations.

In this context, the preparation of solid dispersions of TORSEMIDE using suitable hydrophilic carriers is considered a promising approach to improve its solubility, dissolution behavior, and oral bioavailability. Therefore, TORSEMIDE solid dispersions were developed in pursuit of enhancing its biopharmaceutical performance and therapeutic efficacy.

PLAN OF WORK

- **Selection of drug**
- **Selection of polymer**
- **Preformulation studies of drug**
  - Organoleptic properties
  - Saturation Solubility
  - Melting point
  - UV spectroscopy
- **Method**
  - Solid dispersion
- **Characterization of solid dispersion**
  - Melting point
  - Saturation solubility
- **Project report writing**

MATERIAL AND METHOD

- **Materials**

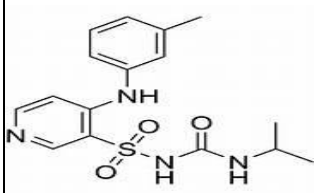
➢ **DRUG AND CHEMICALS:**

1. **TORSEMIDE**
2. **Polyethylene Glycol (4000)**

DRUG AND EXCIPIENT PROFILE

1. Chemistry of TORSEMIDE

Table 2 Chemistry of TORSEMIDE.

Name	**TORSEMIDE**
Structure	
Description	**TORSEMIDE** is a white powder**.**
IUPAC Name	1-[4-[(3-methylphenyl)amino]pyridine-3-sulfonyl]urea
Molecular formula	$C_{16}H_{20}N_4O_3S$
Molecular weight	348.42 gm/ mol
Storage condition	Store protected from light and moisture.
BCS Class	Class II
Category	Loop Diuretic
Bioavailability	80-100%
Log P	2.3-2.8
Solubility	Practically insoluble in water, freely soluble in methanol.
Melting point	163°C to 168^{0}C

2. **Chemistry of Polyethylene Glycol (4000)**

Table 3 Chemistry of Polyethylene Glycol 4000.

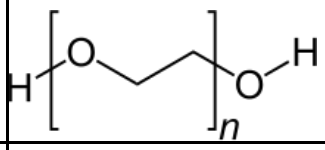
Name	**Polyethylene Glycol 4000**
Structure	
Molecular formula	$C_{2n}H_{4n+2}O_{n+1}$ or Roughly $C_{182}H_{366}O_{92}$
Molecular weight	~ 4000 g/mol
IUPAC Name	poly(oxy-1,2-ethanediyl)
Category	non-ionic hydrophilic polymer
Solubility	630 g/L in water
Boiling point	>200 °C
pH value	4.5-7.5
Melting Point	58-62°C
Applications	Excipient, improve stability, solubility, and bioavailability.

Figure 3 •Method: Solid Dispersion by Kneading Method.

Formulation Of Solid Dispersion Tablet:

Sr.No.	Ingredients	Quantity	Role	Source
1	Solid Dispersion of Torsemide	100mg	Active Pharmaceutical Ingredient	
2	Microcrystalline Cellulose	70mg	Diluent	Pharmaceutics lab SKNCOP
3	Sodium Starch Glycolate	20mg	Disintegrant	Pharmaceutics lab SKNCOP
4	Talc	5mg	Glidant	Pharmaceutics lab SKNCOP
5	Magnesium Stearate	5mg	Lubricant	Pharmaceutics lab SKNCOP

5. EXPERIMENTAL WORK

1) Selection of Drug:

The drug chosen for co-crystallization should be one of those, which are facing problems and can be solved by co-crystallization such as

- Crystallinity of compound
- Poor aqueous solubility
- Poor bioavailability
- Poor flow property
- Non-ionic nature

2) Pre-formulation Studies of Drug:

Drug was evaluated for its colour, odour, and appearance, melting point, solubility.

3) Preparation of solid dispersions:

Solid dispersion of TORSEMIDE with PEG 4000 in different weight ratios **1:1, 1:2, 1:3,** and **1:4** respectively was prepared by the kneading method. Accurately weighed amount of drug and polymer in various ratios was triturated in a pestle and mortar. The obtained amorphous solid dispersion was dried in a desiccator up to 24 hours. Then the powdered dispersion was passed through sieve No. 60 and stored in closed polyethylene zip lock bag.

Table 4 Different Ratios of Solid Dispersion of TORSEMIDE and Polyethylene Glycol 4000.

Formulations	F1	F2	F3	F4
Torsemide (mg)	20	20	20	20
PEG-4000 (mg)	20	40	60	80

4) Saturation Solubility Determination:

The saturation solubility of the different formulations was determined in distilled water by the following procedure:

An amount of TORSEMIDE of each of the solid dispersion was transferred into test tubes containing 2 ml of distilled water until a saturated solution was obtained. Each solution was shaken for 5 minutes and was kept for 24 hours at room temperature. After 24 hours, the solutions were filtered using Whatmann filter paper and the filtrate was analysed by a UV-Visible spectrophotometer at wavelength of 262 nm using distilled water as blank respectively.

Figure 5 Saturation Solubility.

5) In-vitro dissolution studies

1. Preparation of pH 6.8 phosphate buffer:

In a beaker 28.80 gm of disodium hydrogen phosphate was dissolved in 250 ml of distilled water and in another beaker 11.45 gm of potassium dihydrogen phosphate was dissolved in 250 ml of distilled water. And then it was mixed and was made up to volume of 1000ml.

2. The dissolution studies of the solid dispersions were performed using USP Type-I dissolution apparatus (Basket), thermostatically controlled at 37°C ± 1°C and phosphate buffer pH 6.8 was used as dissolution media. Samples of solid dispersions tablet equivalent to 250 mg of TORSEMIDE were introduced into the 900 ml of dissolution medium, stirred at 50 rpm. Samples were withdrawn at 10, 20, 30, 40, 50 and 60 min. The samples were filtered, diluted accordingly, and analysed spectrophotometrically in UV–VIS Spectrophotometer.

Figure c Dissolution Test Apparatus.

1. Angle of Repose

The angle of repose is used to determine the flow property of the powder blend before compression. It indicates whether the powder can flow uniformly into the die cavity during tablet manufacturing.

Formula: θ =tan -1 (h/r)

Interpretation

- Less than 25° → Excellent flow
- 25–30° → Good flow
- More than 40° → Poor flow

2.Bulk Density

Bulk Density is defined as the ratio of the mass of a powder to its bulk volume (including the spaces between particles)

Bulk Density=Bulk Volume/Mass of Powder

3.Tapped Density

Tapped Density is defined as the ratio of the mass of a powder to the tapped volume occupied after mechanically tapping the measuring cylinder.

Tapped Density=Tapped Volume/Mass of Powder

4.Carr's Compressibility Index

Carr's Compressibility Index is used to evaluate the flow property and compressibility of powders.

Carr's Index=Tapped Density/Tapped Density−Bulk Density×100

Interpretation

- 5–15% → Excellent flow
- 16–20% → Good flow
- 21–25% → Fair flow
- Above 25% → Poor flow

5. Hausner Ratio

Hausner's Ratio is defined as the ratio of tapped density to bulk density of a powder.

Hausner's Ratio=Bulk Density/Tapped Density

Interpretation

- 1.00–1.11 → Excellent flow
- 1.12–1.18 → Good flow
- Greater than 1.25 → Poor flow

6. Thickness Test

The thickness test is a quality control test used to determine the uniform thickness of tablets. It ensures that tablets are produced with consistent size and shape during manufacturing.

Apparatus Used

- Vernier caliper

7. Weight Variation Test

The weight variation test is a quality control test used to check whether tablets in a batch have uniform weight. It ensures that each tablet contains the proper amount of drug substance.

Tablet	Weight	%deviation	Pass/Fail	Tablet	Weight	%deviation	Pass/Fail
T1	195.9	0.26	Pass	T11	196	0.31	Pass
T2	196.4	0.56	Pass	T12	192.4	-1.51	Pass
T3	193	-1.21	Pass	T13	196.8	0.72	Pass
T4	194.3	-0.55	Pass	T14	197	0.82	Pass
T5	194.5	-0.45	Pass	T15	199.1	1.90	Pass
T6	196.8	0.72	Pass	T16	190	-2.75	Pass
T7	195	-0.19	Pass	T17	193.5	-0.96	Pass
T8	197.5	1.08	Pass	T18	197	0.82	Pass
T9	194.3	-0.55	Pass	T19	195.2	-0.09	Pass
T10	197	0.51	Pass	T20	196	0.31	Pass

8. Hardness Test

Hardness determines the mechanical strength of tablets.

Instruments Used

- Monsanto hardness tester
- Pfizer hardness tester
- Strong Cobb tester

Ideal Range

Usually 4–8 kg/cm² for conventional tablets.

9. Friability Test

Friability measures the ability of tablets to resist abrasion and shock.

Acceptance Limit

Friability should be less than 1%.

% Weight Variation=Average Weight/Individual Weight−Average Weight×100

10. Disintegration Test

Disintegration test determines the time required for tablets to break into smaller particles.

Limit

Uncoated tablets generally disintegrate within 15 minutes.

9 . RESULT AND DISSCUSSION

1) SELECTION OF DRUG AND POLYMER

1. Selection of drug:

TORSEMIDE was selected for Solid dispersion as there were problems associated with it like poor aqueous solubility and poor bioavailability which can be resolved by this method.

2. Selection of polymer:

The polymer Polyethylene Glycol 4000 (PEG 4000) was chosen for the formulation of solid dispersion with TORSEMIDE due to its favourable characteristics like its excellent solubility, compatibility.

2) PREFORMULATION STUDIES

TORSEMIDE was evaluated for various Pre-formulation parameters like colour, odour and confirmed that they complied with official standards.

Table 5. Pre-formulation Studies of TORSEMIDE

Sr.NO.	Characteristics	Inference
1.	Physical Description	Solid
2.	Colour	White
3.	Odour	Odorless
4.	Melting point	168-171 ^{O}C
5.	Solubility	0.113 µg/L

3)ULTRAVIOLET SPECTROSCOPY

UV calibration curve in phosphate pH 6.8 buffer :

Construction of calibration curve of TORSEMIDE in Methanol:

The calibration curve of the Torsemide was prepared in Methanol. Table shows the absorbance at λmax 262 nm for concentration 2 to 12 µg/ml of Torsemide . Figure shows the calibration curve. The regression coefficient was found to be 0.9837.

Table c UV Absorbance of TORSEMIDE in Methanol at 288nm.

Sr No	Concentration(ug/ml)	Absorbance
1	0	0
2	2	0.116
3	4	0.161
4	6	0.3345
5	8	0.429
6	10	0.5077

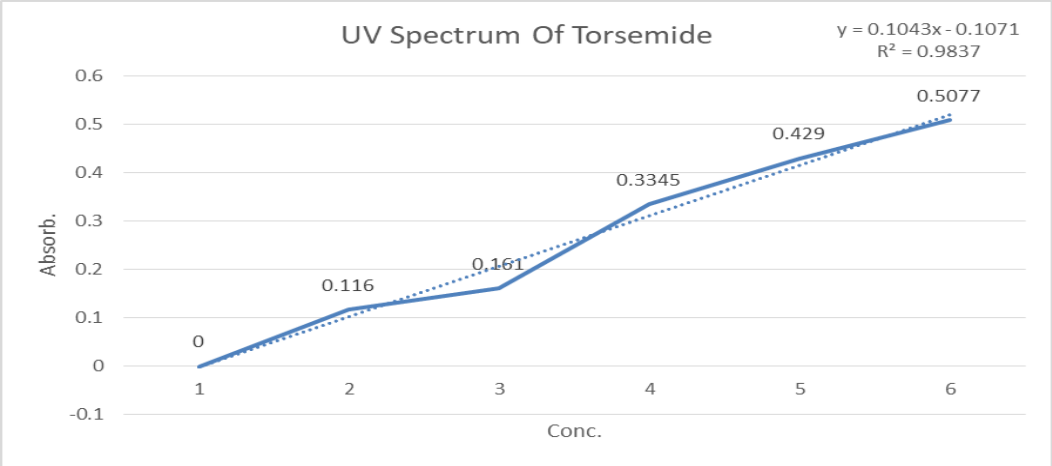


Figure 8. Calibration Curve of TORSEMIDE in Methanol at 288nm.

3)Saturation Solubility of solid dispersions

The saturation solubility of solid dispersions in water was carried out and compared with that of the solubility of pure **Torsemide** in the same solvent.

Table 8: Saturation Solubility of Solid Dispersion.

Sr NO.	Formulation	Solubility (mg/ml) In Water	Solubility Enhanced by folds
1	Torsemide	0.082	-
2	F1 (1:1)	0.124	1.51
3	F2(1:2)	0.256	3.12
4	F3(1:3)	0.198	2.41
5	F4(1:4)	0.754	9.08

From the saturation solubility data, it is observed that there is a significant increase in the solubility of **Torsemide** after conversion into solid dispersion in each formulation. The enhancement in solubility may be attributed to improved wettability, reduced particle size, and possible amorphous transformation of the drug.The maximum increase in solubility was found in the case of **F4 batch (1:4 ratio)**, indicating that a higher carrier concentration leads to greater solubility enhancement.

5) Dissolution Studies

The F4 batch (1:4) solid dispersion of Torsemide demonstrated enhanced solubility, leading to improved dissolution characteristics and potential bioavailability. Compared to the pure drug, the solid dispersion exhibited significantly higher aqueous solubility. To evaluate whether this solubility enhancement translates into improved dissolution, an ***in-vitro*** **release study** was performed.

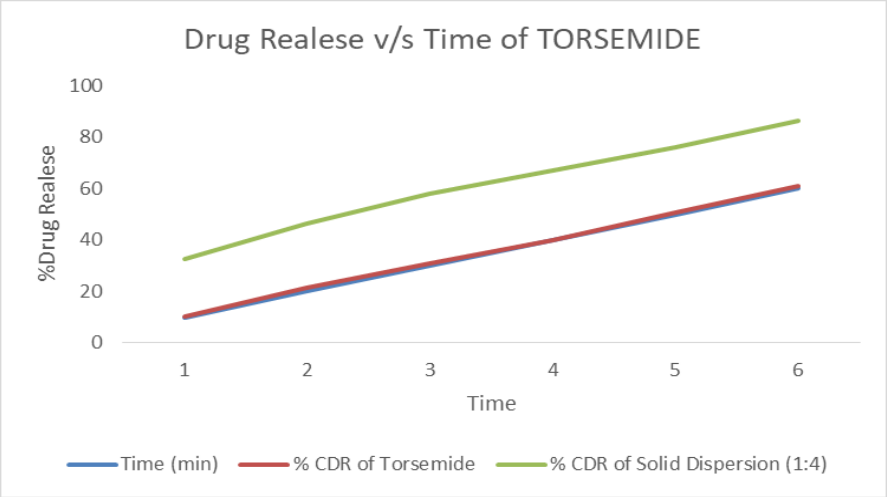
Experimental Conditions:Apparatus: USP Type I (Basket apparatus)

- **Dissolution Medium:** 900 mL phosphate buffer (pH 6.8)
- **Temperature:** 37 ± 0.5°C
- **Rotation Speed:** 50 rpm
- **Sampling:** 10 mL samples withdrawn at 10-minute intervals up to 60 minutes

The withdrawn samples were analyzed using a UV spectrophotometer at an appropriate wavelength for Torsemide (commonly around **288 nm**, adjust based on your calibration data). The results demonstrated a **significant enhancement in dissolution rate** for both solid dispersion and co-crystal formulations compared to pure Torsemide.

Table: Dissolution Data of Torsemide, Solid Dispersion, in Phosphate Buffer.

Time (min)	% CDR of Torsemide	% CDR of Solid Dispersion (1:4)
10	10.2	32.8
20	21.4	46.5
30	30.7	57.9
40	40.1	66.8
50	50.6	75.9
60	60.8	86.3

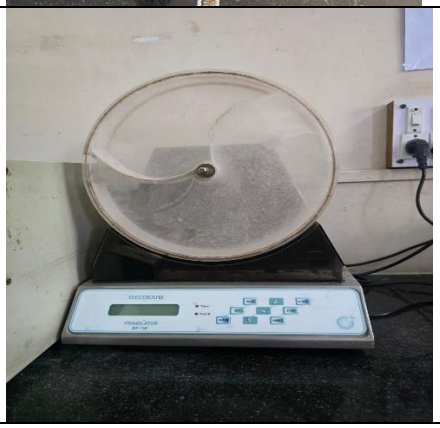


Interpretation

- Pure Torsemide shows **moderate to poor dissolution**, which can limit its bioavailability.
- The **solid dispersion (1:4)** significantly enhances dissolution, likely due to improved wettability, reduced crystallinity, and possible amorphization.
- The **co-crystal formulation** typically provides **faster initial drug release**, indicating improved solubility and surface characteristics.
- At later time points, the **solid dispersion may achieve slightly higher cumulative drug release**, suggesting sustained improvement.

Evaluation Parameters

Sr.No.	Parameters	Observation	Observed Values
1.	Angle of Repose		35.90° Indicates Good Flow.
2.	Bulk Density		0.33g/mL
3.	Tapped Density		0.5 g/mL
4.	Carr's Compressibility Index	Compressibility index = Tapped Density-Bulk Density/Tapped Density×100 =40%	
5.	Hausner's Ratio	Bulk Density/Tapped Density =0.33/0.5 =0.066	

6.	Thickness		
7.	Weight Variability	Individual Weight-Average Weight/Average Weight×100 =195.9-195.3/195.3×100 =0.6/195×100 =**0.30%**	
8.	Hardness		6.33kg
9.	Friability		0.91%

8.CONCLUSION

Torsemide solid dispersions were successfully prepared using the solid dispersion method in different drug-to-polymer ratios. The prepared formulations were evaluated for melting point, saturation solubility, drug content, and in-vitro dissolution studies.

It was observed that the melting point of the solid dispersions was lower than that of pure Torsemide, indicating the formation of molecular dispersion and possible interaction between Torsemide and the carrier polymer (PEG 4000).

The solid dispersions showed enhanced solubility in water and phosphate buffer pH 6.8 when compared with pure Torsemide. Saturation solubility studies demonstrated a significant increase in the solubility of Torsemide after conversion into solid dispersion formulations. Among all formulations, batch F4 (1:4) exhibited the maximum solubility enhancement.

The formulation showing highest solubility was further evaluated for dissolution studies. Dissolution profiles of pure Torsemide and the optimized solid dispersion formulation F4 (1:4) were compared in phosphate buffer pH 6.8. The results showed a significant improvement in the percentage cumulative drug release (%CDR) of the solid dispersion formulation.

Pure Torsemide exhibited lower drug release, whereas the solid dispersion formulation F4 (1:4) showed markedly higher drug release within 60 minutes. The improved dissolution behavior may be attributed to reduced particle size, improved wettability, and conversion of the drug into an amorphous form.

Thus, the study revealed that the solid dispersion of Torsemide prepared with Polyethylene Glycol (PEG 4000) in a 1:4 ratio can be considered a promising and effective approach for enhancing the solubility and dissolution rate of Torsemide.

9)REFERENCE

1. Sandeep Kumar, Pritam Singh. *Various Techniques for Solubility Enhancement: An Overview.* The Pharma Innovation Journal. 2016; 5(1): 23–28.
2. Ladi Alik Kumar, Gurudutta Pattnaik, Bhabani Sankar Satapathy, Sujata Naik, Anup Kumar Dash. *Solubility Enhancement Techniques: Updates and Prospectives.* DOI: 10.47750/pnr.2022.13.S08.353.
3. Mark T. Davis, David P. Egan, Manuel Kuhs, Ciara S. Griffin, John A. Collins. *Amorphous Solid Dispersions of BCS Class II Drugs: A Rational Approach to Solvent and Polymer Selection.* Chemical Engineering Research and Design. 2016; 110: 192–199.
4. Ruba Malkawi, Walla I. Malkawi, Jawad Tawalbeh. *Current Trends on Solid Dispersions: Past, Present, and Future.* Advances in Pharmacological and Pharmaceutical Sciences. 2022; Article ID 5916013.

5. Mohamed Salah Attia, Azza Ali Hasan, Fakhr-Eldin Soliman Ghazy, Eman Gomaa. *Solid Dispersion as a Technical Solution to Boost the Dissolution Rate and Bioavailability of Poorly Water Soluble Drugs.* DOI: 10.5530/ijper.55.2s.103.
6. Vikrant Nikam, Vrushali Kudnar, Kiran Kotade, Sachin Somwanshi, Jyoti Khapare, Nikita Rathod. *Enhancement of Dissolution Profile by Solid Dispersion Using Kneading Technique.* DOI: 10.47750/pnr.2020.13.S09.1300.
7. Avinash Ramrao Tekade, Jyoti Narayan Yadav. *A Review on Solid Dispersion and Carriers Used Therein for Solubility Enhancement of Poorly Water Soluble Drugs.* Adv Pharm Bull. 2020; 10(3): 359–369. doi:10.34172/apb.2020.044.
8. Heike Bley et al. *Characterization and Stability of Solid Dispersions Based on PEG/Polymer Blends.* International Journal of Pharmaceutics. 2010.
9. Swati Sareen, George Mathew, Lincy Joseph. *Improvement in Solubility of Poor Water-Soluble Drugs by Solid Dispersion.* Int J Pharm Investig. 2012; 2(1): 12–17. doi:10.4103/2230-973X.96921.
10. Indian Pharmacopoeia Commission. *Indian Pharmacopoeia 2018, Volume II.*
11. P. S. Argade, D. D. Magar, R. B. Saudagar. *Solid Dispersion: Solubility Enhancement Technique for Poorly Water Soluble Drugs.* Journal of Advanced Pharmacy Education & Research. 2013; 3(4).
12. Duret C., Wauthoz N., Sebti T., Vanderbist F., Amighi K. *Solid Dispersions for Enhanced Dissolution and Solubility of Poorly Water-Soluble Drugs.* International Journal of Pharmaceutics. 2012.
13. *Studies on Enhancement of Solubility and Dissolution Rate of* Torsemide *Using Solid Dispersion Technique with PEG Polymers and Hydrophilic Carriers.*