

# Formulation And Evaluation Of Furosemide Solid Dispersions For Solubility And Bioavailability Enhancement

Mr.Babshetty Rohit Basavraj\*<sup>1</sup>, Dr.Manish Kumar<sup>2</sup>

<sup>1</sup>Research Scholar; Faculty of Pharmaceutical Sciences Madhav University, Abu Road Pindwara Sirohi, Rajasthan, India.

<sup>2</sup>Professor; Faculty of Pharmaceutical Sciences Madhav University, Abu Road Pindwara Sirohi, Rajasthan, India.

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## ABSTRACT

In this study, aim was to formulate Furosemide solid dispersions to modify the drug's solubility and enhance therapeutic effect. Furosemide, loop diuretic, suffers from poor aqueous solubility, which limits its bioavailability. Solid dispersions were prepared using Eudragit L100 as carriers in different drug-to-carrier ratios through solvent evaporation and physical mixing techniques. These dispersions were assessed for bulk density, particle size, tapped density, angle of repose, also drug release profile. The findings indicated a notable improvement in the dissolution rate and solubility of Furosemide in an optimized formulation. The yields of solid dispersions were found to range 67.9%–95.4%, being the drug content of SDF2, the highest (97.63%). Solubility increase was also significant SDF2 showing 0.1100 mg/mL against 0.0697 mg/mL for pure Furosemide). Flow properties were within limits, and SDF2 showed best flow (angle of repose: 22.23°). SDF2 also exhibited the highest drug release (94.95% ± 2.07%) and micro particle size (173–186 µm). As a whole, SDF2 (drug: carrier 1:2) was chosen as the optimal formulation...

**Keywords:** Furosemide, Solid dispersions, Solubility enhancement, Eudragit polymers

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## INTRODUCTION

Oral administration is the most popular route of administration owing to the convenience, no need for medical instruments and relatively low cost, which is more suitable for chronic disease control and patients treated at home. It is also considered to enhance patient compliance than parenteral administration as it frequently needs healthcare monitoring and sometimes could be painful, might carry infection risk<sup>1-4</sup>. Oral drug delivery is favoured for its ease of use, patient compliance, and cost-effectiveness<sup>5,6</sup>. However, poorly water-soluble drugs, such as Furosemide, pose significant challenges in achieving optimal therapeutic efficacy due to limited bioavailability.<sup>7,8</sup> Solid dispersion techniques have emerged as a practical approach to enhancing the solubility of such drugs.<sup>9,10</sup> By dispersing drug in a polymer matrix, solid dispersions enhance the dissolution rate and bioavailability, making them a promising strategy for solubility enhancement.<sup>11,12</sup> This study aimed to develop and optimize Furosemide solid dispersions to enhance drug solubility, release rate, and stability. Solid dispersions were prepared using Eudragit L100 and S100 as carriers.<sup>13,14</sup> These efforts highlight the potential of solid dispersions for improving therapeutic outcomes.<sup>15,16</sup>

## MATERIALS AND METHODS

### Preparation of Solid Dispersions

Formulation development of solid dispersion of Furosemide was carried with the carrier ratios and solvent evaporation method.<sup>17</sup>

**Table 1: Formulation Table for Solid Dispersions**

Batch No	Drug: Carrier	Ratio
SDF1	FUR : Eudragit L100	1:1
SDF2	FUR : Eudragit L100	1:2
SDF3	FUR : Eudragit S100	1:1
SDF4	FUR : Eudragit S100	1:2

### Preparation of physical mixtures of furosemide solid dispersion: Physical mixture with Eudragit L100

The physical mixtures of furosemide with Eudragit L100 were prepared using different proportions/ratios of carrier viz, 1:1, 1:2, & 1:4. Powders were blended using the geometric proportion method using a glass mortar pestle.<sup>18</sup>

### Evaluation of Solid Dispersions

Furosemide solid dispersion batches were evaluated and characterized for different physical parameters such as appearance, color, and odour by visual observation.<sup>19</sup>

### Saturation solubility

Solid dispersions of furosemide were prepared and placed into 25 mL stoppered flasks containing distilled water. The samples were shaken for 24 hours : 25°C to ensure equilibrium. Afterward, the mixtures were filtered through Whatman filter paper followed by a 0.45 µm membrane.

The resulting filtrates were diluted with distilled water and analyzed at 276 nm using a UV-VIS spectrophotometer to determine the furosemide concentration.

The measurements were conducted three times, and the average solubility was determined.<sup>20</sup>

### Flow Properties of Solid Dispersion

#### Bulk density

Bulk density of respective solid dispersions was determined by calculating the proportions of the sample's mass : volume (cm<sup>3</sup>). For this, 5 g of solid dispersion was transferred to a graduated cylinder of size 2mL, and occupied volume was calculated. Formula used for bulk density:

Bulk Density (g/mL) = Mass of Sample in gm / Volume Accumulated in mL.

#### Tapped density

Tapped density was measured by transferring 10 g of powder into a 50 mL graduated cylinder using a glass funnel. The volume was calculated after tapping was done, Formula for Tapped Density:

Tapped Density (g/mL) = Mass of Sample in gm / Volume Accumulated in mL.<sup>21,22</sup>

#### Angle of Repose

The angle of repose refers to the angle formed between horizontal plane and surface of a powder pile.

#### Method:

The angle of repose was determined by allowing the powder blend to flow through a funnel positioned at a height of 4 cm on a burette stand. A sheet of graph paper was placed beneath the funnel to collect the resulting powder pile. The height (h) and radius (r) of the pile were accurately measured, and the angle of repose was calculated using the formula:

$$\theta = \tan^{-1}(h/r)$$

Where:

h = Pile Height

r = Pile Radius.<sup>9,10</sup>

#### Specifications of Angle of Repose

**Less than 20°:** Powders with an angle of repose under 20 degrees exhibit **excellent flowability**, indicating minimal friction between particles and ease of movement.

**20° to 30°:** Powders within this range are classified as having **good flowability**, and suitable for most practical applications.

**30° to 34°:** Powders with an angle of repose in this range show **passable flowability**, indicating moderate resistance to flow that may require adjustments during handling or processing.

**Greater than 40°:** Powders with an angle of repose exceeding 40 degrees exhibit **very poor flowability**, reflecting significant inter-particle friction and difficulty in achieving smooth flow.<sup>23</sup>

#### Drug Content Uniformity:

Solid dispersions containing an equivalent of 10 mg of furosemide were accurately weighed and dissolved in 10

mL of methanol. A 2.5 mL sample was taken and diluted to 25 mL with distilled water in a volumetric flask. The solution was filtered using Whatman filter paper, followed by a 0.45 µm cellulose nitrate membrane. The filtrate was further diluted and analyzed spectrophotometrically at 276 nm, using methanol: distilled water as the blank. Drug content was calculated using a calibration curve within the 5–25 µg/mL range and determined using the formula:

#### %Drug Content □

(Practical amount of solid dispersion/Theoretical amount of solid dispersion) \*100.<sup>24</sup>

### Drug Release Studies from Solid Dispersions

Dissolution testing was conducted using a USP apparatus II with formulations containing approximately 40 mg of furosemide. The test was performed in 900 mL of simulated gastrointestinal fluid (SGF, pH 1.2) maintained at 37 ± 0.5°C, with the paddle speed set at 50 revolutions per minute. At predetermined intervals over 1 hour, 5 mL aliquots were withdrawn while maintaining consistent test conditions. The drug content in the samples was determined using a double-beam UV spectrophotometer at 276 nm.<sup>25</sup>

#### Particle Size Determination:

Particle size of the prepared solid dispersions was evaluated : Simple Sieve Analysis Method.<sup>26</sup>

### Evaluation : Furosemide solid dispersions

The table below summarizes the results for the percentage practical yield, drug content, and solubility of all solid dispersions prepared using the solvent evaporation and kneading techniques.

#### Percent Yield, Drug Content, and Solubility

It outlines the percent yield, drug concentration by weight, and solubility values for the developed batches. The percent yield ranged from 67.9% to 95.4%, with SDF2 exhibiting the highest yield (95.4%), indicating minimal material loss during formulation and processing. This high yield may be attributed to optimal solvent evaporation and polymer-drug compatibility.

The drug concentration by weight was highest in SDF2 (97.63 ± 0.270%), followed closely by SDF1 (96.61 ± 0.005%), suggesting efficient drug loading in these formulations. In contrast, SDF3 and SDF4 showed slightly lower drug content, possibly due to variation in polymer ratios or minor processing losses.

Solubility enhancement was observed in all solid dispersions compared to pure Furosemide (0.0697 ± 0.002 mg/mL). Among the formulations, SDF2 again demonstrated the highest solubility (0.1100 ± 0.001 mg/mL), followed by SDF3 (0.1030 ± 0.002 mg/mL) and SDF1 (0.1010 ± 0.001 mg/mL), highlighting the success of the solid dispersion technique in improving aqueous solubility of the poorly water-soluble drug.<sup>27</sup>

#### Flow Properties, Drug Release, and Particle Size Analysis

The flow properties were assessed through bulk density, tapped density, and angle of repose. All formulations showed acceptable flow characteristics, with angle of

repose values ranging from 22.23° to 29.65°. Notably, SDF2 exhibited the best flow (22.23°), indicative of reduced interparticle friction and improved powder handling.

Drug release studies demonstrated a significant enhancement in release profile compared to pure drug. SDF2 achieved the highest drug release (94.95 ± 2.07%), which correlates well with its higher solubility and drug content. SDF3 and SDF4 showed moderate release (78.47% and 75.29% respectively), whereas SDF1 had a relatively lower release of 65.3 ± 2.98%.<sup>28</sup>

The particle size of all solid dispersion batches was within the desired micron range (173–186 µm). SDF2 had the smallest particle size (173 ± 4 µm), which may have further contributed to its improved dissolution behaviour due to increased surface area.<sup>29</sup>

#### Observations

Solid dispersions of Furosemide were evaluated for preformulation characteristics. The observations include bulk density, tapped density, particle size, and angle of repose. These parameters indicated good flow properties and uniform dispersion. Drug content was found to be uniform across all batches. The dissolution profile of the optimized batch showed a significant enhancement in drug release compared to pure Furosemide, confirming improved solubility due to dispersion in the polymer matrix.

Drug releases from the solid dispersions prepared were significantly higher. Thus, this availability of the dissolved furosemide from the solid dispersion indicated higher absorption and higher bioavailability. The solid dispersion formulation resulted in formation of fine dispersion with a small particle size that permitted faster rate of drug release.

Batch with Eudragit L100, 1:2 gave better release and good results as compared to the other ratios used. The improved dissolution of furosemide from solid dispersions attributed factors influence mechanism dissolution enhancement. Key contributors include the loss of crystallinity (i.e., conversion to an amorphous state), increased wettability and dispersibility, as well as a reduction in particle size. According to the dissolution data of the physical mixtures, the observed enhancement may primarily result from improved wettability and dispersibility.

With the growing number water insoluble drugs, there is an increasing demand for advancements in drug formulation technologies. Solid dispersions serve for particle size reduction. Upon dissolution, drug becomes molecularly dispersed dissolution medium. Method facilitates drug release poorly water-soluble drug and highly soluble carriers.

Particles in solid dispersions exhibited improved porosity. This enhancement in porosity is also influenced by carrier properties. Solid dispersions, linear polymers tend to generate larger, more porous particles compared to those made with reticular polymers, leading to an increased dissolution rate. Moreover, the higher porosity of these particles contributes to an accelerated drug release profile.<sup>30,31</sup>

#### RESULTS AND DISCUSSION

##### Percent Yield, Drug Content, and Solubility

Solid dispersions showed yields ranging from 67.9% to 95.4%. Drug content was highest for SDF2 (97.63%). Solubility of pure Furosemide was 0.0697 mg/mL, whereas SDF2 showed highest solubility of 0.1100 mg/mL.

**Table-2: Physical parameters of solid dispersions**

Batch No	Practical yield in %	Drug content in %	Solubility in mg/ml
Furosemide Pure	-	-	0.0697 ± 0.002
SDF1	77.5	96.61±0.005	0.1010±0.001
SDF2	95.4	97.63±0.270	0.1100±0.001
SDF3	75.4	85.61±0.007	0.1030±0.002
SDF4	67.9	88.50±0.002	0.1001±0.002

Data are expressed: mean ± standard deviation from three repetitions.

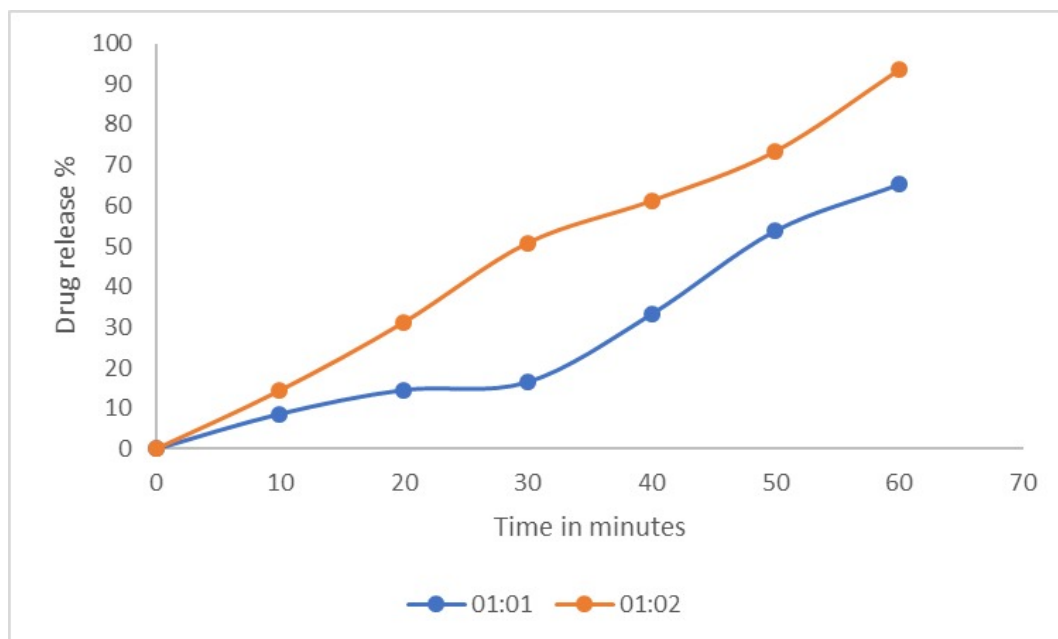
##### Flow Properties, Drug Release, and Particle Size Analysis

Flow properties were acceptable with an angle of repose between 22.23°–29.65°. SDF2 exhibited best flow (22.23°). Drug release was significantly enhanced; SDF2 showed maximum release (94.95% ± 2.07%). Particle size was in micron range (173–186 µm).

**Table 3: Physical parameters of Furosemide solid dispersions**

Batch No	Bulk density in g cm <sup>-3</sup>	Tapped- density	Angle of repose in 0	Drug release in %	Particle size in µm
SDF1	0.255±6	0.322±6	29.65±6	65.3±2.98	186±6
SDF2	0.254±6	0.317±6	22.23±6	94.95±2.07	173±4
SDF3	0.324±6	0.416±6	23.89±6	78.47±1.95	178±6
SDF4	0.344±6	0.402±6	25.62±6	75.29±1.54	176±4

Data are expressed: mean ± standard deviation from three repetitions.



Figures 1 : Percent cumulative drug release of different ratios of furosemide and Eudragit L100.

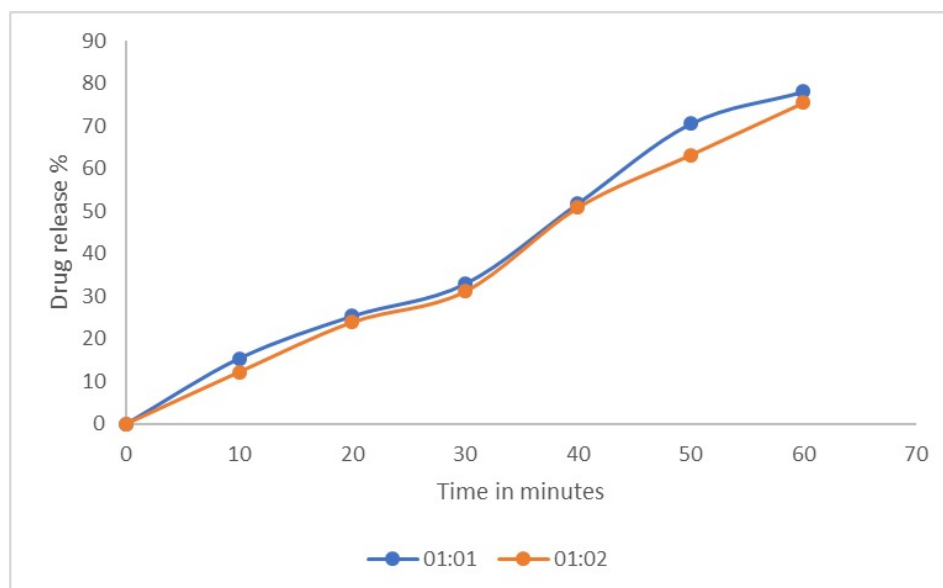


Figure 2 :Percent cumulative drug release of different ratios of furosemide and Eudragit S 100

**DISCUSSION:**

The improved dissolution of Furosemide from solid dispersions was attributed to a reduction in crystallinity, improved wettability, and smaller particle size. SDF2 (1:2 Furosemide:Eudragit L100) showed superior characteristics, establishing it as the optimized formulation.

**CONCLUSION**

The solid dispersions of Furosemide demonstrated significant improvements in solubility, drug release, and physical properties. Among all formulations, SDF2 (Furosemide:Eudragit L100, 1:2) was found to be optimal, with the highest solubility (0.1100 mg/mL), drug content (97.63%), favorable flow properties, and maximum drug release (94.95%). These findings highlight the potential of solid dispersions in improving the oral bioavailability of poorly water-soluble drugs.

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