Valuing Best Poloxamer Carrier for Thiocolchicoside Solid Dispersions

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ABSTRACT

Introduction: The present attempt is aimed to discover the best Poloxamer grade as solid dispersion carrier by taking Thiocolchicoside as a model drug.

Methods: The compatibility of Thiocolchicoside with excipients used was studied by differential scanning calorimetry and Fourier Transform Infrared Spectroscopy. Different formulations of solid dispersions were prepared by using Poloxamer carriers viz., Poloxamer-108, Poloxamer-188, Poloxamer-237, Poloxamer-338, and Poloxamer-407 were prepared by taking Thiocolchicoside: Poloxamer in the ratios ranged from 1:1, 1:2, 1:4 and 1:6. The solid dispersions were prepared by a novel microwave fusion method and compressed using an 8 station tablet compression machine. The fabricated solid dispersion tablets were evaluated for physicochemical characteristics and drug release rates. The release of Thiocolchicoside from the prepared solid dispersions was further analyzed by kinetic models.

Results: Thiocolchicoside was found to be compatible with the Poloxamer carriers used. The solid dispersion formulations were shown satisfactory physicochemical characteristics and Thiocolchicoside release which follows first order release.

Conclusion: Among the Poloxamer carriers used, Poloxamer-188 was found to be the best carrier for increasing the solubility and release rate of Thiocolchicoside from the solid dispersions.

Keywords: Thiocolchicoside, Poloxamer, solid dispersions, evaluation

INTRODUCTION

In Industry the pharmacist makes so many trials with the aim to increase the solubility of the drugs which are poorly soluble, in an inexpensive way. Among the different techniques of increasing solubility, solid dispersion technique was attaining the fame as it is simple, easy and non-tedious compared to other techniques available in the preparation of solid dispersions.

Thiocolchicoside (TCS) is a colchicoside derivative (Gloriosa superba) and Colchicum autumnale. TCS is commonly prescribed a muscle relaxant for the treatment of painful muscle contractions, acute and arthritic problems and pains...
which devoid of sedative side effects unlike other muscle relaxants have. It is prescribed in combination with many NSAIDs\textsuperscript{2-5}. TCS is a yellow crystalline powder which is slightly soluble in Ethyl alcohol and insoluble in chloroform.

The traditional method of preparing solid dispersions by fusion, in which the polymer carriers used for solid dispersions does not expose to a uniform heat from the heat source. To overcome this novel microwave melting technique is adopted. Electromagnetic irradiation in a microwave oven is ranged from 0.3 to 300 GHz of infrared and radio frequencies which resembles wavelengths of 1 mm to 1 m. This technique can be used to get rapid and constant heating even in materials presenting low heat conductivity (E.g., polymers), because the transfer of energy does not trust on heat diffusion\textsuperscript{6, 7}. So, this novel microwave melting method was adopted in the preparation of solid dispersions.

Many researchers succeeded in increasing the solubility of the drugs using Poloxamer viz., Poloxamer- 108 \textsuperscript{8}, Poloxamer- 188 \textsuperscript{9}, Poloxamer- 237 \textsuperscript{10}, Poloxamer- 338 \textsuperscript{11} and Poloxamer- 407 \textsuperscript{12}.

So it is important to increase the solubility of TCS, faster release, absorption and action to relief acute suffering patients. On the other hand for researchers to know which Poloxamer carrier is best for releasing TCS among Poloxamer- 108, Poloxamer- 188, Poloxamer- 237, Poloxamer- 338 and Poloxamer- 407. The present exploration was to increase the solubility of TCS with Poloxamer carriers and finding out the best among the better Poloxamer,

**MATERIALS AND METHODS**

\textit{Materials}

Thiocolchicoside was procured from Yarrow chemicals. (Poloxamer- 108, Poloxamer- 188, Poloxamer- 237, Poloxamer- 338 and Poloxamer- 407) were obtained from Amrutha organics, Hyderabad. Microcrystalline Cellulose, Talc, and Magnesium stearate were acquired from Colorcon, India. Double distilled water was used whenever desirable.

\textit{Solubility studies}

TCS pure drug was tested for solubility in 0.1N HCl, water, pH 4.5 Acetate buffer, pH 6.8 and pH 7.4 Phosphate buffers\textsuperscript{13}.
**Drug-excipient compatibility studies**

The DSC and FTIR studies were carried out to find the interaction among the TCS and carriers used in the study.

**Differential Scanning Calorimetry (DSC)**

Pure drug (TCS), 1:1 ratio of TCS and carriers (solid dispersions) were subjected to the analysis. About 10 mg sample was taken in the pierced DSC aluminum pan and scanned in the temperature range of 50-300°C (DSC-50, Shimadzu, Japan).

**Fourier-transform infrared (FTIR) spectroscopic study**

The interactions between components of the solid dispersions were investigated using FTIR spectroscopy. The FTIR spectra of the TCS alone and in combination with carriers were recorded using an FTIR spectrometer (Bruker) by scanning at 4000-400 cm⁻¹ range.

**Designing of Solid dispersions (physical mixture)**

The drug and carrier solid dispersions were prepared by microwave-induced heating technique \(^\text{14}\). Different ratios of TCS and Carrier were taken (Table 1) into a glass beaker and subjected to microwaves at 560 W in a scientific microwave oven (model # CATA- 2R, Catalytic Systems, Pune, India). Only one beaker at a point of time was placed inside the microwave oven in an accurate place. The samples were exposed to microwave radiation for predetermined durations (3, 4, 5 and 6 min). Then the beakers containing the samples were maintained at room temperature for the samples to solidify \(^\text{15}\). The solid dispersions were collected and placed in a glass desiccator for 24 h and then the product was pulverized using a mortar and pestle. The pulverized powders were passed through an 80# sieve. The various formula of TCS solid dispersions with Poloxamers was shown in table 1.

| Table 1. Drug (Thiocolchicoside): Carrier (Poloxamer) ratios in various formulations |
|--------------------------------------|-----------------|-----------------|
| Drug: Carrier                        | Ratio           | Formulation code |
| TCS: Poloxamer-108                   | 1:1             | TP108-1          |
Evaluation of solid dispersions

Flow properties for solid dispersions

The designed solid dispersions were evaluated for Micromeritic properties viz., angle of repose, true and tapped densities, Carr’s Index, Hausner ratio \(^{16,17}\).

Yield

The % recovery of formulated solid dispersion was resolute after complete removal of moisture. Thus % recovery calculation involves the weight of dried Solid dispersion to sum of the weight of the drug and pharmaceuticals required for the formulation.

\[
% \text{Yield} = \frac{\text{Actual weight of the solid dispersions}}{\text{Total weight of the drug and excipients}} \times 100
\]
Tablet preparation and characterization

In this study, SDs equivalent to TCS were fabricated by direct compression\textsuperscript{18} into the tablet dosage form, after mixing with required amounts of different ingredients as shown in table 2 by using 8 station tablet compression machine (Karnavati Engineering, Ahmedabad, India).

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Quantity per tablet (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid dispersions equivalent to 4 mg of Thiocolchicoside</td>
<td>125</td>
</tr>
<tr>
<td>Lactose</td>
<td>50</td>
</tr>
<tr>
<td>Starch</td>
<td>15</td>
</tr>
<tr>
<td>Micro Crystalline Cellulose</td>
<td>50</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>5</td>
</tr>
<tr>
<td>Talc</td>
<td>5</td>
</tr>
<tr>
<td>The weight of the tablets</td>
<td>250</td>
</tr>
</tbody>
</table>

Evaluation of tablets

The following parameters were tested for TCS solid dispersion tablets\textsuperscript{19-22}.

Morphological characteristics

In this study, tablets were verified for their uniformity in size and shape.

Thickness

The prepared tablets were assessed for their thickness using vernier Calipers (Qumes Enterprises, Mumbai, India). These trails were made in triplicates.

Hardness

The force required to break the prepared tablets were noted using Monsanto tablet hardness tester (Vinsyst Technologies, Mumbai) to know the mechanical strength. These tests were performed in triplicates.
**Uniformity in weight**

20 tablets from each batch were weighed individually using an electronic digital balance (Citizen, CY-104, Mumbai, India) and calculated the average weight and compared with the individual tablet weights. From this, the percentage weight difference was calculated and then checked for IP specifications (Limit ± 7.5% of average weight).

**Friability**

The physical strength of prepared tablets and to check the intactness of prepared tablets when subjected to physical tremor, this test was performed using Roche Friabilator. 10 tablets were weighed before the test ($W_{\text{initial}}$) and moved into a friabilator. The equipment was run at a speed of 25 rpm for the period of 4 minutes and the final weight of tablets ($W_{\text{final}}$) was determined. The loss on friability was then measured by the following equation.

$$F = \frac{W_{\text{initial}} - W_{\text{final}}}{W_{\text{initial}}} \times 100$$

**Thiocolchicoside calibration curve**

The process of determining TCS by UV spectrophotometer at 259 nm was standardized and the drug was found to obey Beer-Lambert’s law in 2-10 µg/mL concentration.

**Uniformity of the drug content**

5 tablets from each batch were taken and weighed and crushed in a mortar and pestle. A weight equal to 4 mg of TCS was dissolved in 100 mL of 0.1M HCl. From this 0.2 mL sample was taken later diluted to 10 mL 0.1M HCl. The absorbance was determined at 259 nm with double beam UV-Visible spectrophotometer (Lab India, Mumbai). The content uniformity was calculated from TCS standard calibration graph.

**Dissolution rate/in-vitro drug release**

The dissolution specifications were as below.
Apparatus used: USP XXIII dissolution test apparatus
Dissolution medium: 0.1M HCl
Volume of dissolution medium: 900 mL
Temperature: 37±0.5°C
Speed of basket paddle: 50 rpm
Sampling intervals: 5 min
Sample withdraws: 10 mL
Absorbance measured at: 259 nm

Kinetic modeling of drug release
The mechanisms of the drug release from the prepared tablets were analyzed and rate kinetics of the dosage form was obtained with the formula shown below. 26, 27
- Cumulative percentage of drug released Vs. Time (Zero order plots)
- Log cumulative percentage of drug remaining Vs Time (First-order plots)
- Cube root of drug remaining Vs. time (Hixson Crowell’s plots)

Accelerated Stability studies of Thiocolchicoside solid dispersions
The prepared TCS solid dispersions tablets were further subjected to stability studies for a period of 6 months under stressed storage conditions to know its strength under the augmented storage conditions (Environmental Chamber- Model 5532) 28.

RESULTS
The present study aimed to prepare novel and efficient solid dispersions of TCS with Poloxamer carriers using MWF technique. In contrast to it, the feasibility of TCS with the carriers used was confirmed by the DSC thermograms which were shown in figure 1.
Figure 1. DSC thermograms of Thiocolchicoside with Poloxamer bases

The compatibility of the TCS drug with the Poloxamer carriers was established by FTIR studies and the FTIR spectra of the TCS with Poloxamer carriers used were shown in figure 2.
Figure 2. FTIR spectrum of Thiocolchicoside with Poloxamer

The prepared solid dispersions were checked for flow properties to confirm their free movements from hopper to tableting machine die wall without adhesion. The flow properties of fabricated TCS solid dispersions were shown in table 3.

Table 3. Flow character specifications

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Angle of repose (°)</th>
<th>Bulk density</th>
<th>Tapped density</th>
<th>Carr's Index</th>
<th>Hausner Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP108-1</td>
<td>33.95±0.03</td>
<td>0.785±0.05</td>
<td>0.799±0.06</td>
<td>1.752±0.01</td>
<td>1.017±0.01</td>
</tr>
<tr>
<td>TP108-2</td>
<td>29.64±0.05</td>
<td>0.458±0.02</td>
<td>0.466±0.01</td>
<td>1.716±0.08</td>
<td>1.017±0.01</td>
</tr>
<tr>
<td>TP108-3</td>
<td>28.45±0.02</td>
<td>0.635±0.01</td>
<td>0.654±0.06</td>
<td>2.905±0.02</td>
<td>1.029±0.02</td>
</tr>
<tr>
<td>TP108-4</td>
<td>29.05±0.05</td>
<td>0.258±0.01</td>
<td>0.268±0.01</td>
<td>3.731±0.05</td>
<td>1.038±0.01</td>
</tr>
<tr>
<td>TP188-1</td>
<td>27.37±0.09</td>
<td>0.528±0.03</td>
<td>0.536±0.04</td>
<td>1.492±0.01</td>
<td>1.015±0.01</td>
</tr>
<tr>
<td>TP188-2</td>
<td>31.22±0.06</td>
<td>0.568±0.07</td>
<td>0.578±0.04</td>
<td>1.730±0.03</td>
<td>1.017±0.03</td>
</tr>
<tr>
<td>TP188-3</td>
<td>31.55±0.05</td>
<td>0.258±0.01</td>
<td>0.268±0.01</td>
<td>3.731±0.07</td>
<td>1.038±0.09</td>
</tr>
<tr>
<td>TP188-4</td>
<td>25.84±0.06</td>
<td>0.269±0.05</td>
<td>0.287±0.02</td>
<td>6.271±0.05</td>
<td>1.066±0.05</td>
</tr>
</tbody>
</table>
TP237-1  26.37±0.05  0.356±0.03  0.398±0.01  10.552±0.09  1.117±0.01
TP237-2  30.50±0.05  0.524±0.05  0.545±0.03  3.853±0.04  1.040±0.03
TP237-3  29.41±0.03  0.425±0.03  0.457±0.01  7.002±0.09  1.075±0.03
TP237-4  29.15±0.04  0.546±0.04  0.555±0.06  1.621±0.05  1.016±0.07
TP338-1  30.50±0.05  0.365±0.05  0.389±0.02  6.169±0.06  1.065±0.08
TP338-2  29.12±0.06  0.358±0.01  0.364±0.02  1.648±0.01  1.016±0.01
TP338-3  25.21±0.03  0.452±0.03  0.457±0.01  0.877±0.05  1.008±0.01
TP338-4  26.09±0.06  0.254±0.08  0.259±0.01  1.930±0.01  1.019±0.07
TP407-1  26.27±0.04  0.524±0.01  0.541±0.03  3.142±0.02  1.032±0.02
TP407-2  30.28±0.06  0.658±0.05  0.666±0.01  1.201±0.01  1.012±0.01
TP407-3  34.52±0.02  0.524±0.05  0.566±0.01  7.420±0.09  1.080±0.08
TP407-4  28.46±0.06  0.254±0.08  0.259±0.01  1.847±0.01  1.018±0.01

All values mentioned as mean ±SD; number of trials (n=3)

The fabricated TCS tablets were observed to have a uniform in size, shape, off white in colour, odorless with a smooth surface. The thickness of prepared formulations, uniformity of weight, hardness, friability, the percent yield, and drug content uniformity were shown in table 4.

Table 4. Physical Characteristics of Prepared solid dispersions

<table>
<thead>
<tr>
<th>Physical parameter</th>
<th>Formulation</th>
<th>Uniformity of weight (mg)</th>
<th>Hardness (cm²)</th>
<th>Thickness (mm)</th>
<th>Friability (%)</th>
<th>Yield (%)</th>
<th>Assay (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP108-1</td>
<td>250.2±2.01</td>
<td>6.5±0.21</td>
<td>4.50±0.01</td>
<td>0.18±0.02</td>
<td>88.2±0.85</td>
<td>102.5±1.23</td>
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</tr>
<tr>
<td>TP108-2</td>
<td>254.3±1.25</td>
<td>5.2±0.09</td>
<td>4.53±0.02</td>
<td>0.62±0.07</td>
<td>89.3±0.65</td>
<td>96.7±0.44</td>
<td></td>
</tr>
<tr>
<td>TP108-3</td>
<td>255.2±0.12</td>
<td>6.9±0.08</td>
<td>4.50±0.03</td>
<td>0.53±0.04</td>
<td>90.5±0.94</td>
<td>99.5±0.77</td>
<td></td>
</tr>
<tr>
<td>TP108-4</td>
<td>255.2±0.98</td>
<td>5.3±0.06</td>
<td>4.51±0.04</td>
<td>0.45±0.03</td>
<td>99.2±0.32</td>
<td>100.6±0.48</td>
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</tr>
<tr>
<td>TP188-1</td>
<td>255.1±0.65</td>
<td>4.9±0.07</td>
<td>4.51±0.02</td>
<td>0.51±0.01</td>
<td>96.8±0.65</td>
<td>97.8±0.05</td>
<td></td>
</tr>
<tr>
<td>TP188-2</td>
<td>250.9±0.54</td>
<td>4.5±0.01</td>
<td>4.53±0.02</td>
<td>0.62±0.09</td>
<td>98.8±1.25</td>
<td>97.3±0.85</td>
<td></td>
</tr>
<tr>
<td>TP188-3</td>
<td>252.3±0.96</td>
<td>5.7±0.01</td>
<td>4.50±0.04</td>
<td>0.53±0.03</td>
<td>97.8±1.95</td>
<td>96.2±0.06</td>
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</tr>
<tr>
<td>TP188-4</td>
<td>253.8±0.08</td>
<td>6.3±0.02</td>
<td>4.51±0.06</td>
<td>0.55±0.04</td>
<td>98.6±3.26</td>
<td>99.0±2.25</td>
<td></td>
</tr>
<tr>
<td>TP237-1</td>
<td>250.5±0.17</td>
<td>5.3±0.03</td>
<td>4.50±0.02</td>
<td>0.61±0.01</td>
<td>95.6±0.68</td>
<td>100.6±0.08</td>
<td></td>
</tr>
<tr>
<td>Code</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
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<td></td>
</tr>
<tr>
<td>TP237-2</td>
<td>250.1±0.07</td>
<td>4.5±0.04</td>
<td>4.50±0.06</td>
<td>0.82±0.01</td>
<td>92.5±0.84</td>
<td>97.1±0.84</td>
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<tr>
<td>TP237-3</td>
<td>254.2±0.84</td>
<td>5.2±0.02</td>
<td>4.51±0.01</td>
<td>0.45±0.02</td>
<td>95.6±1.39</td>
<td>96.8±0.16</td>
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</tr>
<tr>
<td>TP237-4</td>
<td>252.2±0.63</td>
<td>6.0±0.01</td>
<td>4.50±0.04</td>
<td>0.35±0.03</td>
<td>98.5±1.28</td>
<td>97.3±0.08</td>
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<tr>
<td>TP338-1</td>
<td>251.3±0.83</td>
<td>5.3±0.02</td>
<td>4.50±0.02</td>
<td>0.51±0.05</td>
<td>92.3±0.94</td>
<td>96.1±0.09</td>
<td></td>
</tr>
<tr>
<td>TP338-2</td>
<td>252.3±0.10</td>
<td>4.5±0.01</td>
<td>4.51±0.03</td>
<td>0.72±0.01</td>
<td>90.7±0.83</td>
<td>98.5±0.09</td>
<td></td>
</tr>
<tr>
<td>TP338-3</td>
<td>251.2±0.54</td>
<td>7.2±0.07</td>
<td>4.52±0.08</td>
<td>0.63±0.02</td>
<td>97.4±0.64</td>
<td>97.8±0.75</td>
<td></td>
</tr>
<tr>
<td>TP338-4</td>
<td>250.2±1.28</td>
<td>8.3±0.04</td>
<td>4.50±0.03</td>
<td>0.25±0.03</td>
<td>98.3±0.88</td>
<td>96.6±0.84</td>
<td></td>
</tr>
<tr>
<td>TP407-1</td>
<td>250.2±2.26</td>
<td>4.5±0.03</td>
<td>4.51±0.05</td>
<td>0.41±0.03</td>
<td>92.8±1.23</td>
<td>98.9±0.99</td>
<td></td>
</tr>
<tr>
<td>TP407-2</td>
<td>251.2±2.39</td>
<td>4.2±0.02</td>
<td>4.52±0.03</td>
<td>0.52±0.01</td>
<td>96.8±1.29</td>
<td>100.9±2.25</td>
<td></td>
</tr>
<tr>
<td>TP407-3</td>
<td>250.1±1.25</td>
<td>6.3±0.01</td>
<td>4.50±0.04</td>
<td>0.53±0.03</td>
<td>97.9±0.86</td>
<td>97.8±0.23</td>
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</tr>
<tr>
<td>TP407-4</td>
<td>252.1±1.24</td>
<td>5.2±0.01</td>
<td>4.51±0.03</td>
<td>0.65±0.07</td>
<td>99.1±0.35</td>
<td>99.6±0.09</td>
<td></td>
</tr>
</tbody>
</table>

All values mentioned as mean ±SD; number of trials (n=3).

The main theme of preparing solid dispersions is to increase the solubility of drugs. The solubility of prepared solid dispersions was studied in various solvents. The solubility of prepared tablets was found good in distilled water and 0.1N HCl. These values were shown in figure 3.
Figure 3. Solubility of Thiocolchicoside and solid dispersions in various media with
A) Poloxamer-108; B) Poloxamer-188; C) Poloxamer-237; D) Poloxamer-338;
E) Poloxamer-407

Later TCS release from the tablets was studied by *in vitro* drug dissolution. The TCS release from the tablets was determined by plotting a calibration curve of TCS as per the procedure described before and the calibration curve as shown in figure 4.
The solubility of TCS SDs was further proved by *in vitro* drug dissolution studies. All the prepared SDs showed satisfactory drug release pattern. The SDs containing TCS: Poloxamer in the ratio of 1:6 showed good release pattern compared to other formulations and shown in figure 5.
Figure 5. *In vitro* drug dissolution plots of Thiocolchicoside solid dispersions with A) Poloxamer-108; B) Poloxamer-188; C) Poloxamer-237; D) Poloxamer-338; E) Poloxamer-407.

The drug release mechanism from prepared tablets formulations was determined by kinetic treatment of *in vitro* drug dissolution data. The correlation ($R^2$) values were shown in table 5. First order and Hixson Crowell’s plots were shown in figure 6 and 7.
Figure 6. First order plots for formulations with the drug: carrier ratio (1:6)

Figure 7. Hixson Crowell’s plots for formulations with the drug: carrier ratio (1:6)

Table 5. Correlation coefficients ($R^2$) for different release kinetics of Thiocolchicoside solid dispersions

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Zero order</th>
<th>First order</th>
<th>Hixson Crowell’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP108-4</td>
<td>0.9738</td>
<td>0.9936</td>
<td>0.9979</td>
</tr>
<tr>
<td>TP188-4</td>
<td>0.5025</td>
<td>0.9885</td>
<td>0.9868</td>
</tr>
<tr>
<td>TP407-4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TP237-4</td>
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DISCUSSION

The DSC study is the vital tool for obtaining quick evidence about possible interactions between the drug and the carrier by the presence, swing, or vanishing of endothermic/exothermic peaks\textsuperscript{29}. DSC gives a vision into melting and recrystallization activities of SDs. Neither loss of characteristic peaks nor arrival of new peaks were documented upon DSC analyses and confirms the no illogicality between the drug and the carrier used\textsuperscript{30}. The DSC points were attained on pure TCS and physical blend. The thermograms of TCS with Poloxamer combinations were shifted towards left indicating proper impregnation of TCS with carriers used. The characteristic peaks and stretches of TCS pure drug were also found in TCS – Poloxamer carrier combinations indicates no incompatibility of TCS with carriers used.

FTIR spectroscopy is another significant approach to inspect possible chemical interactions among the drug and excipients. The generation and expansion of new absorption bands give the main gestures of the interaction between the drug and the active substance\textsuperscript{31}. The FTIR spectra revealed that typical bands of TCS and polymer individually were not reformed in the physical mixtures, which confirms no interactions between TCS and Poloxamer used.

The spectra of TCS show prominent bands at 1556.6 cm\(^{-1}\), which attributes to the C=O stretching, Tropane ring at 1647.6 \textsuperscript{-1}, Amide II band (N-H stretching) at 3326.98 \textsuperscript{-1} and –OH stretching band at 3413.77 \textsuperscript{-1}. All these bands were found undisturbed even in TCS-Poloxamer blends and are given in Figure 2.

The free flow nature of prepared SDs from the hopper for compression was confirmed by the micromeritic properties. The fabricated TCS SDs showed very good flow properties as the angle of repose (34.52±0.02 to 25.21±0.03\(^{o}\)) as they have nearly spherical particles. The compressibility Index was between 0.877±0.05 to 10.552±0.09, indicating good compression properties while tableting. The fabricated Thiocolchicoside tablets were observed to have a uniform in size, shape, off white in colour, odourless with a smooth surface.
The prepared tablets were found to have a uniform thickness (4.5 mm) and weight indicating the drug and excipients used were added and properly blended. The loss on friability was less than 1% and the hardness was more than 4 Kg/cm² indicating that the prepared tablets having good mechanical strength, this indicates good cohesive properties of solid dispersions for compressing them into tablets. The yield was found to be good (>90%) and the drug content was also found to be uniform.

TCS pure drug checked for its solubility in various media viz., Water, 0.1N HCl, pH 4.5 Acetate buffer, pH 6.8 Phosphate buffer and pH 7.4 Phosphate buffer. The solubility of these was found to have solubility <0.3 µg/ml in indicating the poor solubility of the drug.

The solid dispersion tablets with Poloxamer-108 (TP108-1, TP108-2, TP108-3 and TP108-4) showed good solubility in 0.1 N HCl (up to 0.61±0.05 µg/mL) and in distilled water (up to 0.49±0.03µg/mL). The solid dispersion tablets with Poloxamer-188 (TP188-1, TP188-2, TP188-3 and TP188-4) showed good solubility in distilled water (up to 0.78±0.04 µg/mL) and in 0.1 N HCl (up to 0.68±0.05 µg/mL). The solid dispersion tablets with Poloxamer P-237 (TP237-1, TP237-2, TP237-3 and TP237-4) showed good solubility in 0.1 N HCl (up to 0.58±0.04 µg/mL) and in Acetate buffer (pH 6.8) (up to 0.45±0.03 µg/mL). The solid dispersion tablets with Poloxamer-338 (TP338-1, TP338-2, TP338-3 and TP338-4) showed good solubility in distilled water (up to 0.69±0.04 µg/mL), in 0.1 N HCl (up to 0.68±0.05µg/mL). The solid dispersion tablets with Poloxamer-407 (TP407-1, TP407-2, TP407-3 and TP407-4) showed good solubility in distilled water (up to 0.68±0.05 µg/mL) and in 0.1M HCl (up to 0.58±0.03 µg/mL). The nonionic surfactant property of Poloxamer increases the solubility of Thiocolchicoside in solvents32, 33.

Thiocolchicoside followed Beer’s Lamberts law at the concentration of (2 to 10 µg/mL). The regression (R² value was found to be 0.9998 with the slope of 0.0743x+0.0149. The dissolution of compressed solid dispersion tablets was found good in formulations containing Thiocolchicoside: Poloxamer ratios 1:6 with all carriers viz., Poloxamer-108, Poloxamer-188, Poloxamer-237, Poloxamer-338 and Poloxamer-407.

In addition, the hydrophilic polyoxyethylene part of the co-polymer barred aggregation of individual drug particles, exhibiting high solid-liquid surface tension. Hence, it acted on the hydrodynamic layer adjacent the drug particles ensuing in an in situ inclusion progression that augmented dissolution. It was responsible for
pulling more, insoluble but finely mixed drug into the dissolution medium. Similar observations have been reported for solid dispersions by Viraj et al, 2010. The regression ($R^2$) value was found to be 0.9930, 0.9869, 0.9868, 0.8869 and 0.9980 for first order plots and 0.9979, 0.9868, 0.9206, 0.9860 and 0.9804 for Hixson Crowell’s models for formulations TP108-4, TP188-4, TP237-4, TP338-4 and TP407-4. Accelerated stability studies for the optimized formulation (TP188-4) revealed that these formulations were retained their physical parameters even after stressed storage conditions.

CONCLUSION
The attempt of increasing the solubility was successful using various Poloxamer carriers in 1:6 ratios of drug and carrier (TP108-4, TP188-4, TP237-4, TP338-4 and TP407-4) by making them into solid dispersion formulations. Microwave fusion (MVF) method was better among other techniques of preparing solid dispersions as MWF technique makes the exposure of drug and polymers to a uniform temperature and prevents overheating. TCS and Poloxamer interactions were studied using DSC and FTIR confirms the suitability polymer carrier with TCS. All the solid dispersions were found to increase the solubility of TCS compared to pure drug. Among the SDs the preparations with 1:6 ratio of TCS and Poloxamer-188 (TP188-4) was found to have better solubility, and drug dissolution characteristics compared to (Poloxamer-108, Poloxamer-237, Poloxamer-338, and Poloxamer-407). The advance in formulation technology MWF technique is better than other conventional SDs preparation technique in term of preparation, and drug release. Hence I can conclude that Poloxamer-188 is the best Poloxamer carrier compared to Poloxamer-108, Poloxamer-237, Poloxamer-338, and Poloxamer-407 for preparing Thiocolchicoside solid dispersions.

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Conflict of Interest:
No conflict of interest was declared by the authors.
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