Research Paper

Formulation and Evaluation of Directly Compressible Agglomerates of Celecoxib

V. Rama Mohan Gupta*, K. Srikanth, B. Sree Giri Prasad, G. Naveen Kumar Reddy and B. Sudheer

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ABSTRACT: Prepared spherical crystals of Celecoxib to increase the compressible properties, dissolution rate and bioavailability, using hydrophilic polymers such as PEG-4000, sod.CMC, sod.alginate and PVP K-30. All the formulations were characterized for micromeritic properties, Drug loading, solubility, in vitro drug release and mean dissolution time (MDT). New formulations showed higher dissolution rates and less MDT values than the pure celecoxib. Among all, the crystals prepared with 10 % w/v PVP K-30 exhibited maximum dissolution rate (2.95 ± 0.23%) and very less MDT values (18.50 ± 4.01 min). Hence it was considered as optimized formulation.

KEY WORDS: Celecoxib; Compressibility; Flow properties; Hydrophilic polymers; MDT

Introduction

Insoluble and poorly soluble compounds pose a significant development challenge in formulation field. Therapeutic effectiveness of any drug depends upon the bioavailability which inturn, depends on the dissolution rate of drug molecules. Mechanical micronization of crystalline drugs and incorporation of surfactants during the crystallization process are the techniques commonly used to improve the bioavailability of poorly soluble drugs. The micronization process was found to alter the flow and compressibility of crystalline powders and cause formulation problems. Incorporation of surfactants generally led to less significant increase in aqueous solubility. To overcome this problem, Kawashima et al., 1982, 1984 developed a spherical crystallization technique that led to improving the flow, direct compressibility, dissolution rate, solubility and ultimately bioavailability of many drugs.

Non-steroidal anti-inflammatory drugs (NSAID’s) are used for analgesic, antiphlogistic and antipyretic effects. Today more than 100 NSAIDs preparations are on the market and some are under clinical investigation. The widely prescribed NSAIDs like indomethacin, flurbiprofen, rofecoxib and celecoxib, are poorly soluble, poorly compressible and are more or less irritant to the gastric mucosa. Due to their poor solubility, they have erratic dissolution patterns. The literature survey revealed that celecoxib exhibits poor compressible characteristics (Garima Chawla et al., 2003) and also incomplete, poor oral bioavailability and low aqueous solubility, (G.V.M.M. Babu et al., 2002) and hence it is a suitable candidate for spherical crystallization process to improve the dissolution rate and solubility. Hence, the improvement of compressibility and aqueous solubility in such a case is a valuable goal to improve therapeutic efficacy by increasing the bioavailability. The spherical crystals of celecoxib with HPMC have been investigated (Paradkar et al., 2002), to improve micromeric properties of celecoxib, but the aqueous solubility of spherically crystallized drug was not satisfactorily improved. Therefore, in the present study it was planned to prepare spherical crystals of celecoxib to increase the compressibility characteristics, aqueous solubility, dissolution rate and bioavailability besides improving its micromeric properties using more hydrophilic polymers such as PEG-4000, sod.CMC, sod. alginate and PVP K-30.

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Materials and Methods

Materials

Celecoxib was a gift sample from Aurabindo Pharma, Hyderabad, India. Croscarmellose sodium, crospovidone, sodium starch glycolate a gift sample from Zydus Cadila Healthcare Ltd., Ahmedabad, India. Polyvinylpyrrolidone, Polyethylene glycol 4000, sodiumalginate, sodium carboxymethylcellulose, chloroform, acetone, methanol, sodium lauryl sulphate, methanol (HPLC Grade), water (HPLC grade), acetonitrile (HPLC grade) were obtained from S.D. Fine Chemicals Ltd., Mumbai, India.

Methods

Preparation of Spherical Agglomerates

A solution of celecoxib (2 g) in acetone (3 ml) was added to a solution of hydrophilic polymer (2.5—10% w/v) in 100 ml distilled water. Four hydrophilic polymers namely PVP K 30, PEG-4000, sod.CMC, sod.alginate were used for preparation of spherical agglomerates. The mixture was stirred continuously using mechanical stirrer (Remi Motors, Mumbai, India) at 500 rpm to obtain spherical agglomerates. The bridging liquid (chloroform; 0.5 ml) was added, dropwise. The agglomerates were separated by filtration using Whatman filter paper (No. 1) and dried for 24 h, at room temperature.

Characterization

Infrared spectroscopy, differential scanning calorimetry (DSC) and X-ray diffraction studies

The infrared (IR) spectra of powder celecoxib, physical mixture and the agglomerates were recorded on an IR-spectrophotometer (FTIR 8300, Shimadzu, Japan) by the KBr pellet technique. Differential scanning calorimetry (DSC) analysis was performed using a DSC-60 calorimeter (Shimadzu). The instrument was equipped with a TA-60WS thermal analyzer, FC-60A flow controller and TA-60 software. Samples of celecoxib, physical mixture and agglomerates were hermetically sealed in an aluminum crucible and heated at a rate of 5 °C min⁻¹ up to 200 °C under a nitrogen atmosphere (30 mL min⁻¹). A similar empty pan was used as the reference. Powder X-ray diffraction patterns (XRD) of the pure drug and spherical agglomerates were obtained using an X-ray diffractometer (Seifert 3003 TT, Germany).

The results are given in Table 1 and graphically the data has been shown in Fig 1-15

<table>
<thead>
<tr>
<th>S. No</th>
<th>Sample</th>
<th>Major peaks (wave numbers, cm⁻¹)</th>
<th>Chemical moity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pure celecoxib</td>
<td>3341.51</td>
<td>-NH str., primary amine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1164.58</td>
<td>S=O asymmetric str.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1347.75</td>
<td>S=O symmetric str.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1274.96, 1229.99</td>
<td>-CF₃</td>
</tr>
<tr>
<td>2</td>
<td>10% w/v PEG spherical crystals</td>
<td>3341.09</td>
<td>NH str., primary amine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1164.76</td>
<td>S=O asymmetric str.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1347.81</td>
<td>S=O symmetric str.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1274.81, 1230.07</td>
<td>-CF₃</td>
</tr>
<tr>
<td>3</td>
<td>10% w/v Sodium alginate</td>
<td>3341.12</td>
<td>NH str., primary amine</td>
</tr>
<tr>
<td></td>
<td>spherical crystals</td>
<td>1164.72</td>
<td>S=O asymmetric str.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1347.75</td>
<td>S=O symmetric str.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1274.82, 1229.99</td>
<td>-CF₃</td>
</tr>
<tr>
<td>4</td>
<td>10% w/v Sodium CMC spherical</td>
<td>3341.04</td>
<td>NH str., primary amine</td>
</tr>
<tr>
<td></td>
<td>crystals</td>
<td>1164.68</td>
<td>S=O asymmetric str.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1347.68</td>
<td>S=O symmetric str.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1274.81, 1229.97</td>
<td>-CF₃</td>
</tr>
<tr>
<td>5</td>
<td>10% w/v PVP spherical crystals</td>
<td>3341.15</td>
<td>NH str., primary amine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1164.58</td>
<td>S=O asymmetric str.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1347.68</td>
<td>S=O symmetric str.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1274.82, 1229.92</td>
<td>-CF₃</td>
</tr>
</tbody>
</table>
Fig. 1 FTIR spectra of celecoxib pure drug.

Fig. 2 FTIR spectra of celecoxib spherical agglomerates prepared with PEG 4000.

Fig. 3 FTIR spectra of celecoxib spherical agglomerates prepared with sodium CMC.
Fig. 4 FTIR spectra of celecoxib spherical agglomerates prepared with sodium alginate.

Fig. 5 FTIR spectra of celecoxib spherical agglomerates prepared with PVP K 30.

Fig. 6 DSC thermogram of celecoxib pure drug.
Fig. 7 DSC thermogram of spherical crystals of celecoxib prepared with PEG 4000

Fig. 8 DSC thermogram of spherical crystals of celecoxib prepared with sodium CMC

Fig. 9 DSC thermogram of spherical crystals of celecoxib prepared with sodium alginate

Fig. 10 DSC thermogram of spherical crystals of celecoxib prepared with PVP K 30
Fig. 11 XRD spectra of celecoxib pure drug.

Fig. 12 XRD spectra of celecoxib spherical agglomerates prepared with PEG 4000.

Fig. 13 XRD spectra of celecoxib spherical agglomerates prepared with sodium CMC.
Micromeritic properties

The particle size distribution was studied by the sieve analysis method, Martin et al., 2002. The shape of the crystals was observed under an optical microscope (10x magnification) attached to a computer. The loose bulk density (LBD) and tapped bulk density (TBD) of plain celecoxib and its spherical crystals were determined using a bulk density test apparatus (Kumar Industries, India). Carr’s index and Hausner’s ratio were calculated using LBD and TBD values, Wells et al., 2002. The angle of repose was assessed by the fixed funnel method. A known amount of agglomerates were allowed to flow through a funnel fixed at a constant height (h) and the height and diameter (2r) of the pile of powder were measured to calculate the angle of repose as \( \tan \theta = h/r \). The results are given in Table 2.

Scanning electron microscopy

The surface morphology of the agglomerates was assessed by scanning electron microscopy (SEM) (Leica StereoScan 430, LEO, UK). The crystals were splutter coated with gold before scanning.

Drug loading

The drug loading efficiency of crystals was determined by dissolving 100 mg of crystals in 100 mL of methanol, followed by measuring the absorbance of appropriately diluted solution, spectrophotometrically (PharmaSpec UV-1700, UV-Vis spectrophotometer, Shimadzu) at 253.5 nm. The results are given in Table 3.
Table 2  Micromeritic properties of celecoxib spherical crystals prepared using different hydrophilic polymers

<table>
<thead>
<tr>
<th>Spherical Crystals</th>
<th>LBD (g/ml)</th>
<th>TBD (g/ml)</th>
<th>Carrs Index (%)</th>
<th>Hausners ratio</th>
<th>Angle of Repose</th>
<th>True Density (g/ml)</th>
<th>Porosity (%)</th>
<th>Particle size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sod.algi (2.5%w/v)</td>
<td>0.32±0.01*</td>
<td>0.42±0.01*</td>
<td>19.0±1.32*</td>
<td>1.25±0.02*</td>
<td>31.69±1.85*</td>
<td>1.29±0.17</td>
<td>66.3±1.96</td>
<td>298.53±11.23</td>
</tr>
<tr>
<td>Sod.algi (5.0%w/v)</td>
<td>0.40±0.02*</td>
<td>0.45±0.01*</td>
<td>11.11±1.62*</td>
<td>1.125±0.03*</td>
<td>24.77±1.98*</td>
<td>1.287±0.12</td>
<td>65.03±2.31</td>
<td>530.88±19.63</td>
</tr>
<tr>
<td>Sod.algi (7.5%w/v)</td>
<td>0.40±0.02*</td>
<td>0.42±0.01*</td>
<td>4.76±1.82*</td>
<td>1.05±0.02*</td>
<td>34.42±2.01*</td>
<td>1.24±0.09</td>
<td>67.74±2.90</td>
<td>1333.52±28.33</td>
</tr>
<tr>
<td>Sod.algi (10.0%w/v)</td>
<td>0.35±0.01*</td>
<td>0.40±0.02*</td>
<td>10.10±1.05*</td>
<td>1.10±0.02*</td>
<td>30.12±1.32*</td>
<td>1.36±0.10</td>
<td>70.7±2.12</td>
<td>1888±25.36</td>
</tr>
<tr>
<td>PEG-4000 (2.5%w/v)</td>
<td>0.37±0.01*</td>
<td>0.41±0.01*</td>
<td>10.00±1.31*</td>
<td>1.10±0.01*</td>
<td>28.12±1.30*</td>
<td>1.28±0.18</td>
<td>65±2.01</td>
<td>530.88±12.26</td>
</tr>
<tr>
<td>PEG-4000 (5.0%w/v)</td>
<td>0.32±0.03*</td>
<td>0.42±0.02*</td>
<td>19.0±1.81*</td>
<td>1.23±0.01*</td>
<td>30.31±2.10*</td>
<td>1.26±0.18</td>
<td>66.75±3.0</td>
<td>891.25±11.15</td>
</tr>
<tr>
<td>PEG-4000 (7.5%w/v)</td>
<td>0.35±0.02*</td>
<td>0.40±0.02*</td>
<td>10.10±1.05*</td>
<td>1.15±0.03*</td>
<td>36.12±1.20*</td>
<td>1.21±0.10</td>
<td>71.0±2.61</td>
<td>1000±13.5</td>
</tr>
<tr>
<td>PEG-4000 (10.0%w/v)</td>
<td>0.37±0.01*</td>
<td>0.31±0.02*</td>
<td>9.67±1.25*</td>
<td>1.08±0.02*</td>
<td>26.78±2.13*</td>
<td>1.36±0.11</td>
<td>68.0±1.54</td>
<td>1188.5±18.2</td>
</tr>
<tr>
<td>Sod.CMC (2.5%w/v)</td>
<td>0.37±0.02*</td>
<td>0.42±0.01*</td>
<td>11.1±1.01*</td>
<td>1.16±0.01*</td>
<td>28.12±1.78*</td>
<td>1.30±0.1</td>
<td>68±2.55</td>
<td>789.8±13.23</td>
</tr>
<tr>
<td>Sod.CMC (5.0%w/v)</td>
<td>0.38±0.02*</td>
<td>0.44±0.02*</td>
<td>13.6±1.58*</td>
<td>1.15±0.01*</td>
<td>23.80±2.32*</td>
<td>1.285±0.10</td>
<td>66.77±2.26</td>
<td>944±13.21</td>
</tr>
<tr>
<td>Sod.CMC (7.5%w/v)</td>
<td>0.28±0.01*</td>
<td>0.31±0.01*</td>
<td>9.67±1.01*</td>
<td>1.10±0.02*</td>
<td>35.73±2.11*</td>
<td>1.26±0.12</td>
<td>78.38±1.79</td>
<td>1000±1122</td>
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<tr>
<td>Sod.CMC (10.0%w/v)</td>
<td>0.29±0.01*</td>
<td>0.32±0.01*</td>
<td>10.01±1.20*</td>
<td>1.08±0.02*</td>
<td>26.78±2.25*</td>
<td>1.31±0.13</td>
<td>69.1±2.33</td>
<td>1412.53±15.3</td>
</tr>
<tr>
<td>PVP K 30 (2.5%w/v)</td>
<td>0.42±0.01*</td>
<td>0.45±0.01*</td>
<td>10.20±1.51*</td>
<td>1.18±0.01*</td>
<td>29.31±1.23*</td>
<td>1.22±0.12</td>
<td>59.55±2.36</td>
<td>201.1±10.18</td>
</tr>
<tr>
<td>PVP K 30 (5.0%w/v)</td>
<td>0.40±0.02*</td>
<td>0.45±0.01*</td>
<td>10.10±2.36*</td>
<td>1.10±0.02*</td>
<td>26.47±2.31*</td>
<td>1.25±0.26</td>
<td>65.15±2.16</td>
<td>218.13±12.10</td>
</tr>
<tr>
<td>PVP K 30 (7.5%w/v)</td>
<td>0.37±0.01*</td>
<td>0.41±0.01*</td>
<td>10.10±2.12*</td>
<td>1.10±0.01*</td>
<td>25.61±1.89*</td>
<td>1.28±0.10</td>
<td>71.05±3.01</td>
<td>230.25±11.77</td>
</tr>
<tr>
<td>PVP K 30 (10.0%w/v)</td>
<td>0.39±0.01*</td>
<td>0.44±0.01*</td>
<td>10.10±2.69*</td>
<td>1.10±0.01*</td>
<td>22.88±1.65*</td>
<td>1.25±0.16</td>
<td>64.32±1.36</td>
<td>235.1±12.23</td>
</tr>
<tr>
<td>Pure Celecoxib</td>
<td>0.30±0.0</td>
<td>0.52±0.02</td>
<td>42.00±2.36</td>
<td>1.69±0.03</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>85.55±10.25</td>
</tr>
</tbody>
</table>

All values are expressed as Mean ± SE, n= 3; p < 0.05 compared to pure celecoxib.
Table 3  Drug content and solubility data of the celecoxib spherical crystals and pure drug celecoxib

<table>
<thead>
<tr>
<th>Spherical crystals</th>
<th>Drug content (%)</th>
<th>Solubility (μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Water</td>
</tr>
<tr>
<td>Sod.Alginate (2.5%)</td>
<td>97.18 ± 1.58</td>
<td>3.501 ± 0.28 *</td>
</tr>
<tr>
<td>Sod.Alginate (5.0 %)</td>
<td>98.28 ± 2.18</td>
<td>3.551 ± 0.61 *</td>
</tr>
<tr>
<td>Sod.Alginate (7.5 %)</td>
<td>94.82 ± 1.81</td>
<td>3.928 ± 0.31 *</td>
</tr>
<tr>
<td>Sod.Alginate(10.0%)</td>
<td>93.61 ± 2.26</td>
<td>4.49 ± 0.59*</td>
</tr>
<tr>
<td>PEG-4000 (2.5 %)</td>
<td>94.87 ± 1.81</td>
<td>3.1648 ± 0.30 *</td>
</tr>
<tr>
<td>PEG-4000 (5.0 %)</td>
<td>94.27 ± 1.31</td>
<td>4.0167 ± 0.59 *</td>
</tr>
<tr>
<td>PEG-4000 (7.5%)</td>
<td>92.81 ± 2.50</td>
<td>4.1023 ± 0.91*</td>
</tr>
<tr>
<td>PEG-4000 (10.0%)</td>
<td>95.80 ± 1.80</td>
<td>4.58 ± 0.67 *</td>
</tr>
<tr>
<td>Sod.CMC (2.5 %)</td>
<td>96.49 ± 1.81</td>
<td>3.18 ± 0.25 *</td>
</tr>
<tr>
<td>Sod.CMC (5.0 %)</td>
<td>95.30 ± 2.81</td>
<td>3.26 ± 0.43 *</td>
</tr>
<tr>
<td>Sod.CMC (7.5%)</td>
<td>91.15 ± 1.08</td>
<td>3.59 ± 0.95 *</td>
</tr>
<tr>
<td>Sod.CMC (10.0%)</td>
<td>94.25 ± 1.29</td>
<td>4.02 ± 0.21 *</td>
</tr>
<tr>
<td>PVP K 30 (2.5 %)</td>
<td>95.75 ± 1.25</td>
<td>4.02 ± 0.25 *</td>
</tr>
<tr>
<td>PVP K 30 (5.0 %)</td>
<td>93.89 ± 2.26</td>
<td>4.54 ± 0.69 *</td>
</tr>
<tr>
<td>PVP K 30 (7.5%)</td>
<td>95.61 ± 2.12</td>
<td>5.28 ± 0.95 *</td>
</tr>
</tbody>
</table>

**Solubility studies**

A quantity of crystals (about 100 mg) was shaken with 10 mL of distilled water and a solution of sodium lauryl sulphate (SLS) (2%, m/V) in a shaking water bath (100 agitations per min) for 24 h at room temperature. The solution was then passed through a 0.45 mm membrane filter and the amount of the drug dissolved was analyzed spectrophotometrically. The results are given in Table – 3.

**In vitro dissolution studies**

The in vitro dissolution studies were carried out using 8 station USP XXIII dissolution testing apparatus (Electrolab, Mumbai, India) for three hours. The dissolution medium used was 900 ml of distilled water and 2 % w/v sodium lauryl sulphate. The agglomerates containing 100 mg of celecoxib and celecoxib agglomerates prepared using different concentrations of hydrophilic polymers were weighed and then introduced into the dissolution medium. The medium was stirred at 100 rpm using paddle at 37 ± 0.5 °C. The samples were collected and analyzed, spectrophotometrically.

The percentage drug release and MDT data of all spherical crystals were compared with the pure celecoxib data. The results are given in Table 4.

**Statistical analysis**

The results were analyzed by two tailed Student’s t-test using the Graph Pad Instat Software (GPIS; Version: 1.13), (Muthalik et al., 2006). The mean dissolution time (MDT) was calculated using the Origin software.
### Table 4 Percentage of drug release at the end of 180 min and mean dissolution time and pure drug celecoxib

<table>
<thead>
<tr>
<th>Spherical Crystals</th>
<th>Water</th>
<th>SLS (2% w/v)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CXB Released (%)</td>
<td>CXB Released (%)</td>
</tr>
<tr>
<td></td>
<td>(180 min)</td>
<td>(180 min)</td>
</tr>
<tr>
<td></td>
<td>MDT (min)</td>
<td>MDT (min)</td>
</tr>
<tr>
<td>Sod.Alginate (2.5%)</td>
<td>2.21 ± 0.31</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>20.16 ± 2.85*</td>
<td>60.16 ± 3.58*</td>
</tr>
<tr>
<td>Sod.Alginate (5%)</td>
<td>2.33 ± 0.29</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>19.56 ± 2.16*</td>
<td>58.46 ± 2.76*</td>
</tr>
<tr>
<td>Sod.Alginate (7.5%)</td>
<td>2.25 ± 0.44</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>21.87 ± 3.51*</td>
<td>59.61 ± 1.27*</td>
</tr>
<tr>
<td>Sod.Alginate (10%)</td>
<td>2.20 ± 0.33</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>22.06 ± 2.68*</td>
<td>61.79 ± 2.15*</td>
</tr>
<tr>
<td>PEG 4000 (2.5%)</td>
<td>2.28 ± 0.58</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>19.60 ± 3.15*</td>
<td>66.56 ± 4.28*</td>
</tr>
<tr>
<td>PEG 4000 (5%)</td>
<td>2.38 ± 0.20</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>19.16 ± 3.26*</td>
<td>53.79 ± 5.19*</td>
</tr>
<tr>
<td>PEG 4000 (7.5%)</td>
<td>2.16 ± 0.22</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>20.15 ± 1.28*</td>
<td>67.16 ± 3.58*</td>
</tr>
<tr>
<td>PEG 4000 (10%)</td>
<td>2.10 ± 0.58</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>20.68 ± 2.26*</td>
<td>55.68 ± 2.78*</td>
</tr>
<tr>
<td>Sod. CMC (2.5%)</td>
<td>2.09 ± 0.32</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>18.79 ± 3.15*</td>
<td>61.56 ± 5.34*</td>
</tr>
<tr>
<td>Sod. CMC (5%)</td>
<td>2.15 ± 0.21</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
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<td>19.16 ± 3.75*</td>
<td>59.76 ± 4.68*</td>
</tr>
<tr>
<td>Sod. CMC (7.5%)</td>
<td>2.19 ± 0.43</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
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<td></td>
<td>20.18 ± 4.16*</td>
<td>62.66 ± 5.12*</td>
</tr>
<tr>
<td>Sod. CMC (10%)</td>
<td>2.06 ± 0.23</td>
<td>100 ± 0.0 (180 min)</td>
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<td></td>
<td>17.85 ± 2.56*</td>
<td>58.75 ± 4.62*</td>
</tr>
<tr>
<td>PVP K 30 (2.5 %)</td>
<td>2.28 ± 0.41</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>21.89 ± 3.23*</td>
<td>61.56 ± 5.34*</td>
</tr>
<tr>
<td>PVP K 30 (5.0 %)</td>
<td>2.39 ± 0.55</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
<td></td>
<td>20.19 ± 4.56*</td>
<td>59.76 ± 4.68*</td>
</tr>
<tr>
<td>PVP K 30 (7.5%)</td>
<td>2.65 ± 0.51</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
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<td></td>
<td>20.08 ± 5.66*</td>
<td>62.66 ± 5.12*</td>
</tr>
<tr>
<td>PVP K 30 (10.0%)</td>
<td>2.95 ± 0.23*</td>
<td>100 ± 0.0 (180 min)</td>
</tr>
<tr>
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<td>18.50 ± 4.01*</td>
<td>58.75 ± 4.62*</td>
</tr>
<tr>
<td>Pure Celecoxib</td>
<td>1.80 ± 0.20</td>
<td>100 ± 0.0 (90 min)</td>
</tr>
<tr>
<td></td>
<td>49.25 ± 3.01</td>
<td>24.89 ± 3.66*</td>
</tr>
</tbody>
</table>

### Results and Discussion

FTIR spectra and DSC studies of all the batches of agglomerates showed that, the drug was stable in the prepared formulations indicating no interaction between celecoxib and hydrophilic polymers. The data has been graphically represented in Fig 1-10

Comparison of powder X-ray diffraction spectra of celecoxib and spherical agglomerates indicate considerable decrease in crystallinity of spherical agglomerates. After the recrystallization no polymorphic phenomenon is detected, as all powder X-ray diffraction patterns of primary crystals consisting of agglomerates were consistent with the pattern of original crystals. The data is graphically presented in Fig 11-15.

The shape of agglomerates was spherical with all the batches, except with the agglomerates of sodium alginate wherein the shape was irregular.

All the batches of spherical agglomerates showed good packability, flowability and compressibility compared to pure celecoxib. Spherical crystals prepared with hydrophilic polymer PVP K-30 were shown to have uniform size and spherical shape and exhibited good micromeritic properties compared to spherical crystals prepared with other hydrophilic polymers.

The drug content of spherical agglomerates was high and uniform in all batches indicating no loss of drug during crystallization process.

From the results of solubility and dissolution studies, the spherical agglomerates prepared from PVP K-30 (10% w/v) showed maximum solubility and drug release in water compared to pure drug and other batches of spherical agglomerates. The data is graphically presented in Fig 18.

The spherical crystals as well as pure drug exhibited high dissolution rate in 2% w/v SLS solution (dissolution medium), due to surfactant effect on the drug and complete dissolution of drug was observed within 90-180 minutes. Owing to availability of very large surface area due to fineness of powder, pure drug exhibited high dissolution rate and low MDT, but here also the spherical agglomerates prepared with 10% PVP K-30 showed very low MDT value compared to other spherical agglomerates. The data is graphically presented in Fig 16 & 17.

Hence, the spherical agglomerates prepared with 10% w/v PVP K-30 is selected as optimized batch.
Fig. 16 Percentage Drug Release at the end of 180min from all Formulations

Fig. 17 Mean Dissolution Time of All Formulations

Fig. 18 Drug Solubility from Celecoxib Spherical Crystals of All formulations
Then optimized batch of spherical crystals were made into dense compacts with 10%w/w of sodium starch glycolate, crosspovidone and crosscarmellose-sodium, separately to study the effect of super disintegrant on dissolution in water and 2% w/v SLS solution as dissolution medium and compared with the market product (capsule).

The drug release in water from dense compacts prepared with 10% crosscarmellose-sodium as super disintegrant and the market product were found to be almost similar.

Also, the release of drug in 2% w/v SLS solution as dissolution medium was found to be 100% within 45 and 60 minutes from the market product and dense compacts prepared with 10% crosscarmellose-sodium, respectively. The reason for faster release of drug in case of capsules (market product) may be due to lesser particle size of drug which might have enhanced the dissolution in 2% w/v SLS solution.

It indicates that the efficiency of our formulation is comparable to that of market product (capsule).

**Conclusion**

Spherical agglomeration technique may be useful to improve flow properties of poorly compressible celecoxib drug. This technique has not only shown improvement in the flow properties but also showed enhancement in the solubility and dissolution rate of celecoxib.

**References**


