FORMULATION, DEVELOPMENT, AND EVALUATION OF TOLPERISONR HYDROCHLORIDE FILM-COATED TABLETS

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ABSTRACT

Among all the different routes of administration, oral route of administration continues to be the most preferred route due to various advantages including ease of ingestion, avoidance of pain, versatility and most importantly patient compliance. Likewise, among all dosage forms tablet is the most popular dosage form existing today because of its convenience of self-administration, compactness and easy manufacturing. Sometimes immediate onset of action is considered obligatory immediate release tablets are the final option. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer and lead to better patient compliance. In the present work, we engage in discussion about formulation, development, and evaluation of immediate release tablets. An immediate release dosage form allows a manufacturer to extend market exclusivity. They are also a tool for expanding markets, extending product life cycles and generating opportunities. Pharmaceutical products designed for oral delivery and currently available on the prescription and over-the-counter markets are mostly the immediate rel

Objective

The objective of this study was to formulate and evaluate Tolperisone hydrochloride film-coated tablets using wet granulation and compression technique, and to investigate their physical and chemical properties.

Methodology

Pre-formulation studies were performed to assess the physicochemical properties of Tolperisone hydrochloride. Formulations were prepared using wet granulation and compression technique. The prepared tablets were subjected to various physicochemical evaluations such as weight variation, thickness, hardness, friability, drug content, disintegration time, and in-vitro release studies.

Findings

The formulated Tolperisone hydrochloride film-coated tablets were found to be acceptable with regard to their physical and chemical properties. The tablets showed uniformity in weight, thickness, and drug content. The friability values of the tablets were within the acceptable limits. The disintegration time of the tablets was found to be within the specified limits. In vitro release studies showed that the formulation exhibited sustained release of the drug substance.

Significance

The study reveals that Tolperisone hydrochloride film-coated tablets can be successfully formulated using the wet granulation and compression technique, which is a cost-effective method. The developed formulation can be a potential alternative for commercially available tablets. The study also supports the development of sustained-release formulations of Tolperisone hydrochloride.
Keywords
Tolperisone hydrochloride, film-coated tablets, wet granulation, compression, sustained-release.

Introduction
Among all the different routes of administration, oral route of administration continues to be the most preferred route due to various advantages including ease of ingestion, avoidance of pain, versatility and most importantly patient compliance. Likewise among all dosage forms tablet is the most popular dosage form existing today because of its convenience of self-administration, compactness and easy manufacturing. Sometimes immediate onset of action is considered obligatory immediate release tablets are the final option. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer and lead to better patient compliance. In the present work, we engage in discussion about formulation, development, and evaluation of immediate release tablets. An immediate release dosage form allows a manufacturer to extend market exclusivity. They are also a tool for expanding markets, extending product life cycles and generating opportunities.

Pharmaceutical products designed for oral delivery and currently available on the prescription and over-the-counter markets are mostly the immediate release type, which are designed for immediate release of drug for rapid absorption. Immediate release drug delivery systems are designed to provide immediate drug levels in short period of time. In recent decades, a variety of pharmaceutical research has been conducted to develop new dosage forms considering quality of life, most of these efforts have been focused on ease of medication. Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer, has quick onset of action is economical and lead to better patient compliance. They are also a tool for expanding markets, extending product life cycles and generating opportunities. Superdisintegrants are first choice of excipients which are extensively used for the formulation development of the immediate release tablets as they effectively result into the immediate disintegration, release and absorption of the drug after administration into the body. Cross carmelllose sodium which is commonly known as Ac-di-sol is cross linked carboxy methyl cellulose sodium and sodium starch glycolate is a carboxy methyl starch and both of which are stable through hygroscopic material.

MATERIALS AND METHODS:
MATERIALS: Tolperisone HCl (Active), Hypromellose, Lactose Monohydrate, Croscarmellose Sodium, PVP K-30, Microcrystalline Cellulose, Colloidal Anhydrous Silica, Purified Talc, Magnesium Stearate, Opadry white excipient used in formulation development. Weighing balance(sartorius lab), UV-Spectrophotometer(U.V. i1900 Shimadzu, Japan), Dissolution apparatus(Electrolab), Tablet machine (Chamunda Pharma), Hardness tester(Pfizer type), Roche Friabilator(electro lab), pH Meter(Lab India), FTIR(Shimadzu, Japan.)

METHODS:
PREFORMULATION STUDY: Study of Organoleptic properties of pure drug Tolperisone Hydrochloride was tested for organoleptic properties such as appearance, solubility, odour, colour, melting point etc.

Determination of λmax and calibration curve of drug
Preparation of diluent
Mixed water and methanol in the ratio of 20:80 v/v mix well.

Determination of λmax
Weigh and transfer 160 mg of Tolperisone Hydrochloride into 200 ml volumetric flask add 150 ml diluent sonicated to dissolve. Make up with diluent mix well. Further transfer 5 ml of above solution into 50 ml volumetric flask make up with diluent mix well, to obtain the concentration of 80µg/ml. It was scanned for maximum absorbance by UV-spectrophotometer (Shimadzu, Japan) in range of 200-400 nm using diluent as a blank.

Preparation of standard calibration curve of Tolperisone Hydrochloride
Weigh and transfer 160 mg of Tolperisone Hydrochloride into 200 ml volumetric flask add 150 ml diluent sonicated to dissolve. Make up with diluent mix well. This solution was used as stock solution. Further transfer of 1 ml, 2.5 ml, 3.7 ml,
5 ml and 6 ml of stock solution were transferred in to series of 50 ml volumetric flask. Make up with diluent. The concentration of these solution was 16 µg/ml 40 µg/ml, 59 µg/ml, 80 µg/ml, 96 µg/ml. Finally, the absorbance of each sample was measured at 259 nm against blank phosphate buffer of pH 6.8. Standard curve of concentration vs. absorbance was plotted.

Compatibility study

The compatibility of the active substance with excipients:

Compatibility studies of all active ingredients were carried out with the commonly used excipients under stressed conditions of 60°C for 6 hours and 80°C for 30 minutes. This aided in ruling out apparently incompatible excipients. The drug and the excipients were mixed in the 1:1 ratio (drug: excipients) to make a binary mixture. To analyze the compatibility of drug and polymer the FTIR spectrum of pure drug and combination of drug with polymer was recorded by using Fourier transform infrared spectroscopy and the spectrum analysis was done.

FORMULATION DEVELOPMENT OF TOLPERISONE HYDROCHLORIDE FILM COATED TABLET

Following formulations of Tolperisone Hydrochloride film coated tablets were used for developmental work.

Table 1.1: Formulation development batches for Tolperisone HCl tablet

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Ingredients</th>
<th>F 1</th>
<th>F 2</th>
<th>F 3</th>
<th>F 4</th>
<th>F 5</th>
<th>F 6</th>
<th>F 7</th>
<th>F 8</th>
<th>F 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>For Dry Mix</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Tolperisone Hydrochloride</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
<td>50</td>
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<tr>
<td>2</td>
<td>Hypromellose</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>40</td>
<td>40</td>
<td>35</td>
<td>35</td>
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<tr>
<td>3</td>
<td>Lactose Monohydrate</td>
<td>35</td>
<td>40</td>
<td>40</td>
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<td>35</td>
<td>38</td>
<td>38</td>
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<tr>
<td>4</td>
<td>Croscarmellose Sodium (Ac-di-sol SD 711)</td>
<td>3</td>
<td>5</td>
<td>10</td>
<td>6</td>
<td>6</td>
<td>7</td>
<td>7</td>
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<td>II</td>
<td>For Paste Preparation</td>
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<td>Povidone (PVP K 30)</td>
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<td>3</td>
<td>5</td>
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<tr>
<td>6</td>
<td>Purified water</td>
<td>--</td>
<td>--</td>
<td>q.s</td>
<td>q.s</td>
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<td>7</td>
<td>Isopropyl alcohol</td>
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<td>III</td>
<td>For Lubrication</td>
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<td>8</td>
<td>Microcrystalline cellulose (PH 102)</td>
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<td>20</td>
<td>25</td>
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<td>15</td>
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<td>9</td>
<td>Croscarmellose Sodium (Ac-di-sol SD 711)</td>
<td>3</td>
<td>3</td>
<td>6</td>
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<td>10</td>
<td>Colloidal Anhydrous Silica</td>
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<td>11</td>
<td>Purified Talc</td>
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<td>12</td>
<td>Magnesium Stearate</td>
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<tr>
<td>13</td>
<td>Opadry white</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>5</td>
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<td>14</td>
<td>Total weight of Core tablet</td>
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<td>122</td>
<td>153</td>
<td>173</td>
<td>172</td>
<td>155</td>
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<tr>
<td>IV</td>
<td>Film Coating</td>
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<tr>
<td>No.</td>
<td>Name of Key Equipment</td>
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<td>Weighing Balance</td>
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<td>2</td>
<td>Vibratory Sifter</td>
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<td>3</td>
<td>Rapid Mixer Granulator</td>
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<td>4</td>
<td>Mechanical Stirrer</td>
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<td>5</td>
<td>Multimill</td>
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<td>6</td>
<td>Fluid Bed Dryer</td>
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<td>7</td>
<td>Steam Jacketed Kettle</td>
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<td>8</td>
<td>Double Cone Blender / Octagonal Blender</td>
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<td>9</td>
<td>Compression Machine B-Tooling</td>
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<td>10</td>
<td>Punch Set, Upper Punch: Circular, Shallow concave and Plain. Lower Punch: Circular, Shallow concave and Plain.</td>
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<tr>
<td>11</td>
<td>Coating Pan with Spray Gun (Bullows)</td>
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<tr>
<td>12</td>
<td>Ganscoater with Spray Gun (Spraying System)</td>
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<tr>
<td>13</td>
<td>Inspection Belt</td>
<td></td>
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</tr>
</tbody>
</table>

**MANUFACTURING PROCEDURE & INPROCESS CONTROLS:**

**General Processing Instructions:**

Line clearance checks shall be carried out before carrying out any operations of manufacturing as per current updated SOP.

All equipment and machines are to be cleaned and operated as per Standard Operating Procedure for individual equipments and machines.

Ensure the environmental conditions (Temperature, Pressure differential & Humidity) as per specific product requirement.

Ensure wearing of gloves and masks in the manufacturing area.

Use calibrated balance only.

Use appropriate balance depending upon the quantity to be dispensed.

Carry out dispensing of raw materials in dispensing area as per current updated SOPs.

All materials selection, weighing and additions to be carried out under supervision of Approved staff.

In-process checks shall be carried out wherever necessary.

Table 1.2: List of Key Equipments used in manufacturing:

<table>
<thead>
<tr>
<th>No.</th>
<th>Name of Key Equipment</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>Isopropyl Alcohol q.s</td>
</tr>
<tr>
<td>15</td>
<td>Dichloromethane q.s</td>
</tr>
<tr>
<td></td>
<td>Total weight of Coated Tab 119 124 155 176 177 160 166 167 167</td>
</tr>
</tbody>
</table>
Manufacturing Procedure:

Weighing and Dispensing:

Weigh accurately active and inactive raw materials and dispense as per the formula.

Stage- 1.0 SIFTING:

Sift below ingredients through specified mesh with the help of Vibratory Sifter:

<table>
<thead>
<tr>
<th>№</th>
<th>Ingredients</th>
<th>Sieve size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tolperisone Hydrochloride IH</td>
<td>30#</td>
</tr>
<tr>
<td>2</td>
<td>Hypromellose</td>
<td>30 #</td>
</tr>
<tr>
<td>3</td>
<td>Lactose Monohydrate BP</td>
<td>30 #</td>
</tr>
<tr>
<td>4</td>
<td>Croscarmellose Sodium USPNF (Ac-Di-Sol SD- 711)</td>
<td>30 #</td>
</tr>
</tbody>
</table>

Collect the sifted material separately in prelabeled polybags.

Stage- 2.0 DRY MIXING:

Load the previously sifted material from Stage- 1.0 to RMG and mix for 30 min with slow speed of Impeller. Chopper off.

Stage- 3.0 BINDER PREPARATION:

Take Purified Water in a Steam Jacketed Vessel & heat it to 50°C- 55°C.

Then transfer heated Purified water BP in another S.S Vessel & add slowly Povidone BP (PVP K 30) in it under continuous stirring and dissolve it completely.

Then add and mix Isopropyl Alcohol BP to above solution under continuous stirring and mix it completely and use this solution for binding.

Stage- 4.0 WET GRANULATION:

Add Stage 3.0 to Stage 2.0 under continues mixing.

If required use extra quantity of Purified Water BP and Isopropyl Alcohol BP (1:1) to form wet mass of desired consistency.

Note down the extra quantity of Purified Water BP and Isopropyl Alcohol BP used.

Stage- 5.0 WET MILLING (If required)

Pass the wet mass obtained from Stage 4.0 through 10 mm screen of multimill with knife forward direction & at a medium speed.
Stage- 6.0 DRYING:
Initially air dries the wet mass for 20 minutes in Fluid Bed Dryer (without temperature) & then at Inlet temperature 50ºC & Outlet temperature: 45ºC – 50ºC.
Record the Inlet and Outlet temperature of the FBD and drying time.
Rake the granules after every 30 min. interval.
Check the LOD on Moisture analyzer at 80ºC (Limit: 2 % to 3 % w/w)

Stage- 7.0 DRY SIFTING/SIZE REDUCTION:
Sift the dried granules from Stage 6.0 through 20# sieve by using Vibratory Sifter. Pass the oversized granules through 2.0 mm screen of multi mill with knife forward direction, at fast speed and again sift through 20# sieve of sifter.

Storage of dried granules:
Storage Condition: Store the dried granules in duly labeled double polybag inside an airtight HDPE container at temperature 20 ºC – 25ºC and Relative Humidity 45% to 55%.
Storage period: Not more than 48 hrs.

LUBRICATION:
Load the dried & sifted granules from stage 7.0 to Double Cone Blender/Octagonal Blender.
Sift the following ingredients separately with the help of Vibratory Sifter.

<table>
<thead>
<tr>
<th>No</th>
<th>Ingredients</th>
<th>Sieve size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Microcrystalline Cellulose (PH 102) BP</td>
<td>30 #</td>
</tr>
<tr>
<td>2</td>
<td>Colloidal Anhydrous Silica BP along with</td>
<td>30 #</td>
</tr>
<tr>
<td></td>
<td>Croscarmellose Sodium USPNF (Ac-Di-Sol SD- 711)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Purified talc BP</td>
<td>30#</td>
</tr>
<tr>
<td>4</td>
<td>Magnesium Stearate BP</td>
<td>30#</td>
</tr>
</tbody>
</table>

Load above sifted ingredients (without Magnesium Stearate BP) to Double Cone Blender/Octagonal Blender & mix as per limit mentioned in the below table
Add previously sifted Magnesium Stearate BP to Double Cone/Octagonal Blender, close the blender. Mix as per limit mentioned in the below table.
Table 1.3: Blending time

<table>
<thead>
<tr>
<th>Equipment Name</th>
<th>Equipment Capacity</th>
<th>RPM</th>
<th>Mixing time before addition of Magnesium Stearate</th>
<th>Mixing time after addition of Magnesium Stearate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Double cone Blender</td>
<td>50.0 L</td>
<td>35</td>
<td>5 min</td>
<td>5 min</td>
</tr>
<tr>
<td>Octagonal Blender</td>
<td>500 L</td>
<td>15</td>
<td>10 min</td>
<td>5 min</td>
</tr>
</tbody>
</table>

Storage of blend: Store the blend in duly labeled double polybag inside an airtight HDPE container at temperature 20 ºC -25ºC and Relative Humidity 45% to 55%. until released for compression.

COMPRESSION:
Transfer the blend to Compression cubicle.

Note the No. of containers transferred to the compression in BMR.

Set the Compression machine using punch sets
Upper punch : Circular, shallow concave, plain
Lower Punch: Circular, shallow concave, plain

Operate the Compression machine as per current updated SOP and Compress the lubricated granules. Certify it after compliance with the Compression Parameters and record the results.

Table 1.4: In-process Checks during compression

<table>
<thead>
<tr>
<th>No.</th>
<th>Parameter</th>
<th>Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Description</td>
<td>White to off-white colored, Circular, biconvex uncoated tablet plain on both sides.</td>
</tr>
<tr>
<td>2</td>
<td>Weight of 20 tablets</td>
<td>3.24g ± 10% (2.91 g to 3.56g)</td>
</tr>
<tr>
<td>3</td>
<td>Average weight per tablet</td>
<td>167 mg ± 10% (145.8 mg to 178.2mg)</td>
</tr>
<tr>
<td>4</td>
<td>Uniformity of Weight</td>
<td>± 10% of average weight</td>
</tr>
<tr>
<td>5</td>
<td>Hardness</td>
<td>NLT 3 kg/cm²</td>
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<tr>
<td>6</td>
<td>Friability</td>
<td>NMT 1 % w/w</td>
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<tr>
<td>7</td>
<td>Thickness</td>
<td>3.8 mm ± 0.2 mm (3.6 mm to 3.10 mm)</td>
</tr>
<tr>
<td>8</td>
<td>Diameter</td>
<td>9.0 mm ± 0.1 mm (8.9 mm to 9.1 mm)</td>
</tr>
<tr>
<td>9</td>
<td>Disintegration Time</td>
<td>NMT 15 minutes at 37ºC ± 2ºC</td>
</tr>
</tbody>
</table>
Storage of compressed tablets:

Storage condition: Store the compressed tablets in duly labeled double lined polybag inside an airtight HDPE container at temperature 20ºC-25ºC and Relative Humidity 45% - 55% until it is released for coating.

FILM COATING SUSPENSION PREPARATION:

Film coating suspension should be freshly prepared & used within 24 hrs from preparation.

Take Isopropyl Alcohol BP in clean S. S. Vessel & stir it to form a vortex. Add Opadry white slowly in it. If require increase the speed of stirrer to form vortex.

Add Dichloromethane BP and stir it for 40 min.

Filter coating suspension through 100# nylon cloth.

FILM COATING PROCESS:

Load the dedusted tablets in Coating Pan, carry out the prewarming of the tablet at 50ºC for 10 min. Inch the pan during prewarming.

Maintain the tablet bed temperature as mentioned in film coating parameters with respect to coating pan at the time of coating.

Start the coating pan, commence and continue the coating.

Spray the coating suspension on the rolling tablet bed till weight gain is achieved. The film coating suspension in the vessel should be stirred slowly during coating.

Carry out the in-process checks as per parameters given in table of In-process Checks Parameters.

After completion of film coating dry the film coated tablet in the coating pan with the hot air for 10 min. Then transfer it in to duly labeled double polybag inside an airtight HDPE container.
Table 1.5: Coating in-process checks parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Yellow colored, circular, biconvex, film coated tablet, plain on both sides.</td>
</tr>
<tr>
<td>Weight of 20 tablets</td>
<td>3.34 g ± 7.5% (3.0 g to 3.67 g)</td>
</tr>
<tr>
<td>Average Weight</td>
<td>167 mg ± 7.5% (150 mg to 183 mg)</td>
</tr>
<tr>
<td>Uniformity of Weight</td>
<td>± 7.5% of average weight</td>
</tr>
<tr>
<td>Thickness</td>
<td>3.4 mm ± 0.2 mm (3.2 mm to 3.6 mm)</td>
</tr>
<tr>
<td>Diameter</td>
<td>9.5 mm ± 0.2 mm (7.3 mm to 8.7 mm)</td>
</tr>
<tr>
<td>Disintegration Time</td>
<td>NMT 30 minutes at 37°C ± 2°C</td>
</tr>
</tbody>
</table>

Then transfer the film coated tablets in a double lined poly bag in HDPE container.

RESULTS AND DISCUSSION

PREFORMULATION STUDY

2.1 Organoleptic properties of drug

The sample of Tolperisone Hydrochloride received was studied for its organoleptic characteristics such as colour, odour, appearance. The results are given in Table 7.1

Table 1.6 Physical characteristics of drug

<table>
<thead>
<tr>
<th>Characters</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>White, Crystalline powder, it has slight characteristic odor, hygroscopic powder</td>
</tr>
<tr>
<td>Solubility</td>
<td>Very soluble in acetic acid (100%), freely soluble in water and in ethanol (95%), soluble in acetic anhydride, slightly soluble in acetone, practically insoluble in diethyl ether</td>
</tr>
<tr>
<td>Colour</td>
<td>White</td>
</tr>
<tr>
<td>Odour</td>
<td>characteristic odor</td>
</tr>
<tr>
<td>Melting point</td>
<td>167°C - 174°C</td>
</tr>
</tbody>
</table>

Preparation of standard calibration curve of Tolperisone Hydrochloride

Calibration curve was plotted by taking values of concentration and absorbance

Table 2.1: Concentration and absorbance of Tolperisone Hydrochloride

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Concentration (µg/ml)</th>
<th>Absorbance (at 259 nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>0.1653</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>0.3883</td>
</tr>
<tr>
<td>4</td>
<td>59</td>
<td>0.5727</td>
</tr>
<tr>
<td>5</td>
<td>80</td>
<td>0.7766</td>
</tr>
<tr>
<td>6</td>
<td>96</td>
<td>0.9319</td>
</tr>
</tbody>
</table>
Fig Calibration curve of Tolperisone HCl

The correlation coefficient ($R^2$) = 0.999

From the graph it is showed that it follows Beer-Lambort’s law.

Compatibility studies

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Tolperisone HCl IH + Excipients</th>
<th>Observations on Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Initial (Color)</td>
</tr>
<tr>
<td>1</td>
<td>Hyromellose</td>
<td>White Powder</td>
</tr>
<tr>
<td>2</td>
<td>Lactose Monohydrate</td>
<td>White Powder</td>
</tr>
<tr>
<td>3</td>
<td>Croscarmellose Sodium (Ac-Di-Sol SD-711)</td>
<td>White Powder</td>
</tr>
<tr>
<td>4</td>
<td>Povidone (PVP K-30)</td>
<td>White Powder</td>
</tr>
<tr>
<td>5</td>
<td>Microcrystalline Cellulose (PH 102)</td>
<td>White Powder</td>
</tr>
<tr>
<td>6</td>
<td>Colloidal Anhydrous Silica</td>
<td>White Fluffy Powder</td>
</tr>
<tr>
<td>7</td>
<td>Purified Talc</td>
<td>White Powder</td>
</tr>
<tr>
<td>8</td>
<td>Magnesium Stearate</td>
<td>White Powder</td>
</tr>
<tr>
<td>9</td>
<td>Opadry white</td>
<td>Yellow Powder</td>
</tr>
<tr>
<td>10</td>
<td>Purified Water</td>
<td>Clear Solution</td>
</tr>
</tbody>
</table>
2.1 FTIR spectra of Tolperisone Hydrochloride

Fig. 2.2: FTIR spectra of Tolperisone Hydrochloride

2.3 FTIR spectra of physical mixture Tolperisone HCl and excipients

Fig. 2.4: FTIR spectra of physical mixture Tolperisone HCl and Excipients

Summary:
No evidence of physical change was found between the active drug with excipients indicating that Tolperisone Hydrochloride IH and all excipients are compatible with each other. From the FTIR study of drug and polymer it was clear that drug and polymer are compatible.

2.2.1 EVALUATION PARAMETER

2.2.1 Precompression parameter

The powder blend of each formulation were evaluated for bulk density, tapped density, Carr’s index, Hausner’s ratio, angle of repose and result obtained are shown in Table 2.3
Table 2.5: Precompression parameter of formulations

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Bulk density (gm/cm³)</th>
<th>Tapped density(gm/cm³)</th>
<th>Carr’s index</th>
<th>Hausner ratio</th>
<th>Angle of repose (θ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.44±0.017</td>
<td>0.51±0.017</td>
<td>13.72</td>
<td>1.15</td>
<td>30°.55±0.36</td>
</tr>
<tr>
<td>F2</td>
<td>0.41±0.011</td>
<td>0.47±0.023</td>
<td>12.76</td>
<td>1.14</td>
<td>28°.80±0.33</td>
</tr>
<tr>
<td>F3</td>
<td>0.47±0.023</td>
<td>0.58±0.028</td>
<td>12.96</td>
<td>1.14</td>
<td>27°.99±2.01</td>
</tr>
<tr>
<td>F4</td>
<td>0.43±0.020</td>
<td>0.49±0.020</td>
<td>13.04</td>
<td>1.15</td>
<td>29°.40±1.01</td>
</tr>
<tr>
<td>F5</td>
<td>0.46±0.025</td>
<td>0.53±0.024</td>
<td>12.95</td>
<td>1.14</td>
<td>28°.80±1.20</td>
</tr>
<tr>
<td>F6</td>
<td>0.42±0.018</td>
<td>0.48±0.020</td>
<td>13.47</td>
<td>1.15</td>
<td>27°.95±1.01</td>
</tr>
<tr>
<td>F7</td>
<td>0.44±0.021</td>
<td>0.51±0.022</td>
<td>12.86</td>
<td>1.14</td>
<td>28°.10±1.02</td>
</tr>
<tr>
<td>F8</td>
<td>0.45±0.023</td>
<td>0.54±0.023</td>
<td>13.55</td>
<td>1.15</td>
<td>30°.75±0.67</td>
</tr>
<tr>
<td>F9</td>
<td>0.45±0.023</td>
<td>0.55±0.017</td>
<td>13.54</td>
<td>1.15</td>
<td>30°.77±0.68</td>
</tr>
</tbody>
</table>

*Values are expressed in mean ±SD (n=3)

1. Bulk density

The bulk density values less than 1.2 gm/cm³ indicate good packing and values > 1.5 gm/cm³ are indicates poor packing. The bulk density values for all formulation of powder bulk varied in the range of 0.41±0.011gm/cm³ to 0.47±0.023gm/cm³. The values obtained lies within acceptable limits.

2. Tapped density

The tapped density values for all formulation of powder bulk varied in the range of 0.47±0.023 gm/cm³ to 0.58±0.028 gm/cm³. The values obtained lies within acceptable limits.

3. Carr’s index

The percent compressibility of formulation of powder bulk was determined by Carr’s compressibility index. The percent compressibility for all formulation lies within the range of 12.76 % to 13.72 % indicates acceptable flow property.

4. Hausner’s ratio

Hausner’s ratio was found to be in the range of 1.14 to 1.15 which shows acceptable flow property and good packing ability.

5. Angle of repose

The of angle of repose for all formulation of powder blend were found to be in the range of 27°.90±2.01 to 30°.77±0.68 indicating good flow property. It can be concluded that the powder blend for all batches possess good flow characteristic.

6. Post compression parameter

All the formulations evaluated for the postcompression parameters, result obtained were shown in Table 7.4. The average weight from all the formulation were found be in the range 150.62 mg to 183.12 mg, indicates that the all batches have the average weight as per the official standards. The drug contents in all the batches in the range of 95.56 to 105. All the batches have good hardness and friability as per standards. Surface pH of the tablets were found in the range of 5.72±0.04 to 6.78±0.05 that indicates no risk of mucosal damage or irritation. The thickness of the tablet was in the range of 3.2 ±0.04 mm to 3.6± 0.02 mm.
Table 2.6: Post compression parameter of formulation

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Hardness (kg/cm²)</th>
<th>Thickness (mm)</th>
<th>Friability (%)</th>
<th>Weight variation (mg)</th>
<th>Drug content (%)</th>
<th>Surface pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>2.67±0.20</td>
<td>3.08±0.02</td>
<td>0.57±0.04</td>
<td>117.86±1.89</td>
<td>98.59</td>
<td>5.89±0.04</td>
</tr>
<tr>
<td>F2</td>
<td>3.43±0.35</td>
<td>3.18±0.05</td>
<td>0.64±0.02</td>
<td>122.61±3.42</td>
<td>99.44</td>
<td>5.72±0.04</td>
</tr>
<tr>
<td>F3</td>
<td>4.53±0.30</td>
<td>3.48±0.04</td>
<td>0.61±0.03</td>
<td>153.66±4.87</td>
<td>100.08</td>
<td>6.66±0.05</td>
</tr>
<tr>
<td>F4</td>
<td>5.97±0.41</td>
<td>3.53±0.02</td>
<td>0.67±0.03</td>
<td>173.66±4.56</td>
<td>98.19</td>
<td>5.43±0.06</td>
</tr>
<tr>
<td>F5</td>
<td>5.48±0.21</td>
<td>3.82±0.02</td>
<td>0.59±0.03</td>
<td>172.66±4.16</td>
<td>99.81</td>
<td>5.64±0.03</td>
</tr>
<tr>
<td>F6</td>
<td>5.10±0.34</td>
<td>3.80±0.03</td>
<td>0.60±0.03</td>
<td>155.66±2.94</td>
<td>99.67</td>
<td>5.70±0.09</td>
</tr>
<tr>
<td>F7</td>
<td>4.86±0.64</td>
<td>3.27±0.05</td>
<td>0.57±0.03</td>
<td>161.66±3.41</td>
<td>99.06</td>
<td>5.37±0.03</td>
</tr>
<tr>
<td>F8</td>
<td>4.60±0.41</td>
<td>3.63±0.04</td>
<td>0.39±0.03</td>
<td>162.66±5.68</td>
<td>99.97</td>
<td>5.90±0.04</td>
</tr>
<tr>
<td>F9</td>
<td>4.61±0.20</td>
<td>3.60±0.04</td>
<td>0.37±0.02</td>
<td>162.31±5.72</td>
<td>100.40</td>
<td>6.08±0.05</td>
</tr>
</tbody>
</table>

*Values are expressed in mean ±SD (n=3)

Table 2.7: Average cumulative percentage of drug released of formulations

<table>
<thead>
<tr>
<th>Media</th>
<th>900ml of 0.1 N HCl at 75 rpm in USP Type I apparatus (basket)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time (min)</td>
<td>% Cumulative Drug Release (%CDR)</td>
</tr>
<tr>
<td>05</td>
<td>76</td>
</tr>
<tr>
<td>10</td>
<td>84</td>
</tr>
<tr>
<td>20</td>
<td>96</td>
</tr>
<tr>
<td>30</td>
<td>98</td>
</tr>
<tr>
<td>45</td>
<td>100</td>
</tr>
<tr>
<td>60</td>
<td>101</td>
</tr>
</tbody>
</table>

Fig: Comparative dissolution profile of F1 to F9 in 0.1 N HCl
Acceptance Criteria:

In case where more than 85% of the drug is dissolved within 15 min for at least 3 media, the dissolution profiles may be accepted as similar without further mathematical evaluation.

Conclusion:

Considering more than 85% drug release of sample & innovator within 15 min in 3 media (0.1 m HCl, pH 4.5 & pH 6.8), The product Tolperisone HCl Tablets 50 mg is comparable with innovator sample (Mydocalm 50) in dissolution profile in different dissolution media as per WHO guideline reference phosphate buffer pH 6.8

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