A REVIEW ON TOLPERISONE – CENTRALLY ACTING MUSCLE RELAXANT AND ITS ANALYTICAL METHODS

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ABSTRACT
Method development is the process of proving that analytical method is acceptable for use to measure the concentration of active pharmaceutical ingredient in a specific compounded dosage form which must be validated to provide reliable data for regulatory submissions. Tolperisone is a piperidine derivative, centrally acting muscle relaxant, indicated for use in the treatment of pathologically increased tone of the cross striated muscle caused by neurological diseases (damage of pyramidal tract, multiple sclerosis, myelopathy, encephalomyelitis) and of spastic paralysis and other encephalopathy’s manifested with muscular dystonia. This article examines published analytical methods reported so far in the literature for the determination of Tolperisone in biological sample and pharmaceutical formulations. They include various techniques like spectrophotometry, High performance liquid chromatography, High performance thin layer chromatography and liquid chromatography-mass spectrometry.

KEYWORDS: Tolperisone, analytical methods, muscle relaxant.

INTRODUCTION

Tolperisone has the unique property of mediating muscle relaxation without concomitant sedation and it does not cause incoordination, weakness and mental confusion or withdrawal phenomena in contrast to other muscle relaxant. It belongs to cholinergic muscarinic antagonist pharmacological group on the basis of mechanism of action and also classified in gastrointestinal anticholinergic or antispasmodic pharmacological group. Tolperisone hydrochloride is extremely water soluble, it is more soluble in acidic medium (pH<4.5), because it is disposed to decomposition in aqueous solution, which is faster at higher pH 2-4.
The advantages of Tolperisone include a low adverse event profile, lack of sedation and no interaction with alcohol as well as no potential for tolerance and addiction. The structure of Tolperisone is given below.

![Structure of Tolperisone](image)

**Figure 1: Structure of Tolperisone.**

### PHYSICAL PROPERTIES OF TOLPERISONE

- **Molecular formula**: C_{16}H_{23}NO.HCl
- **Molecular mass**: 281.83
- **IUPAC name**: 2-methyl-1(4-methyl phenyl)-3-piperidine-1-yl propan-1-one hydrochloride
- **Appearance**: white crystalline powder
- **Nature**: basic
- **Pka**: 9.4
- **Solubility**: soluble in water, methanol, chloroform, and ethanol. Slightly soluble in acetone, insoluble in benzene and ether

### MECHANISM OF ACTION OF TOLPERISONE

Tolperisone is a centrally acting muscle relaxant. Tolperisone acts at the level of spinal cord by blocking sodium channels and calcium channels. Tolperisone exerts its spinal reflux inhibitory action mainly via pre synaptic inhibition of the transmitter release from the primary afferent endings via combined action on voltage gated sodium and calcium channels. Tolperisone causes muscle relaxation by its action on central nervous system. It also leads to membrane stabilization and has analgesic activity. This muscle relaxation is dose dependent.

### Pharmacokinetics of Tolperisone

- **Absorption**: Well absorbed from GI tract. Peak plasma concentration is 0.5-1hr
- **Bioavailability**: 20%
Metabolism: Extensively metabolized by liver and kidney.
Excretion: Excreted via urine as metabolites.

REPORTED ANALYTICAL METHODS

Table 1: Chromatographic Methods.

<table>
<thead>
<tr>
<th>Title</th>
<th>Method</th>
<th>Mobile Phase</th>
<th>Stationary Phase</th>
<th>Wave Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simultaneous estimation of Diclofenac and Tolperisone hydrochloride in bulk and tablet dosage form by RP-HPLC</td>
<td>RP-HPLC</td>
<td>Acetonitrile:water (65:35v/v) PH adjusted to 3 with Ortho Phosphoric acid</td>
<td>250X4.6mm, i.d 5µm C18column</td>
<td>262nm</td>
</tr>
<tr>
<td>Chemo metrics Assisted UV spectrophotometric and RP-HPLC method for the simultaneous determination of Tolperisone hydrochloride and Diclofenac sodium in their combined pharmaceutical formulation</td>
<td>UV-HPLC</td>
<td>Methanol; Acetonitrile:Water 60:30:10v/v PH adjusted to 3 with ortho phosphoric acid</td>
<td>Reverse phase c18 column</td>
<td>275nm</td>
</tr>
<tr>
<td>Development and Validation of HPTLC method for simultaneous determination of Tolperisone hydrochloride and Diclofenac sodium in combined dosage form</td>
<td>HPTLC</td>
<td>Toluene:Ethyl acetate:Methanol 4:4:2v/v</td>
<td>Merck TLC aluminium sheets of silica gel 60 F 254</td>
<td>282nm</td>
</tr>
<tr>
<td>Reverse phase HPLC method for simultaneous estimation of Tolperisone hydrochloride and Etodolac in combined fixed dose oral formulation</td>
<td>HPLC</td>
<td>Phosphatebuffer: Methanol:Acetonitrile:Triet hylamine(40:40:20:15). pH is adjusted to 5.5 with ortho phosphoric acid</td>
<td>Phenomax c-18,prepacked column</td>
<td>257nm</td>
</tr>
<tr>
<td>Method development and validation for the simultaneous estimation of Tolperisone hydrochloride and Diclofenac sodium by RP-HPLC</td>
<td>HPLC</td>
<td>Phosphate buffer: Acetonitrile: Methanol 60:20:20 pH adjusted to 3 with ortho phosphoric acid</td>
<td>C18 column</td>
<td>242nm</td>
</tr>
<tr>
<td>Stability indicating RP-HPLC method for determination and validation of Tolperisone hydrochloride and Etodolac in pharmaceutical dosage form.</td>
<td>HPLC</td>
<td>Ammonium acetate buffer:Acetonitrile (52:48 v/v). PH is adjusted to 3.7 with ortho phosphoric acid</td>
<td>Kromasil column</td>
<td>210nm</td>
</tr>
<tr>
<td>RP-HPLC method for simultaneous determination of Tolperisone hydrochloride and Diclofenac sodium in pharmaceutical dosage form.</td>
<td>HPLC</td>
<td>Acetonitrile: Phosphate buffer (70:30 v/v). pH is adjusted to 3 with Ortho phosphoric acid</td>
<td>C18 column</td>
<td>240nm</td>
</tr>
<tr>
<td>RP-HPLC method development and validation for simultaneous estimation of Diclofenac sodium and Tolperisone in tablet dosage form</td>
<td>HPLC</td>
<td>Acetonitrile:Phosphate buffer (30:70 v/v) at PH 3.4.</td>
<td>XDB C-18 column</td>
<td>260nm</td>
</tr>
</tbody>
</table>
Development and validation of RP-HPLC method for simultaneous determination of Tolperisone hydrochloride and Diclofenac sodium in synthetic mixture

Estimation of centrally acting muscle relaxant drug Tolperisone hydrochloride using HPTLC method

Development and validation of a precise, single HPLC method for the determination of Tolperisone impurities in API and pharmaceutical dosage form

Simultaneous determination of Tolperisone and Lidocaine by HPLC

Development of stability indicating LC method for the estimation of Tolperisone in bulk and pharmaceutical dosage form

Reverse phase HPLC method for simultaneous estimation of Tolperisone hydrochloride and Etodolac in combined oral formulation

Determination of tolperisone in human plasma by liquid chromatography/tandem mass spectrometry for clinical application

<table>
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<tr>
<th>Title</th>
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<th>Linearity</th>
<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>[13] Development and validation of a precise, single HPLC method for the determination of Tolperisone impurities in API and pharmaceutical dosage form</td>
<td>HPLC</td>
<td>Pottassium dihydrogen buffer: acetonitrile. PH is adjusted to 8 with diethylamine.</td>
<td>C18 column</td>
<td>254nm</td>
</tr>
<tr>
<td>[14] Simultaneous determination of Tolperisone and Lidocaine by HPLC</td>
<td>HPLC</td>
<td>Acetonitrile: water (70:30 v/v)</td>
<td>Spherisorb ODS column</td>
<td>254nm</td>
</tr>
<tr>
<td>[15] Development of stability indicating LC method for the estimation of Tolperisone in bulk and pharmaceutical dosage form</td>
<td>LC</td>
<td>Methanol: Water (60:40v/v) PH adjusted to 7.5 with Triethylamine</td>
<td>Reverse phase C18 sun fire column</td>
<td>261nm</td>
</tr>
<tr>
<td>[16] Reverse phase HPLC method for simultaneous estimation of Tolperisone hydrochloride and Etodolac in combined oral formulation</td>
<td>HPLC</td>
<td>Phosphate buffer: Methanol: Acetonitrile: Triethylamine (40:40:20:15) PH adjusted to 5.5 with ortho phosphoric acid</td>
<td>C18 prepacked column</td>
<td>257nm</td>
</tr>
<tr>
<td>[17] Determination of tolperisone in human plasma by liquid chromatography/tandem mass spectrometry for clinical application</td>
<td>LC-MS/MS</td>
<td>10Mm ammonium formate buffer (PH 3.5)- methanol (12:88 v/v)</td>
<td>Reverse phase Luna C18 column (2.0 mm x 50mm, 5µm)</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 2: Spectrophotometric Methods.

<table>
<thead>
<tr>
<th>Title</th>
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<th>Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>[18] Spectrophotometric Determination of Tolperisone using 2,4-dinitrophenyl hydrazine reagent</td>
<td>UV-VISIBLE spectrophotometer</td>
<td>254nm</td>
<td>2.5-15µg/ml</td>
<td>99.18%</td>
</tr>
<tr>
<td>[19] The simultaneous estimation of Paracetamol and Tolperisone hydrochloride in tablet by UV spectrophotometric methods.</td>
<td>simultaneous equation method &amp; Q analysis method</td>
<td>260nm</td>
<td>4-12µg/ml and 2-18 µg/ml</td>
<td>102.03±3.79 % 100.4±1.80%</td>
</tr>
<tr>
<td>[20] Simultaneous UV spectrophotometric estimation of Diclofenac and Tolperisone hydrochloride in tablet dosage form</td>
<td>simultaneous equation method &amp; Q analysis method</td>
<td>260nm</td>
<td>5-50 µg/ml and 5-60 µg/ml</td>
<td>100%</td>
</tr>
<tr>
<td>[21] Development and validation of UV spectrophotometric methods for simultaneous estimation of Tolperisone hydrochloride and Diclofenac sodium in tablet dosage form</td>
<td>UV</td>
<td>254nm</td>
<td>4-12µg/ml and 8-16 µg/ml</td>
<td>99.73% and 98.87%</td>
</tr>
</tbody>
</table>
CONCLUSION
A large number of techniques are available for the estimation of Tolperisone in pharmaceutical formulations and biological samples. The study of analytical data revealed that HPLC and UV methods are predominant for the estimation of Tolperisone alone or in combinations. These methods provide faster analysis time and more separation than other techniques. These analytical methods are important for both qualitative and quantitative determination of Tolperisone.

REFERENCE


