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Formulation and Characterization of Tolperisone Mouth Dissolving Tablet

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ABSTRACT :

Even elderly folks have trouble taking the conventional medications. Therefore, pills that dissolve quickly or dissolve in the mouth must be developed to address this issue. The current study's objective was to create and formulate tolperisone hydrochloride mouth-dissolving tablets. To evaluate the purity of tolperisone, a performulation study was carried out. This study could also be used to test for Tolperisone's physicochemical properties. Using normal processes, the resulting powder blend was examined for various rheological parameters, including bulk density, tapped density, Hausner's ratio, and angle of repose. The results were good. Crospovidone and sodium starch glycolate, two superdisintegrants, were used in different ratios to produce Tolperisone tablets using the direct compression method.

Keywords: Tolperisone hydrochloride, Sodium starch glycolate, Mouth dissolving pills, cross povidone

INTRODUCTION

Mouth dissolving tablets

As per the Food and Drug Administration (FDA), MDT is tablet which disintegrates within seconds after putting upon the tongue. After disintegration of DT form gel like substances, and this facilitate the patients in easy swallowing of drugs. The Pharmacopoeia mentioned that the disintegration time of MDT varies from a few seconds to more than a minute[9-11].

Ideal Properties of MDTs

It should not need aqua for consuming. It should ideally in the mouth less than few seconds.

- Taste should be palatable.
- Should withstand handling and packing forces.
- Should leave pleasant after feel in mouth.
- Following administration of MDT, it is supposed to not leave any residues of tablets in the mouth.
- It resists the humidity and temperature during transportation.

Material and Method

Drug/Excipient	**Manufacturer/Supplier**
Tolperisone	Aristo Pharma Ltd. Baddi
Crospovidone	Micro Labs, Bangalore
Sodium starch glycolate	Micro Labs, Bangalore
Microcrystalline cellulose	Central Drug House, Mumbai
Mannitol	Central Drug House, Mumbai
Mg. Stearate	Oxford Laboratory, Mumbai

Talc	Central Drug House, Mumbai
Aspartame	Central Drug House, Mumbai

Sr. No	Equipments	Manufacturer/Supplier
1.	Tablet punching machine 12 station	Cadmach
2.	Tablet Hardness Tester	Shankar
3.	Friability Tester	Electrolab
4.	Digital vernier caliper	Mitutoyo
5.	Dissolution Tester	Electro lab
6.	Bulk density Apparatus	Electro lab

Experimental Work

Pre-formulation studies of pure drug

Determination of λ_{max}

In our study we determined the λ_{max} of Tolperisone by using UV spectroscopy. The solution of Tolperisone containing concentration of 10µg/ml was prepared in water and ethanol respectively, and UV spectrum was taken using UV spectrophotometer. The sample was scanned in the range of 200-400 cm^{-1}

Preparation of calibration curve in pH 6.8 phosphate buffer

Making a calibration curve in a phosphate buffer with a pH of 6.8 In a 100 ml volumetric flask, a precisely weighed 100 mg of tolperisone was dissolved in a tiny amount of pH 6.8 phosphate buffer, and the volume was increased to 100 ml using the same pH 6.8 phosphate buffer. Using a pH 6.8

Drug excipients interaction study by FTIR,

1 ml, 2 ml, 3 ml, 4 ml, 5 ml, 6 ml, 7 ml, 8 ml, 9 ml, and 10 ml of this stock's solution were taken out and diluted up to 10 ml with the pH 6.8 Phosphate Buffer in a 10 ml volumetric flask to obtain a concentration of 1µg. To determine whether the medicine and polymer are compatible while creating a mouth-dispersing tablet of Tolperisone the drug and excipients mixture of quantity 10 mg and 400 mg of KBr were acquired in a mortar and were triturated. A little volume of the triturated sample was seized and kept on to the sample holder and examined from 4000cm^{-1} to 400cm^{-1} in FTIR Spectrophotometer. The spectra obtained were matched with that of the peaks obtained from the FTIR study of the pure drug sample and interpreted for the interaction of drug and excipients if any.

Solubility analysis

The preparation of any dosage form, it required to know the solubility of drug. The solid dose form has a pharmacological effect on the body and requires a specific solvent to dissolve. Furthermore, the drug's bioavailability in solid dose form

Determination of melting point

The melting point of drugs indicates the purity of drug. Every drug has its own melting point at particular conditions. If there is any alteration in melting point of drug it inferred the change in therapeutic response of drug. When active constituents are incorporated with foreign particles or adulterants, it changes the melting point of active constituents

Preparation of Tolperisone tablets by direct compression method

Tablets using the direct compression technique Tolperisone tablets were made using the direct compression process. In a mortar and pestle, all of the formulation ingredients listed in formulation tables 1 and 2 were combined after being weighed appropriately. After a short period of drying, this powder mixture was thoroughly mixed once more and run through sieve number 60. Blends were then used for additional processing.

Ingredients	T1	T2	T3	T4	T5
Tolperisone	150	150	150	150	150
Crospovidone	8	8	8	8	10
Sodium starch glycolate	7	9	11	13	7
Microcrystalline cellulose	20	20	20	20	20
Mannitol	114	112	110	108	112
Mg. Stearate	3	3	3	3	3
Talc	1	1	1	1	1
Aspartame	2	2	2	2	2
Theoretical Weight	305	305	305	305	305

Table: Formulation of mouth dissolving Tolperisone tablets

Ingredients	T1	T2	T3	T4	T5
Tolperisone	150	150	150	150	150
Crospovidone	8	8	8	8	10
Sodium starch glycolate	7	9	11	13	7
Microcrystalline cellulose	20	20	20	20	20
Mannitol	114	112	110	108	112
Mg. Stearate	3	3	3	3	3
Talc	1	1	1	1	1
Aspartame	2	2	2	2	2
Theoretical Weight	305	305	305	305	305

Evaluation of pre-compression

Bulk density

The bulk density was measured as reported in research paper. The mixtures were filled in a measuring cylinder, and after that the complete The loudness was recorded. A digital weighing balance was used to determine the powder mixture's gravity. The bulk density was calculated using the following formula: The density that is taped After determining the appropriate density, the combinations were put into a measuring cylinder. Following then, 100 taps were made on the measuring cylinder. Calculate the total weight of the powders. The following formula was used to determine the tapped density: Tapped Density = Powder Weight / Tapped The powder's volume **Repose angle**

The fennel was positioned 6 cm above the graph paper during this procedure. The powder clung to the fennel and gradually pulled it away. The heap's height was measured using the scale. The angle of repose was calculated by applying following formula:

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

Where, h = height of heap of granular bed, r = radius of heap of granular bed.

Hausner's ratio

The Hausner's ratio The following formula was used to calculate Hausner's ratio, which was then stated as a percentage,

H=Dt/Db.

Where Dt stood for the powder's tapped density. Db stood for the powder's bulk density.

Compression of powders into tablets

Before compression of powder into tablets, the Lubricant (talc) and glidant (magnesium stearate) were mixed to the prepared powders. By the help of compression the powder were punch into tablets using 10mm diameter, flat faced punches.

Evaluation of compression characteristics of tablets

After formulation of tablets it required to check the suitability of dosage form for proper therapeutic response. The various parameters are used for evaluation of compression ot tablets. Weight fluctuation, hardness, thickness, friability, and dissolution test were evaluated for prepared tablets using standard procedures.

Weight variation test

In this process the 20 tablets were weighed separately. The average weight of one tablet was calculated by taking average mean. On I.P. it has mentioned that No more than two tablets result in noticeable weight. According to I.P., there should be more than two unique weights that deviate from the mean weight, and none of them should be more than twice as aberrant as the proportion stated in the monographs.

Thickness test

The micrometer-scale thickness of the tablets. Three readings were averaged, and the mean's outcomes were documented (n = 3).

Test of hardness

The hardness of the prepared tablets was assessed using the Monsanto hardness tester. The hardness was measured in kilograms per square centimeter. Three measurements were made, and the average was recorded.

Friability test

Test of Friability In order to measure the Roche friabilator. Measure the weight of 20 tablets and kept in the friabilator chamber. The friabilator was rotted at speed of 4 minutes at 25 rpm. Following the friabilator tablet rotation, the tablets were weighed, and the percentage weight loss was computed using a formula.

Drug content

Content of drugs The three pills were triturated to a fine powder in a mortar and pestle in order to determine the drug content. One tablet's weight in powder form was dissolved in phosphate with a pH of 6.8. Determine the absorbance of a diluted Tolperisonet sample using a UV-Visible Spectrophotometer at 260 nm. The standard calibration curve was used to determine the drug content.

Wetting time

Time spent wetting The tablets were placed in Petridish to determine the wetting time. Six milliliters of filtered water and two folded pieces of tissue paper made up the petridish. It was measured how long it took for the tablets to completely wet. Ratio of water absorption The water absorption ratio was calculated using the same method as wetting time.

In-vitro disintegration time

Disintegration time in vitro The primary function of mouth-dissolving tablets is determined by their rate of disintegration. The purpose of the disintegrating agents is to facilitate the breakdown of oral dissolving tablets. The disintegrants facilitate the tablets' absorption of moisture. The following variables influence how quickly mouth-dissolving pills dissolve. Drug release research in vitro To create an oral dosage form, in vitro dissolution has been adequately established. It is employed to forecast pill dissolving in vivo. Tablet dissolution test device USP XXIII, apparatus I, was used to measure the in vitro release of mouth-dissolving tablets. Phosphate buffer pH6.8 (900 mL) was the medium used in the dissolving device, which was kept at 37 ± 1°C. The sample of 10 mL was withdrawn at different interval and volume of media was maintained by putting fresh media in chamber. The aliquots were evaluated spectrophotometrically at 260 nm for Tolperisone.

7. Result and Discussion

Identification of drug by UV spectroscopy

The Tolperisone were identified by UV spectroscopy method.
The Tolperisone exhibited maximum absorption at 260 nm respectively. These wavelengths were considered as λ_{max} for samples and all the observations by UV spectrophotometer to calculate the amount of drug were taken at this wavelength.

Standard curves of Tolperisone

Tables 6.1 to 6.2 show the results of the preparation of the standard curves for tolperisone using phosphate buffer pH 6.8 and 0.1 N NaOH.

Table:Tolperisone medication absorbance in a pH 6.8 phosphate buffer at varying concentrations

S. No.	Concentration in µg/ml	Absorbance at 260 nm
1.	1	0.023
2.	2	0.042
3.	3	0.073
4.	4	0.098
5.	5	0.121

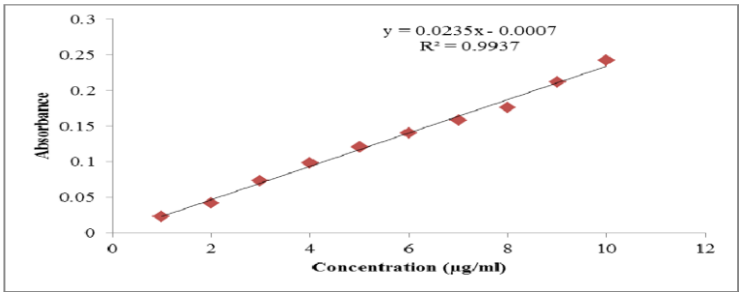
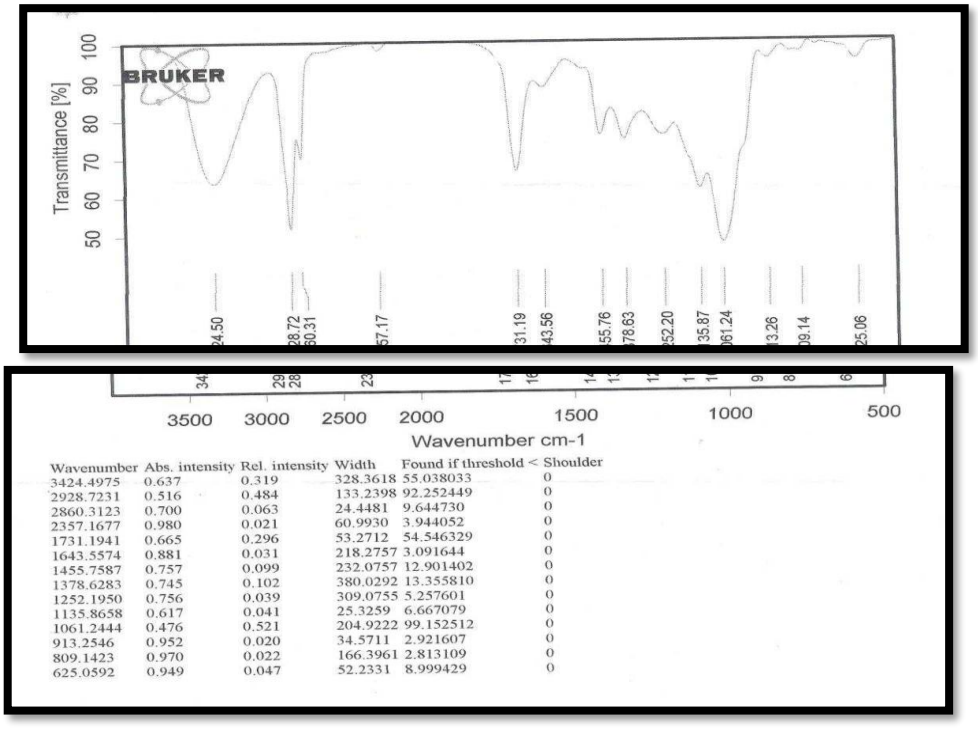


Fig: FTIR spectra of Tolperisone



FTIR

Determination of melting point

Melting point of pure Tolperisone was found to be 175-178 ˚C was in range of 176˚- 178 ˚C, actual melting point of Tolperisone as per pharmacopoeia.

Evaluation of pre-compression of Tolperisone powder blend

The tapped density and bulk density of several formulations were computed. The tapped density ranges from 0.565 to 0.698, whereas the bulk density ranges from 0.473 to 0.574. The results showed that the Compresibility Index ranged from 12.74 to 19.34 and Hausner's ratio was between 1.14 and 1.23. The powdered blend's angle of repose showed good to exceptional flow characteristics (Table 6.5).

Table: Data of pre-compression characteristics of Tolperisone powder blend

Parameters	**T1**	**T2**	**T3**	**T4**	**T5**
Mean Angle of repose* ± S.D.	36°25 ± 0.02	29° 36'±0.11	31°28'±0.5	30° 57' ±0.08	29° 91' ± 0.09
Mean Apparent bulk density* (g/cm^3) ± S.D	0.473 ± 0.02	0.565 ± 0.04	0.547 ± 0.06	0.513 ± 0.01	0.574 ± 0.03
Mean Tapped bulk density* (g/cm^3) ± S.D.	0.565 ± 0.03	0.689 ± 0.01	0.672 ± 0.03	0.621 ± 0.06	0.698 ± 0.04
Compresibility Index* (%)	12.74	15.09	17.11	17.39	14.89
Hausner's Ratio*	1.14 ± 0.01	1.17 ± 0.02	1.20 ± 0.04	1.21 ± 0.02	1.17 ± 0.05

Table : Evaluation of Tolperisone mouth dissolving tablets

Parameters	**T1**	**T2**	**T3**	**T4**	**T5**
Uniformity of weight (mg)*	305.20 ± 1.12	304.17 ± 1.07	304.84 ± 2.01	305.07 ± 1.81	304.6 ± 1.92
Thickness (mm)*	3.21 ± 0.01	3.50 ± 0.04	3.10 ± 0.03	3.34 ± 0.02	3.17 ± 0.01
Friability (%)*	0.28 ± 0.02	0.19 ± 0.01	0.24 ± 0.03	0.27 ± 0.01	0.29 ± 0.05
Tablet Hardness (Kp)*	3.29 ± 0.06	3.18 ± 0.03	3.51 ± 0.06	3.05 ± 0.04	3.62 ± 0.07

Table : Evaluation of wetting time of Tolperisone mouth dissolving tablets

Formulation	**Wetting time (Sec)**
T1	35.07±0.02
T2	30.52±0.05
T3	28.36±0.12
T4	25.73±0.19

T5	28.46±0.08

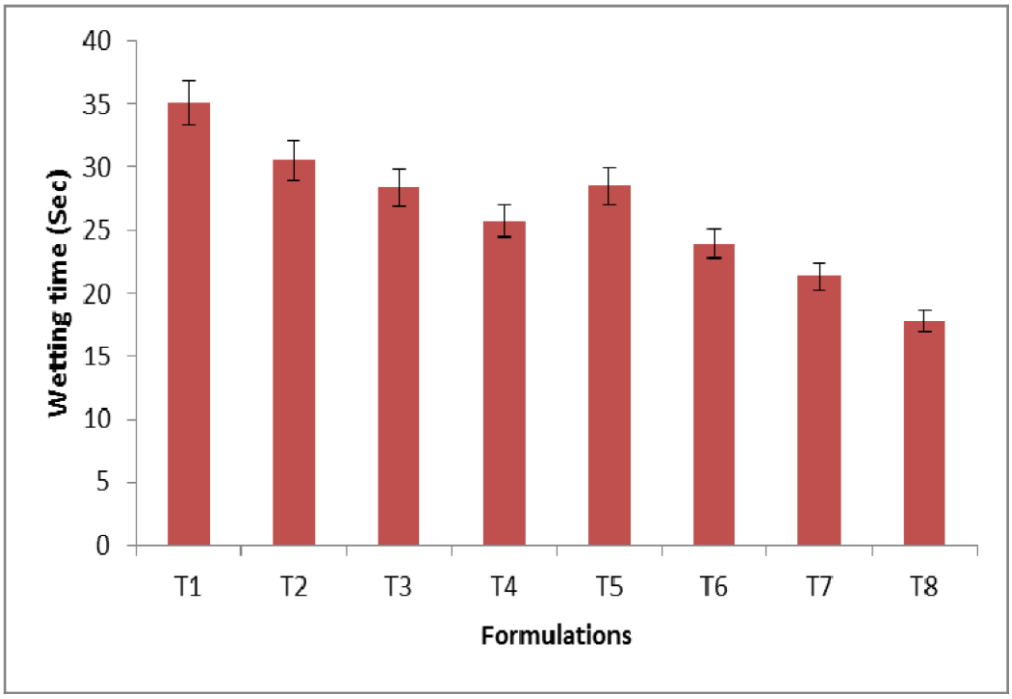
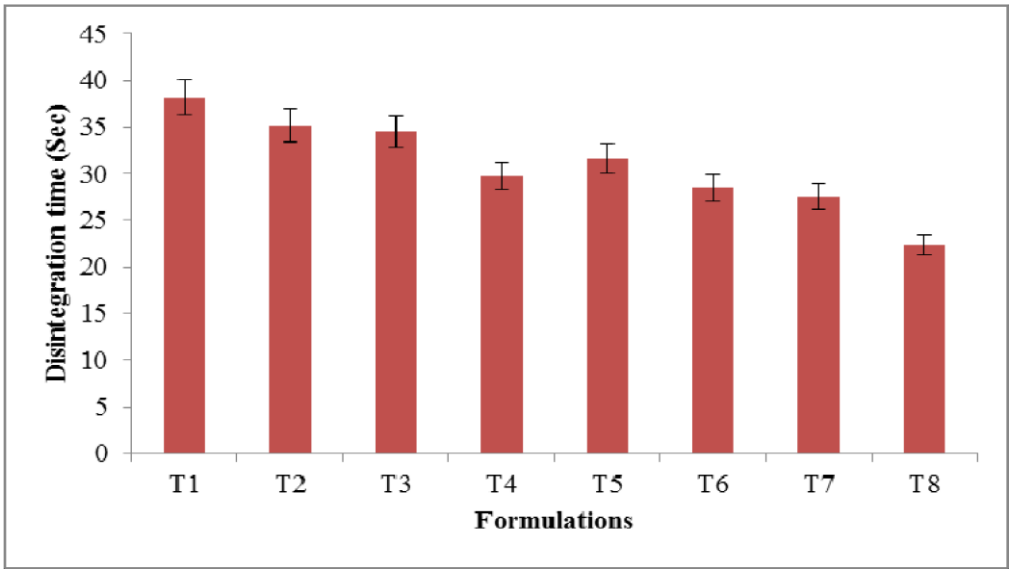


Fig : Wetting time of Tolperisone mouth dissolving tablets

Table: Evaluation of *in-vitro* disintegration time of Tolperisone mouth dissolving tablets

Formulation	***In-vitro* disintegration time (sec)**
T1	38.21±0.08
T2	35.18±0.12
T3	34.52±0.07
T4	29.73±0.08
T5	31.61±0.19



Conclusion

It was concluded that the direct compression method was a successful way to formulate MDTs of tolperisone. To improve pill disintegration, superdisintegrants were incorporated into the formulation. It results in more effective tablet therapy and improved patient compliance. Additionally, by utilizing aspartame as a flavor masking ingredient, the bitter medication can be readily made into mouth-dispersing tablets. Additionally, it was discovered that the superdisintegrants work best at a specific concentration; the gelling effects of the formulation are improved when the ratio of sodium starch glycolate to crospovidone is increased above its optimal value. The outcomes of the formulations were superior to those of other

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