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Evaluation of Floating Matrix Tablets of Tolperisone Hydrochloride.

MRS. RITU SAINI (ASSISTANT PROFESSOR STIBAS)

MS. DEVIKA RANI (M. PHARAM), MS. SHILPA SINGH (M. PHARMA),MR.VIPUL GUPTA (M.PHARMA), MR WASIF RAO (M PHARM)

ABSTRACT

The goal of every medicine delivery system is typically understood to be to deliver a therapeutic dose of medication to the appropriate region in the body without causing any obvious adverse effects. Because of its numerous advantages, including as patient compliance, convenience of administration, formulation flexibility, etc., oral drug delivery systems have long been the most popular and clinically acknowledged mode of drug administration. It must, however, also fulfill a number of other important criteria, including physical and chemical stability, the capacity to be produced in vast quantities and at a reasonable cost while guaranteeing the accurate dose of the medicine in each and every dosage unit.

Optimal drug solubility and availability from absorptions commensurate with intended usage (i.e., immediate or prolonged release) are the main design requirements for matrix tablets. accuracy and consistency of medication composition. Stability includes the capacity of the pharmacological ingredient to remain stable over time as well as the overall tablet composition, pace, and amount of dissolution. Manufacture ease: The formulation should be designed in a way that makes it simple and affordable to produce the necessary batches.

KEYWORD-: TOLPERISONE HCL , FLOATING AGENTS.

INTRODUCTION

Controlled release dosage forms can be produced by including the medication into a matrix that also contains a hydrophilic, rate-regulating polymer. Those made from cellulose, including hydroxypropyl methylcellulose (HPMC), are the most often used polymers. Drug release from these sorts of systems is controlled by the hydration of HPMC, which forms a gelatinous harrier layer at the matrix's surface and enables the contained drug to permeate through it. In addition, the degree of viscosity of the HPMC controls how erosion-resistant such a gel layer is. While water-soluble medications are predominantly released via diffusion of dissolved drug molecules over the gel layer, poorly water-soluble pharmaceuticals are primarily released by the erosion process. Tolperisone HCl is a white, crystalline powder with a somewhat distinguishing odor. It has a high solubility in acetic acid (100), is easily soluble in water and ethanol (95%), soluble in acetic anhydride, and has a low solubility in acetone. It is also hygroscopic. A Tolperisone HCI solution has a pH between 4.5 and 5.5. A centrally acting muscle relaxant called Tolperisone works at the spinal cord level by obstructing sodium and calcium channels.

Material

Analytical Methods

The powder form of Tolperisone hydrochloride is white and crystalline. One gram of the medication dissolves roughly in 1.5 ml of water or 6 ml of alcohol and has a pka of 9.4 and
3.0. The routine determination of Tolperisone hydrochloride in dissolution fluids derived from the suggested formulation is the focus of the current work. The UV spectrophotometric approach is utilized in the study, despite the fact that numerous methods have been published for the determination of Tolperisone hydrochloride in pharmaceutical dosage form and biological fluids.

Standard curve of Tolperisone Hydrochloride in S.G.E

Stock Solution Preparation: In simulated gastric fluid (SGF) devoid of enzymes, a stock solution of Tolperisone hydrochloride comprising 100 mg/100 ml was made.

Standard Dilutions: Different concentrations of Tolperisone hydrochloride, including 2, 4, 6, 8, 10, 12, 14, 16, and 20 g/ml, were prepared from the stock solution by dilution with SGF without enzymes at pH 1.2, and their absorbance was measured at 260 nm using a UV/Visible double beam spectrophotometer (THERMOSCIENTIFIC. INDIA). The following table contains the absorbances of the aforementioned solutions. Tolperisone Hydrochloride concentration (pg/ml) and absorbance (Y-axis) were used to generate a graph.

METHOD OF FORMULATION

Formulation of different batches of floating matrix tablets

The direct compression approach was used to create the matrix tablets. Before being utilized in the formulations, the excipients (polymers, Tolperisone Hydrochloride, and other excipients) were passed through filter No. 40. Pharmaceutical grade was used for all of the substances.
Tolperisone hydrochloride's pharmacokinetic characteristics 145, 146, and 147 were utilized to create a speculative drug release profile for a 12-hour dose form.

$$\text{Total Dose (Dr)} = \text{Loading Dose (D)} + \text{Maintenance Dose (D) Loading Dose (D) (Cs Va)/F}$$

$$\text{Maintenance Dose (DM)} = \underline{C_{ss} x Cl_T x T / F}$$

Following the calculation of the drug dose, all of the ingredients—including the calculated amount of drug, the polymers, the diluents, and sodium bicarbonate (the gas-generating agent)—were uniformly mixed using the formulas before being compressed into a powder. The mixture was subsequently crushed in a 13 mm single punch tablet compression machine (Cadmic, Ahmedabad) after being passed through sieve no. 40. All of the formulation batches from FI through F9 maintained the same medication dosage.

Composition and Formulations

Formulation	Tolperisone HCL	HPMC K100M	HPMC K15M	HPMC K4M	Chitosan	Carbopol 71G	MCC PH-102	Lactose	sodium Bicarbonate
F1	150	100	100	50	------	20	50	50	50
F2	150	100	100	50	------	30	40	50	50
F3	150	100	100	50	------	40	30	50	50
F4	150	100	100	50	------	50	20	50	50
F5	150	100	100	------	50	50	20	50	50
F6	150	50	50	100	50	50	20	50	50
F7	150	100	50	50	50	20	50	50	50
F8	150	50	100	50	50	20	50	50	50
F9	150	50	50	100	50	20	50	50	50

CHARACTERIZATION OF PREPARED TABLETS

All of the batches of prepared tablets were tested for a variety of evaluation criteria, including tablet hardness, friability, weight variation, uniformity of the drug content, floating properties (FLT and TFT), mass degrees of swelling, permeability, in-vitro drug release studies, and final statistical analysis. Utilizing FTIR and Differential Scanning Calorimetry (both from Shimadzu, Japan) for drug polymer interaction research, the improved formulation has also undergone stability testing.

Thickness of Tablets

Digital thickness gauge (India: Mitutoyo Ltd. The individual crown-to-crown thickness of 10 tablets was calculated for each batch. Standard deviation and sample mean were calculated.

Hardness

Digital hardness tester (Expo Pvt. Ltd. India) was used to measure the hardness of five tablets from each formulation. The standard deviation and average of five data were presented.

Friability

Using (Electro lab Pvt. Ltd. India), ten tablets from each of the formulations were evaluated for friability. Each formulation's twenty pills were weighed. then put in a Friabilator and spun it for 4 minutes at 25 rpm. The weight reduction % was then recorded after the pills had been powdered and weighed once more.

Weight Variation (Indian Pharmacopoeia 2007)

Each of the twenty tablets, made up of all the formulas, was weighed precisely. The 20 readings were averaged, and this was reported. The weight of any one tablet should not deviate from the average by more than 5% or more than 10% for any more than two of the twenty tablets. The uncoated tablets must pass the test for weight uniformity as specified in the IP 2007 regulations.

Floating Properties (Buoyancy Study)

A dissolution vessel containing 900 ml of SGF (pH 1.2, temperature 3 = 1°C, paddle rotation 50 rpm) without enzymes was used to measure the times it took for the tablet to emerge on the water's surface (Floating Lag Tin [FLT]) and to float on the surface [Total Floating Tim [TFT]].

Drug Content Uniformity

Five tablets were collected from each batch of manufactured tablets, pulverized finely, and a quantity equal to 100 mg of the medication was taken, combined with 50 ml of simulated stomach juice, and thoroughly shaken for 15 minutes. The volume was then increased to 190nd and filtered. After the proper dilution, this filtrate was examined using a UV-Visible double beam spectrophotometer for the presence of Tolperisone hydrochloride at 260 nm.

Mass Degree of Swelling

By adjusting each tablet formulation with 100 ml of water for Sh, the mass degree of swelling of the hydrogels was discovered. After being taken out, the pills were wiped with tissue paper (148), then weighed. The formula "Q=Mass of the swollen gel/Mass of dry polymer" was used to determine the mass degree of swelling (Q).

Drug-Polymer Interaction Study FTIR Study

By scanning the sample in ATR mode on an FTIR Spectrophotometer from Bruker in the United States, infrared spectrum analysis was performed. Over the wave number range of 4000-400 cm, the spectra of pure drugs, pure polymers, and physical mixtures of drugs & polymers as per various formulations were collected. After holding samples at 37°C/75% RH for three months, the IR spectra of the medication in the improved formulation and physical mixes were also measured. Then, to determine whether there was any compatibility between the drug and excipients, various spectra were compared with the spectra of the pure drug.

Differential Scanning Calorimetric (DSC) Analysis

The best formulation (F1 after tablets were stored at a temperature of 37°C and a relative humidity of 75%) for three months was the subject of a DSC research. to assess any potential drug-polymer, drug-other component, or drug-degradation during melting interactions. The sample was heated from 20°C to 250°C at a heating rate of 10°C/min, in a nitrogen atmosphere (nitrogen gas flow rate of 20 ml/min), to perform a Differential Scanning Calorimetry (DSC) examination of the pure drug and drug in formulation (F1). The resulting thermograms were then contrasted to look for any potential interactions between the medication and formulation polymers.

In Vitro Release Study

Utilizing the eight-stage dissolving paddle apparatus type of USP XXIV, experiments on in vitro release rate were conducted. As the dissolving media, 900 ml of simulated stomach fluid without enzymes with a pH of 1.2 was utilized, which was kept at 37° 1°. 50 rpm was used to manage the paddle speed. At various times, including 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 hours, aliquots of 5 ml of the media were taken out and replaced with 5 ml of fresh medium. After the samples had been appropriately diluted, the drug content of the samples was evaluated by UV/Visible spectroscopy at 260 nm. The results of three separate dissolution trials were averaged.

Permeability

The parameter is helpful for researching hydrogel medication delivery. Given that the drug is disseminated throughout the hydrogel, the drug diffusion coefficient, K or (D), may be calculated from the slopes of the plot of square root time, where Q is the amount that is sometimes released.

Drug Release Mechanism and Kinetics

in order to determine the drug's release mechanism from matrix tablets. Different kinetic models were fitted to the experimental data. Different mathematical kinetic models, including zero order, first order, Higuchi's model, Kors Meyer model, and Hixson-Crowell models, were used to the drug release data. These models are employed when the release mechanism is unknown or when it is possible that different types of release phenomena are present.

"n'' value	Mechanism
0.5	Fiskian Diffusion (Higuchi Matrix)
0.5<n> 1	Anomalous transport
1	Case11 transport (Zero order release)
n>1	Super case 11 transport

Table: Characterization of release Mechanism as per Kors Meyer Release Exponent (n)

Stability Study

A study of the improved formulation's short-term stability was conducted. According to ICH short term stability protocols, samples (Tablets) from the improved formulation (FI) were stored at 37°C/75% RH for a period of three months. After three months, samples were examined by FTIR research and DSC analysis for any changes in physical characteristics, drug content, in-vitro drug release profile, and any potential drug-polymer interactions.

Statistical Analysis

Similarity Factor Analysis (f_2 values)

Using the following equation, the theoretical (anticipated) 12 hour modified dissolution profile of Tolperisone hydrochloride was compared with all batches F1 to F9 through determine the similarity factor (f), as described by Moore and Flanner (1996).

$F_2 = 50 \log_{10} \{1+1/n \sum^{n}_{i=1} W_t (R_t - T_t)^2\} \times 100$ Where, w, -50/f_2TH

& Th-50 logo 11 (R. -Ta) 100

Similarity factor: W, -Optional weight factor, & 6Th - Conversion factor R-% Drug Released of reference

& T% Drug Released of test (At time t')

Photographs of floating Tablets from Formulation F1

(a) At Initial State **(b) After Five Minutes**

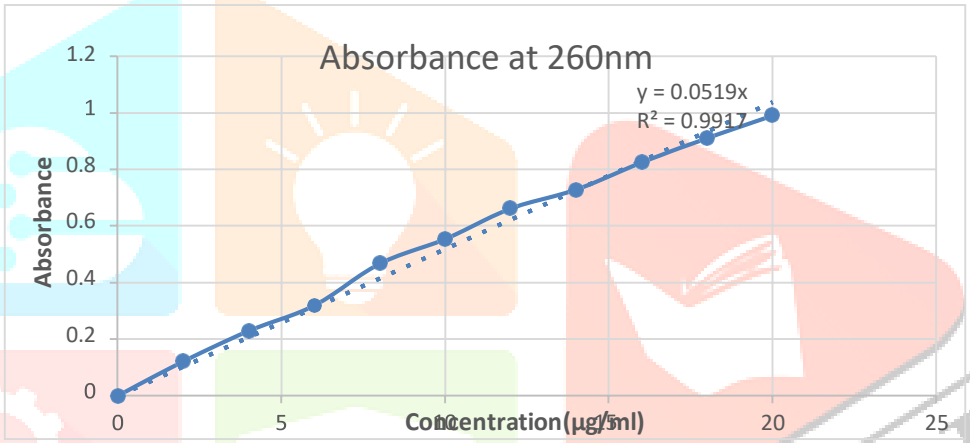

Fig: Standard Curve of Tolperisone HCL

FTIR Study

First, the IR spectra of pure polymers and the medication Tolperisone hydrochloride were collected. Then, after three months at 37°C/75% RH, the IR spectra of the physical combination of the drug, polymers, and drug in the improved formulation (FI) were recorded.

Tolperisone Hydrochloride's pure FTIR spectrum exhibits typical absorption peaks as stretching vibrations in wave number: 643, 833, 1382, and 1453 centimeters. 1604, 1673,
1706, 2859, and 2940 millimeters

The absorption peak of the spectra for Tolperisone hydrochloride in the different physical mixtures with polymers and in the optimized formulation (F1) showed no significant shift and no disappearance of characteristic peaks in comparison to the pure drug, indicating that there is no interaction between the drug and polymer matrices or degradation in the Tolperisone hydrochloride molecule. Different medication concentrations might be the cause of the transmittance variances.

RESULTS AND DISCUSSION:

The drug and excipient, which is selected to form the sustained release tablet were tasted for Compatibility study. The drug should be kept individually and in combination with excipient In 1:1 ratio in closed vial for 30 days and found drug and excipient of all in combination are Compatible with each other in following manner.

CONCLUSION

Tolperisone Hydrochloride was produced with HPMC K100M, HPMC K15M, Chitosan, and Carbopol 71G. The dissolution profiles obtained by direct compression demonstrated that the combination of these polymers allows for effective drug release control. Each formulation's produced tablets have physical characteristics that are within the permitted range. A regulated gastric retention strategy utilizing sodium bicarbonate has been used for the produced tablets. A buoyancy investigation showed that tablets may float in the medium of dissolution for the full 12-hour drug release period. Throughout the whole term of their release, tablets were able to keep their physical integrity.
variable formulations have variable dissolving rates, which can be due to variations in the concentration and viscosity of polymers.

The release of the drug from the matrix is increased in tablets manufactured with reduced polymer content and viscosity due to their higher rates of dissolution. In particular, when it comes to highly water-soluble drugs like Tolperisone hydrochloride, synthetic polymers Carbopol 71G and Chitosan are more effective in controlling drug release than HPMC polymers. First order kinetics are used to release the medication from the matrix, according to analysis of dissolution patterns (R2 values). There was no chemical interaction between the study's polymers and the medicine Hydrochloride, according to FTIR and DSC analyses. According to the stability analysis of the improved formulation F1, all of the formulations need to be maintained in airtight containers and kept out of direct sunlight.

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