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Formulation Development of Tolperisone Hydrochloride Film Coated Tablet

Survase Sandeep *[1], Dr. Hingane L. D[1]
1. Aditya Pharmacy College, Nalwandi Naka Beed. 431122

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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 release type, which are designed for immediate release of drug for rapid absorption. Tolperisone Hydrochloride Film Coated Tablets 50 mg was prepared using various excipients listed as in formula. The tablets were prepared by wet granulation method using concave plane punch on multi-station compression machine. The formulations were evaluated
for their physical characteristics like thickness, hardness and friability, weight variation, content uniformity study was carried out. Evaluated for chemical analysis like Assay, disintegration and dissolution. In-vitro comparative dissolution study was performed with the help of U.S.P dissolution test apparatus-II with 900 ml of 0.1 N HCL, Acetate buffer pH 4.5 & 0.1 M HCL Acid at the 75 rpm for 45min.

Keywords: Tolperisone Hydrochloride, film Coating Muscle Relaxant.

I. INTRODUCTION:

Tolperisone HCl (TOL) is a centrally acting muscle relaxant which is used in the treatment of different pathological conditions like acute and chronic muscle spasm, electroconvulsive therapy, neurological conditions and orthopedic manipulation, myelopathy, encephalomyelitis, spondylosis, spondylarthrosis, cervical and lumbar syndrome, arthrosis of the large joints obliterating artherosclerosis of the extremity vessels, diabetical angthromboangitis obliterans, raynauds syndrome. It is recently launched drug in India for acute and chronic back pain and spasticity of neurological origin. Tolperisone hydrochloride is a "Class-I" drug according to Biopharmaceutics Classification System (BCS), possessing both high solubility and high permeability absorption characteristics. Tolperisone hydrochloride is rapidly and completely absorbed from the gastrointestinal tract. Peak plasma concentrations are reached 0.9-1.0 hours after oral dosing and its elimination half-life ranges from 1.5 to 2.5 hr.

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 [1-8]. 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

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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 carmellose 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.

The objective of this study was to prepare film Coated tablet of Tolperisone HCl for the effective treatment of patient with acute musculoskeletal spasm or acute low back pain, in an attempt to improve bioavailability and to get maximum therapeutic benefits and applicable for long term therapy with better patient compliance about the treatment .

Two different film formers which possessed moisture protective ability were used to protect tolperisone hydrochloride from degradation.In this experiment, tolperisone hydrochloride core tablets were prepared by direct compression and then coated with either Methocel E15LV or Eudragit® E100. The film coated tablets were stored at ambient temperature, and 45 C, 75 %RH. The amount of active ingredient and piperidine hydrochloride was determined spectrophotometrically at 0, 2 and 4 weeks. It was indicated that tolperisone hydrochloride tablets coated with Eudragit®E100 decomposed less than those coated with Methocel E15LV. This was attributable to the higher water permeability of Methocel E15LV films, resulting in higher decomposition. However, film coating of tolperisonehydrochloride tablets with Methocel E15LV and Eudragit®E100 still could not well protect drug decomposition. Further development of coating solution and selection of appropriate film formers were needed.

II. MATERIAL & METHOD:

Materials: Tolperisone HCl (Active), Hypromellose, Lactose Monohydrate, Croscarmellose Sodium, PVP K- 30, Microcrys-talline 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:

Preparation of Tolperisone HCl floating matrix tablets :

Tablets were prepared by direct compression technique. Tolperisone HCl was mixed with the required components except magnesium stearate by geometric mixing. The powder blend was then lubricated with magnesium stearate (1%) and manually compressed on 10 station rotary tablet machine using 12 mm standard concave face punch. The tablet characteristics were shape, round and concave: size, average diameter of 12 ± 0.1 mm and thickness of 4.0 ± 0.2 mm; and hardness, range of 6 to 7 kg/cm.

In vitro buoyancy study :

The in vitro buoyancy was characterized by floating lag time (FLG) and total floating time (TFT). The test was performed using USP 24 type II paddle apparatus using 900 of 0.1 N HC1 at 100 rpm at 37±0.5°C. The time required for tablet to rise to surface of dissolution medium and duration of time the tablet constantly float on dissolution medium were noted as FLG and TFT, respectively (n=3).

In vitro drug release study :

The in vitro drug release was performed using USP 24 type II paddle apparatus using 900 ml of 0.1 N HC1 at 100 rpm at 37±0.5°C. The samples were withdrawn at predetermined time intervals for period of 12 hr and replaced with the fresh medium. The samples were filtered through 0.45 µm membrane filter, suitably diluted and analyzed at 260 nm using double beam UV/Vis spectrophotometer. The content of drug was calculated using calibration curve.

Full Factorial Design :

The goal of pharmaceutical formulation and development centre is to develop anacceptable pharmaceutical formulation in the shortest possible time using minimum number of personnel, time and raw materials. The formulae developed by the formulation and development centre is then tried at the pilot plant scale and manufacturing scale. Ideally, minor changes are to be made during scale up. It is therefore very essential to study the formulation from all perspectives[4, 5]. In addition to the art of formulation, statistical techniques are available that can aid in the pharmacist's choice of

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formulation components which can optimize one or more formulation attribute[6]. It is well known that the traditional experiments involve a good deal of efforts and time especially when complex formulations are to be developed. A very efficient way to enhance the value research and to minimize the process development time is through various experimental designs[7, 8]. Factorial designs are used in experiments, where the effects of different factors or conditions on experimental results are to be evaluated[9]. In factorial designs, levels of factor are independently varied, each factor at two or more levels. A factor is an assigned variable such as concentration, temperature, lubricating agent, drug treatment or diet. Factor may be qualitative or quantitative. The levels of a factor are the values or designations assigned to the factors. The runs or trials that comprise full factorial experiments consist of all combinations of all levels of all factors. The effect of a factor is the change in response caused by varying the levels of the factor. The important objective of a factorial experiment is to characterize the effect of changing the levels of factor or combination of factors on the response variable. The predictions based on results of an undersigned experiment will be less variable. The optimization procedure is facilitated by construction of an equation that describes the experimental results as a function of the factors. A 32 randomized full factorial design was used in development of dosage form. In this design, two factors were evaluated each at three levels and experimental trials were performed at all possible nine combinations. The content of polymer (X1) and ratio of HPMC K4M to HPMC K100M (X2) were selected as independent variables. Percentage drug release at 2 hr (Q2), 6 hr (Q6), 12 hr (Q12), 18 hr (Q18), 24 hr (Q24), release rate constant (K) and diffusion exponent (n) were selected as dependent variables. The content of polymer was evaluated at 125mg, 150mg, and 175mg while the ratio of HPMC K4M and HPMC K100M was evaluated at 75:25, 50:50 and 25:50. The experimental design with corresponding formulations is outlined in Table 2, 3, 4. A statistical model incorporating interactive and polynomial terms was utilized to evaluate the response (equation 1) [9]

$$Y = bo + b1X1 + b2X2 + bl2X1X2 + b11X1X1 + b22X2X2 \quad (1)$$

Where Y is the dependent variable, βo is the arithmetic mean response of the 9 runs, and bi is the estimated coefficients for the factor X. The main effect (X1 and X2) represents the average result of changing one factor at a time from its low to high value. The interaction term (X1X2) shows how the response changes when two factor are change simultaneously. The polynomial term (X1X1, X2X2) are included to investigate nonlinearity. The magnitude of the coefficients represents the relative importance of each factor. Once the polynomial equation has been established, an optimum formulation can be found by grid analysis.

III. CONCLUSION:

In this study the attempt was made to develop once a day film coated tablet of Tolperisone HCl using different grade of hydroxy propyl methyl cellulose as a matrix forming polymer. Tablets had desired buoyancy characteristics. It was found that total content of had dominant role on retardation of drug release from floating matrix tablets compared to polymer ratio of HPMC K15M to HPMC K100M, although the presence of later component in formulation is essential to improve the integrity of tablet. Use of combination of polymer in tablet reduces the total content of polymer used. From the conducted investigation it can be concluded that once a day Tolperisone HCl delivery is feasible using hydroxy propyl methyl cellulose film Coating tablet.

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