International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 2(2): March-April 2012

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences **Research Article……!!!**

Received: 03-03-2012; Accepted: 10-03-2012

DEVELOPMENT AND VALIDATION OF DISSOLUTION METHOD OF TOLPERISONE HYDROCHLORIDE FILM COATED TABLETS AND ITS COMPARATIVE IN VITRO DISSOLUTION STUDY

Komal B. Patel*, Dushyant A. Shah, Rajesh R. Parmar

Department of Quality Assurance, APMC College of Pharmaceutical Education and Research, College Campus, Motipura, Himmatnagar – 383001, India

Keywords:

Tolperisone hydrochloride, Dissolution method validation, UVspectrophotometer, in vitro dissolution testing

For Correspondence:

Komal B. Patel

Department of Quality Assurance, APMC College of Pharmaceutical Education and Research, College Campus, Motipura, Himmatnagar – 383001, India

E-mail:

kpkomalpatel711@gmail.com

ABSTRACT

The aim of this work is to develop and validate a dissolution method for 150mg Tolperisone hydrochloride film coated tablets using a UV spectroscopic method. Tolperisone HCl as a frequently used as centrally muscle relaxants has no dissolution method in its monograph in Japanese pharmacopeia. After test sink conditions, dissolution medium, the best conditions were: Basket apparatus at 75 rotations per minute (rpm) stirring speed, 0.1 N HCl as dissolution medium volume of 900 ml. The quantitation method was also adapted and validated. More than 95% was achieved over 30 min in the basic one. The dissolution profile for tablets was considered satisfactory. And in comparative study three marketed brands of Tolperisone HCl 150mg tablets have been evaluated using dissolution test in 0.1N HCl media with the aim to assess bioequivalence. The dissolution test developed was adequate for its purpose and could be applied for quality control of Tolperisone hydrochloride tablets. Minutes. The in vitro release profiles of various tests were compared for their similarity using the f2 test. Results of this test indicate that in most cases dissolution profiles of the different marketed brands were significantly different from each other. The first objective of this study was to assess the interchangeability of the available Tolperisone HCl products on the basis of their in vitro dissolution characteristics using USP Apparatus 2(Basket type). The second objective was to compare dissolution profiles in simulated fasted and fed states and determine whether there is a change in the mechanism of drug release.

INTRODUCTION

Dissolution is a qualitative and quantitative tool which can provide valuable information about biological availability of a drug as well as batch to batch consistency, new formulation development guide and ensure product quality and performance after changes in the manufacturing process. Like many performance tests in regulated environment, the dissolution is considered to be one of the most important control tests performed on pharmaceutical dosage forms and developing and validation of dissolution methods is an important part of good manufacturing practices. Here, highlights of some specific method development and validation guidelines used in developing and validating dissolution test methods. Dissolution testing is an in vitro laboratory test method that is designed to demonstrate how efficiently an active drug substance is extracted out of a solid oral dosage form. In vitro dissolution testing is an important physicochemical tool used to measure drug release rates during both early and late stages of drug development.

Tolperisone Hydrochloride ($C_{16}H_{23}NO.HCl$) is official in Japanese pharmacopoeia, Molecular weight 281.82 g/ mol g/mol ,with chemical name: 1-piperidino-2-methyl-3-(p-toll)-3-propanonehydrochloride. It being, centrally acting muscle relaxant, tolperisone acts at the level of spinal cord by blocking sodium channels and calcium channels.

Difference factor (f1), similarity factor (f2) were calculated and compare for dissolution data obtained from two dissolution media. Difference factor f1 is the percentage difference between two curves at each point and is a measurement of the relative error between the two curves. The similarity factor (f2) is a logarithmic reciprocal square root transformation of the sum of squared error and is a measurement of the similarity in the percent (%) dissolution between the two curves. The following equations were used to calculate difference factor f1 and similarity factor.

$$f_1 = \left\{ \frac{\sum_{t=1} |R_t - T_t|}{\sum_{t=1}^{n} R_t} \right\} X100 \quad f_2 = 50 \log \left\{ \left(1 + \frac{1}{n} \sum_{i=1}^{n} (R_t - T_t)^2 \right)^{-0.5} X100 \right\}$$

where n is the number of time points, Rt is the dissolution value of reference product at time t and Tt is the dissolution value for the test product at time t. Two dissolution profiles are considered similar and bioequivalent, if f1 is between 0 and 15 and f2 is between 50 and 100 (FDA, 1997).

MATERIALS AND METHODS

Chemicals and Reagents

Tolperisone HCl was obtained as a gift sample from zydus cadila health care ltd, ahmedabad, Gujarat, India. Marketed film coated tablets contains 150mg TOLPERISONE HCl. All other chemicals used were of analytical grade. Distilled water and caliberated glasswares were used throughout the work.

Apparatus

A shimadzu model 1700 (Japan) double beam UV-Visible spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. A Reptech electronic weighing analytical balance based on EMFC technology was used in the study, Dissolution apparatus.

Preparation of standard stock solutions

An accurately weighed quantity of TOLPERISONE HCl (100 mg) was transferred to a separate 100 ml volumetric flask and dissolved and diluted to the mark with 0.1 N HCl to obtain standard solution having concentration of TOLPERISONE HCl (1000 µg/ml). Accurately measured 10 ml of the solutions was transferred to 100ml of volumetric flask and diluted to the mark with 0.1N HCl to obtain solution having concentration 100 µg/ml of TOLPERISONE HCl.

Method

Dissolution was conducted using a dissolution tester using USP Apparatus 2 (Basket type apparatus) at a temperature of 37.0 ± 0.5 ºC with use of 0.1 N HCl. For all experiments filtered with whatman filterpaper , aliquots (5 ml) were withdrawn with replacement at appropriate time intervals at duration of 5min up to 45 min, using a 5mL bulb pipette. Dilute the appropriate withdrawal sample up to 100ml in 100 ml volumetric flask with help of 0.1 N HCl All the sample solutions were protected from the light until being analyzed. Due to the limited number of samples, 6 tablets per formulation were tested in the development and validation stage, and six in the optimized conditions. The cumulative percentage of Drug released (%DR) was determined by UV spectrometer at 260 nm. This procedure was repeated during 45min.The results of these studies revealed no significant loss of API. This method proceeds for different three brands of tolperisone hydrochloride.

Validation of the proposed method:

The proposed method was validated according to the International Conference on Harmonization (ICH) guidelines.

Linearity (Calibration curve)

The calibration curves were plotted over a concentration range of 2-18µg/ml for TOLPERISONE HCl. Accurately measured standard solutions of (2, 6, 10, 14, and 18 ml) TOLPERISONE HCL was transferred to a series of 100 ml of volumetric flasks and diluted to the mark with 0.1 N HCl. The absorbance of the solutions was measured at 260 nm against 0.1 N HCl as blank. The calibration curves were constructed by plotting absorbances versus concentrations and the regression equations were calculated.

Precision

The repeatability of dissolution procedure was accomplished by submitting six samples of each product (A,B,C) to the optimized dissolution test. Aliquots were collected and evaluated by spectrophotometry at 260 nm. The intermediate precisions were determined similarly but a second analyst repeated the procedure in a different day. The R.S.D values for determinations were calculated.

Accuracy (recovery study)

The accuracy was evaluated by adding known amounts of the reference substance to the placebo sample in the dissolution medium at 80, 100 and 120% of the nominal assay of TOLPERISONE HCl, corresponding to the concentrations of 116.8,146,175.2mg,115.20,144,172.80mg& 117.60,147,175.40mg for product A,B,C respectively. Aliquots was collected and analyzed by spectrophotometry at 260nm in 0.1N HCl. The accuracy was calculated as the percentage of the drug recovered from the formulation matrix and also expressed as the percentage relative error (bias %) between the measured mean concentrations and added concentrations. These studies were performed in triplicate.

ILLUSTRATIONS: TABLES AND FIGURES

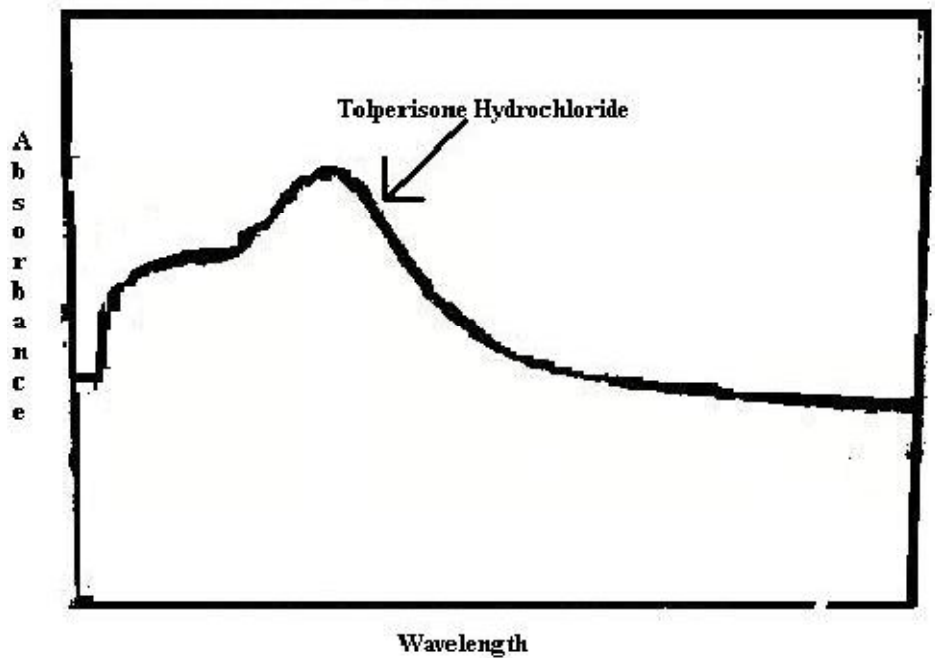

FIGURE 1: spectrum of Tolperisone HCl in 0.1 N HCl

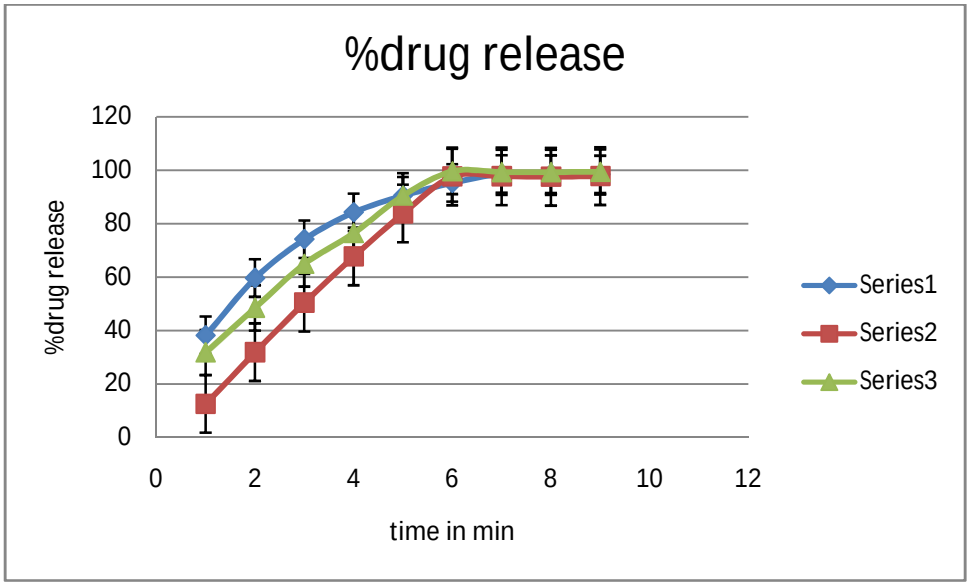

FIGURE 2: Dissolution profile of 150 mg film coated tablets of tolperisone HCl products codified as A, B and C under optimal dissolution conditions using UV spectroscopic method, series 1- A,2-B,3-C(Bars indicate the standard deviation.)

TABLE-1 REGRESSION ANALYSIS DATA AND SUMMARY OF VALIDATION PARAMETER OF THE CALIBERATION CURVES

Parameters	TOLPERISONE HCl
Wavelength (nm)	260nm
Beer's law limit (µg /ml)	2-18 µg /ml
Regression equation (y = a + bc) Slope (b) Intercept (a)	y = 0.044x + 0.007 0.007 0.044
Correlation coefficient (r^2)	0.999
LOD (µg/ml)	0.080
LOQ (µg /ml)	0.241

TABLE-2 REPEATABILITY AND INTERMEDIATE PRECISION OF THE DISSOLUTION OF TOLPERISONE HCl

Intraday(*n*=6),set3	Mean observed value (%release) ± SD			RSD (%)		
	A	B	C	A	B	C
Day-I	98.85±0.660	97.80±0.290	99.61±0.457	0.668	0.297	0.450
Day-II	98.41±0.503	97.77±0.168	99.47±0.293	0.511	0.172	0.294
Day-III	98.52±0.533	97.79±0.168	99.50±0.531	0.541	0.172	0.534
Interday precision (n=3)	98.53±0.205	97.77±0.030	99.52±0.075	0.208	0.031	0.075

TABLE-3 RESULTS OF THE RECOVERY STUDY

Std addition of drugs in mg	Mean recovery % (n=6)		
	A	B	C
80%	99.14	97.45	98.55
100%	99.95	98.32	99.45
120%	99.55	97.82	99.23
Mean absolute recovery (%) ± SE (*n* = 18)	99.55 ± 0.429	97.77±0.377	98.96±0.471

TABLE-4 f1, f2 OF TOLPERISONE HCl

BRANDS	F1	F2
A(std)	-	-
B	2.46	60.70
C	13.58	23.86

ABRREVIATIONS

HCl-Hydrochloride, API-Active Pharmaceutical Ingredient, USP-United State Pharmacopoeia

RESULTS AND DISCUSSION

The proposed methods were found to be simple, accurate and rapid for the routine determination of TOLPERISONE HCL 150 mg film coated tablets(A,B,C). To study the validity and reproducibility of proposed methods, recovery studies were carried out. The methods were validated in terms of linearity, accuracy, precision. In this method linearity was observed in the concentration range of 2-18 µg/ml for TOLPERISONE HCl. Validation parameters are presented in Table-1. Marketed brand of 150mg of film coated tablets (A,B,C) was analyzed % drug release determined by proposed methods was 98.85% , 97.80%,and 99.61% respectively (Table-2). The proposed methods were validated as per ICH guideline. The accuracy of method was determined by calculating mean percentage recovery at 80, 100 and 120 % level. The % recovery ranges from 97.45 to 99.55 % release for TOLPERISONE HCl respectively for drug product A,B,C and are presented in Table-3. Precision was calculated as inter and intraday variations for drugs. The comparison of in vitro dissolution study of different brands of product is calculated by f1,f2 where f1 is between 0 and 15 and f2 is between 50 and 100 .

ACKNOWLEDGEMENT:

The authors are thankful to Cadila Healthcare Ltd, Ahmedabad, Gujarat, India for providing Tolperisone HCl for research. The authors are highly thankful to APMC College of Pharmaceutical education and research, Himatnagar, Gujarat, India for providing all the facilities to carry out the work.

REFERENCES

1. Japanese Pharmacopoeias JP15 pp. 1190.
2. Vaghela B, Kayasstha R, Bhatt N, Rathod D, Pathak N," Development And Dissolution
3. Procedure", Journal of Applied Pharmaceutical Science, 2011: 01(03); 50-60.
4. B.R.Babu "Method development and validation for dissolution testings" Research Journal of Pharmaceutical, Biological and Chemical Science ,January – March 2011, 2(1): 561 -574.
5. Chung chaw chan,Y.C.Leo,Harman Lam, Analitycal method validation and instrument performance verification, A John Wiley & Sons, Inc., Publication,51-66.
6. British Pharmacopoeia, Vol II London, The British Pharmacopoeia Commission, Ghaziabad, 2007, pp-A-223.
7. FDA Division of Pharmaceutical Analysis, Mechanical Qualification of Dissolution apparatus 1 and 2, Document # DPA- LOP.002, Version 2.0, June 2006.
8. Skoog D.A et al., "Introduction to UV Spectroscopy in, Principle of Instrumental Analysis", Fifth edition, Thomson Brooks/Cole publication, pp. 301, 893-934
9. Beckett .A.H., Stenlake .J.B., "Practical Pharmaceutical Chemistry", CBS Publishers and distributors, 14th Edition;1997; pp. 275-337.
10. Banker U.V., "Pharmaceutical Dissolution Testing", Informa health care, New York London,Vol.49:pp19-52
11. httm:/www.sanochemia.at/en/research-devlopment/product- pipeline/tolperisone /#1779
    httm://www.drug-pro.com/other/mydoca/m.html