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Research Article

DOSAGE FORM DESIGN AND EVALUATION OF EPERISONE HYDROCHLORIDE MATRIX FILM COATED EXTENDED RELEASE TABLETS

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ABSTRACT

The object of this present study was to develop extended release matrix film coated tablets of Eperisone hydrochloride to enhance the therapeutic efficacy, reduce the frequency of administration and improve the patient compliance. The matrix film coated tablets were prepared by wet granulation method, using different polymers such as Hydroxyl propyl methyl cellulose (HPMC K4M, K100M), Ethyl Cellulose (EC), Microcrystalline cellulose pH 101 (MCC), alone or in combinations and other standard excipients. The granules of different formulations were determined for bulk density, tapped density, compressibility Index and Hausner ratio. Formulated tablets were evaluated for physical characteristics viz. hardness, thickness, friability, percentage weight variation and drug content. Further, tablets were evaluated for *In-vitro* release characteristic for 12 hrs. Tableting of granules was showed good flow properties and fabricated tablets were exhibited desired compressibility characteristics. Formulation (F5) exhibited an *In-vitro* drug release up to of 90% and the release kinetics of drugs was best explained by Krosmeyer- peppas model. The optimized formulation was passed the stability studies carried out at room temperature (25ºC±2º/60º±5%RH) as per ICH guidelines and an accelerated stability conditions (40ºC±2º/ 75%±5%RH) for 3 months. The designed Eperisone hydrochloride matrix film-coated tablets have a potential for Extended-release dosage forms.

Keywords: Eperisone hydrochloride, Extended release, Release kinetics

INTRODUCTION

Eperisone (4-ethyl-2-methyl-3-piperidino) propiophenone hydrochloride (Formulated as the Eperisone hydrochloride salt) is a new generation antispasmodic drug. It belongs to Anticholinergic agent pharmacological group and the Molecular Weight of the drug is 295.80[1]. It exhibits both skeletal muscle relaxant and vasodilator properties because of its actions within the central nervous system and on vascular smooth muscles and demonstrates a variety of effects such as cervical spondylosis, headache and low back pain [2-5].

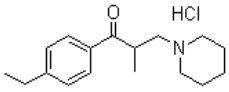

Fig. 1: Chemical structure of Eperisone hydrochloride.

It reduces alpha- and gamma-efferent activities and inhibits spinal cord activities by acting on the spinal cord and supra spinal structures. In addition to its relaxant effect, Eperisone hydrochloride exerts a vasodilatatory activity, thus increasing muscle blood flow. Importantly, it has not demonstrated sedative effects, differing from other muscle relaxant agents. In spite of its favorable clinical response and lack of significant draw backs, chronic therapy with Eperisone hydrochloride, suffers from certain problems of which the most prominent is the dose level fixation. Eperisone hydrochloride has a biological half-life of 1 to 4.3 hrs i.e., it requires three-times a day dosing [6-8]. Multiple daily dosing is inconvenient to the patient and can result in missed doses, made up doses and patient incompliance with the therapeutic regimen. The success of therapy depends on selection of appropriate delivery system as much as it depends on the drug itself. Extended release dosage forms are designed to complement the pharmaceutical activity of the medicament in order to achieve better selectivity and longer duration of action. Thus, Eperisone hydrochloride is chosen as a suitable candidate for extended release drug delivery system. In this study, an attempt was made to design and formulate the matrix film coating extended release tablets of Eperisone hydrochloride.

MATERIALS AND METHODS

Materials

Eperisone hydrochloride was obtained as a gift sample from Macleod's Pvt Ltd. (India). Hydroxy propyl methyl cellulose (HPMC K4M &K100) was procured from Colorcon Asia Bio limited. (India). Ethyl Cellulose was from Hercules Incorporated. (USA). Micro crystalline cellulose (MCC) was purchased from FMC. (USA), Magnesium stearate and Calcium stearate were obtained from Ferro Industry. (Quimicas). Talc was from Accord labs. (Hyderabad). Hydroxy propyl cellulose (HPC) was received from Nitika Chemicals. (India).Titanium dioxide was purchased from Travancore Titanium product Ltd. (India). All other chemicals and solvents used were analytical grades.

Methods

Compatibility study of Eperisone hydrochloride by DSC

Differential scanning calorimetry (DSC) analysis was performed with a Mettler DSC 822e (Mettler Toledo, Greifensee, Switzerland). In this study, the mixture of drug and polymer samples were weighed hermetically sealed in aluminum containers and scanned in the temperature range of 35 to 300ºC at 10ºC/min and thereafter heat transfer was measured [29]. Measurements resulted in an endothermic peak upon increase in temperature, where CMT (critical micelle temperature) was taken as the onset of the endothermic peak.

Preparation of matrix tablets

Different tablet formulations were prepared by the wet granulation technique. Drug (Eperisone hydrochloride) and excipients (HPMC K4M & K100M, MCC, HPC, Ethyl cellulose, Calcium stearate, and Magnesium stearate) were accurately weighed as mentioned in the Table 1. Drug, Hydroxy propyl methyl cellulose and Micro crystalline cellulose were passed through sieve 40#. Cosift all the three ingredients in geometric proportions by passing through sieve 30#. These ingredients were mixed for 3 minutes and binding solution was prepared by dissolving hydroxy propyl cellulose/Ethyl cellulose in Iso propyl alcohol. After, mass of cohesive material was passed through sieve 22# and 44#. These granules were dried in tray dryer till the desired limit for loss on drying is achieved. The dried granules were passed through sieve 20# and Magnesium stearate/Calcium stearate were passed through sieve 60# and uniformly mixed with the dried granules in the polybag for 5 minutes. Then the blend was compressed (9.5mm, diameter, flat punches) using multipunch tablet compression machine (Cadmach, Ahmadabad, India) in such a way that each tablet should contains 150mg of Eperisone HCl.

Measurements of flow properties

Angle of repose of different formulations was determined by a fixed funnel method. It has been used to characterize the flow properties of granules .The granules were poured through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation [9].

$\tan \theta = h/r$

Where, θ= Angle of repose, h= height of cone, r= radius of cone.

Table 1: Composition of extended release matrix film coated tablets of Eperisone Hcl

S. No	Ingredients	Quantity used in mg						
		F1	F2	F3	F4	F5	F6	F7
1.	Eperisone	150	150	150	150	150	150	150
2.	HPMC K4M	135	110	120	100	60	71	90
3.	HPMC K100M	-	-	-	16	20	14	22
4.	MCC pH 101	-	29	21	23	57	54	27
5.	Hydroxy propyl cellulose	-	-	6	8	10	8	8
6.	Ethyl cellulose	10	8	-	-	-	-	-
7.	Iso propyl alcohol (ml)	250	190	60	85	95	95	85
8.	Dichloromethane (ml)	325	265	-	-	-	-	-
9.	Magnesium stearate	5	-	-	-	-	-	-
10.	Calcium stearate	-	3	3	3	3	3	3
	Coating							
11.	HPMC E5M	8	8	8	8	8	8	8
12.	Titanium dioxide	2	2	2	2	2	2	2
13.	Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5
14.	Ethyl cellulose (7 cps)	-	-	2	2	-	2	2
15.	Propylene glycol (ml)	5	5	5	5	5	5	5
16.	Iso propyl alcohol (ml)	120	120	120	120	120	120	120
17.	Dichloromethane (ml)	190	190	190	190	190	190	190

Bulk density was determined by placing pre-sieved drug excipient blend in to a graduated cylinder and measuring the volume and weight as it is [10]

$$\text{Bulk density} = \frac{\text{Mass of the Powder}}{\text{Bulk Volume}}$$

Tapped density is the ratio of mass the powder taken to the volume occupied after specific tapping. It was determined by USP method II, tablet blend was introduced in the 100 ml graduated cylinder of tap density tester, which was operated for fixed number of taps until the powder bed volume has reached a minimum, thus was calculated using the following formula.

$$\text{Tapped density} = \frac{\text{Mass of the Powder}}{\text{Tapped Volume}}$$

Compressibility Index (CI) has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content, and cohesiveness of materials because all of these can influence the observed compressibility Index [11]

$$\text{Compressibility (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped volume}} \times 100$$

Hausner's ratio has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content, and cohesiveness of materials because all of these can influence the observed hausner's ratio [12]

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk}}$$

Loss on Drying (LOD)

The moisture content of the granules was analyzed by using Infra Red Moisture Analyzer. 1.0 gm or more quantity of granules was heated at 105ºC until the change in the weight was no more observed by the instrument. The % loss in weight was recorded [13].

Evaluation of tablets

Average Weight variation

Weight variation test was done as per USP methods, twenty tablets were selected at a random and average weight was calculated. Then individual tablets were weighed (Shimadzu, Japan), and the individual weight was compared with an average weight [14].

Hardness and Thickness

Hardness was measured using Monsanto hardness tester (Paramount science Instruments), India, for each batch six tablets were tested. Thickness was done by using Screw-gauge micrometer (Campbell Electronics, India.) Twenty tablets from each batch were randomly selected and thickness was measured [15].

Friability

Friability was determined according to British Pharmacopoeia with Roche friabilator (Electro lab, India). Twenty tablets were weight and placed in the Roche friabilator and it was operated at 25 rpm for 4 min. After revolution the tablets were weighed and calculated the percentage friability [16].

Assay of tablets

Twenty tablets from each batch were weighed and powdered. Powder equivalent to the average weight of the tablet was accurately weighed and transferred into a 100ml volumetric flask and dissolved in a suitable quantity of buffer pH 6.8. The solution was made up to the mark and mixed well. A portion of the sample was filtered and analyzed by a UV spectrophotometer (Shimadzu UV-150, Japan) at 260nm.

In-Vitro release

In vitro drug release was determined by using USP XXIII dissolution apparatus II. The release studies were performed at 100 rpm in 900 ml of using 0.1NHcl for first 2 hrs and followed by phosphate buffer pH 6.8 up to 12 hrs. The temperature was maintained at 37 ± 0.5ºC. Ten milliliters of sample was withdrawn at predetermined time intervals and the volume of the dissolution medium was maintained by adding the same volume of fresh prewarmed buffer every time. The withdrawn sample was filtered through a 0.8µm filter membrane and the absorbance was measured spectrophotometrically (Shimadzu UV-150, Japan) at 260nm.

The content of Eperisone hydrochloride was determined at 260 nm by UV spectrophotometry Calibration curve was prepared using 0.1N HCL in the concentration range of 1 – 15 µg/ml. The drug was analyzed spectrophotometrically (Shimadzu UV-150, Japan) at 260 nm (Regression coefficient r^2 = 0.9988 in 0.1N HCL). Similarly Calibration curve of Eperisone HCL for pH 6.8 was prepared (Regression coefficient r^2 = 0.9997 pH 6.8).

Release kinetics

Release kinetics models are assumed to reflect different release kinetics mechanisms. The zero order rate (equation one) describes the systems where the drug release rate is independent of its concentration [17]. The first order equation two, describes the release from systems where release rate is concentration dependent [18]. Higuchi (1963) described the release of drugs from insoluble matrix as a square root of time dependent process based on Fickian diffusion equation (equation three)[19]. The Hixson-Crowell cube root law (equation four) describes the release from systems where there is a change in surface area and diameter of tablets or particles [20].

$C = k_o t$ (i)

Where, K_0 is zero-order rate constant expressed in units of concentration/time and t is the time.

LogC = Log-Co kt / 2.303 (ii)

Where, C_0 is the initial concentration of drug and K is first order constant.

$Q = Kt^{½}$ (iii)

Where, K is the constant reflecting the design variables of the system.

$Q_0^{1/3} – Qt^{1/3} = KHC\ t$ (iv)

Where, Qt is the amount of drug released in time t, Q_0 is the initial amount of the drug in tablet and KHC is the rate constant for Hixson-Crowell rate equation.

The release of drugs from the matrix tablets can be analyzed by release kinetics theories .To describe the kinetics of drug release from matrix tablets, release data was analyzed according to Korsmeyer- Peppas equation (equation 5)[21].

$$Mt/M_\infty = Kt^n \text{ (v)}$$

Where,

$Mt/M\infty$ = fraction solute release

t = release time

K = kinetic constant characteristic of the drug/ polymer system n = exponent that characterizes the mechanism of release of traces

Stability studies

These studies were carried out for the optimized batch for a period of three months at room temperature (25ºC±2º /60º±5%RH) as per ICH guidelines and an accelerated stability conditions (40ºC±2º /75%±5%RH). Then the tablets at specific intervals were evaluated for appearance, average weight, drug content and *In-vitro* release [22,23,28].

RESULT AND DISCUSSION

Results

Compatibility study of Eperisone hydrochloride by DSC

Drug excipient compatibility studies were carried out to check whether any compatibility related problems are associated between drug and excipients used in the formulations. Differential Scanning Calorimetry results revealed that the physical mixture of Eperisone hydrochloride with excipients showed superimposition of the thermograms. There is no considerable change observed in melting endotherm. The DSC thermograms are shown in Figure 2-4. Differential Scanning Calorimetry, result revealed that there is no significance interaction between the drug and the excipients used in the formulation. Hence the polymers are compatible with drug [24-26, 29].

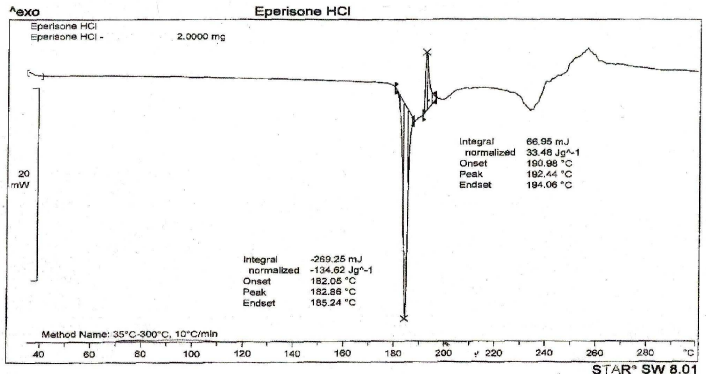

Fig. 2: DSC thermogram of Eperisone hydrochloride

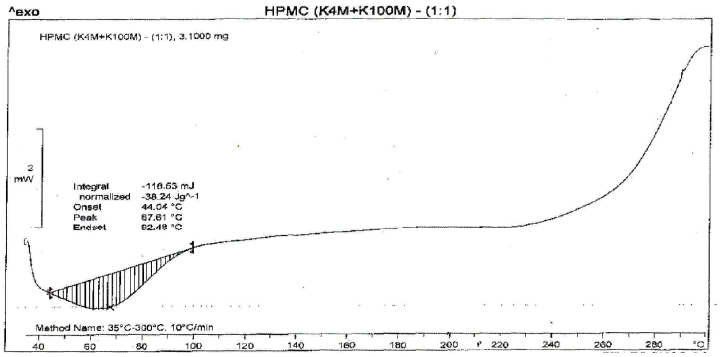

Fig. 3: DSC Thermogram of Hydroxy propyl methyl cellulose (K4M+K100M)

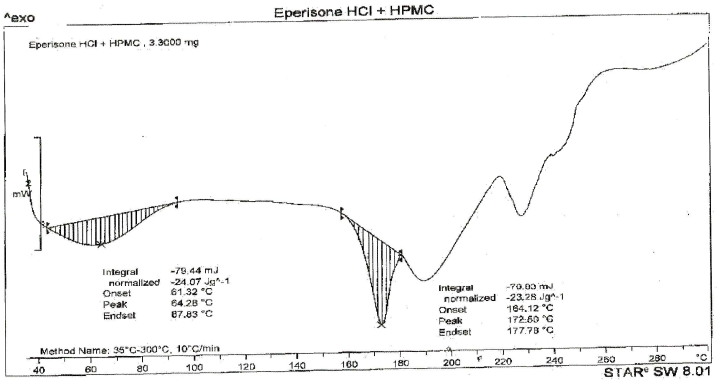

Fig. 4: DSC thermogram of Eperisone hydrochloride: Hydroxy propyl methyl cellulose

Evaluation of granules

The granules of various formulations were prepared and evaluated for bulk density, tapped density, compressibility index, and Hausner's ratio. Results of angle of repose (Ø) ranged from 21.30 ± 0.01 to 26.65 ± 0.91. Bulk density and tapped density were found 0.302 ± 0.00 to 0.387 ± 0.00 g/ml and 0.421 ± 0.06 to 0.538 ± 0.03g/ml. The bulk density depends on particle size, shape and cohesiveness of the particles. The Hausner's ratio was found from 1.19 ± 0.002 to 1.39 ± 0.002, which is well within the possible. The compressibility index, ranged from 20.33 ± 2.45 %to 24.65% ± 2.01 as indicates pass to possible flow properties. All these results were given in Table 2.

The tablets of different formulations (F1 to F7) were evaluated for various parameters such as, percentage weight variation, thickness, hardness, friability and drug content. The results of these parameters are gives in Table 3.

Table 2: Measurements of flow properties*

Parameters	Observations						
	F1	F2	F3	F4	F5	F6	F7
Angle of repose (Ø)	22.1± 0.11	25.66± 0.38	23.99± 0.12	21.99± 0.95	24.65± 0.65	26.65± 0.91	24.84± 0.03
Bulk density (g/ml)	0.387±0.00	0.344±0.00	0.302±0.00	0.320±0.00	0.351±0.00	0.357±0.00	0.330±0.00
Tapped density (g/ml)	0.538±0.03	0.432±0.04	0.447±0.03	0.427±0.08	0.421±0.06	0.425±0.04	0.4109±0.02
Compressibility index (%)	28.07±0.04	20.33±2.45	32.85±1.5	24.65±2.01	17.0±0.05	16.05±1.05	23.65±2.28
Hausner's ratio	1.39±0.002	1.25±0.005	1.48±0.003	1.38±0.003	1.22±0.002	1.19±0.002	1.36±0.006
Loss on drying (%)	2.48	3.05	2.94	2.37	2.40	2.23	2.49

* All values are expressed as mean ± SD

Table 3: Evaluation of Eperisone hydrochloride release matrix film coated tablets

Parameters	Observations						
	F1	F2	F3	F4	F5	F6	F7
Average weight(mg)	300.05±0.98	302.45±0.88	299.88±1.00	300.43±1.06	300.23±1.23	301.03±1.80	299.45±1.01
Thickness (mm)	4.1-4.8	4.5-4.6	4.4-4.6	4.47-4.52	4.1-4.5	4.2-4.8	4.47-4.52
Hardness (kg/cm^2)	10.5±0.45	10.5±0.82	9.45±0.77	9.89±0.16	10.21±1.30	9.52±1.08	9.75±0.66
Friability (%)	0.38±0.03	00.45±0.02	0.14±0. 01	0.21±0.02	0.32±0.06	0.28±0.01	0.24±0.09
Assay (%)	74.34	83.36	95.0	95.25	95.22	95.45	97.84

In-vitro drug release

The percentage drug release profiles of Eperisone hydrochloride from seven formulations were used with different polymers and in their combinations. It was observed that the polymers influence the drug release pattern. A significantly higher rate and extent of release was observed from batches based on hydroxy propyl cellulose and micro crystalline cellulose than those based on hydroxy propyl methyl cellulose alone. The combination of MCC and HPMC K4M sustains the drug release for longer time. The varying amount of HPMC K4M didn't affect the drug release. Formulations containing combinations of different grades of hydroxy propyl methyl cellulose were evaluated.

An addition of Ethyl cellulose was decrease the drug release. The formulations F4 and F5 drug release is faster than other formulations. The formulations were showing the drug release data in Table 4 and the drug release profile was depicted in Figure 5 and 6.

Table 4: In-vitro drug release profile of Eperisone hydrochloride different formulations

Time (hrs)	Formulations*						
	F1	F2	F3	F4	F5	F6	F7
2*	17.23±1.20	19.61±1.89	42.25±1.20	36.34±1.49	41.07±1.72	37.65±1.07	32.10±1.36
4	27.66±2.55	30.84±1.27	66.84±0.91	58.18±1.69	58.39±1.63	54.69±2.17	48.50±2.07
6	33.80±1.32	44.87±2.05	72.55±1.30	72.88±1.23	68.68±1.37	64.07±1.46	55.50±0.93
8	42.41±1.66	46.87±2.12	76.82±1.87	82.26±1.49	74.37±2.52	69.45±1.28	61.20±1.87
10	53.61±1.93	56.27±1.65	80.14±1.32	86.93±1.35	85.74±1.57	68.07±2.19	64.70±1.32
12	58.32±2.80	59.45±1.19	81.37±1.65	90.01±2.05	99.38±1.19	67.65±1.44	71.32±2.80

***First two hour in pH 0.1 N HCl and followed by phosphate buffer pH6.8 medium

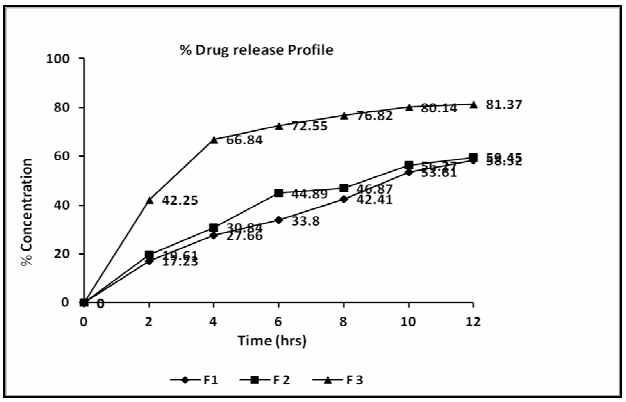

Fig. 5: Dissolution release profile of Eperisone hydrochloride

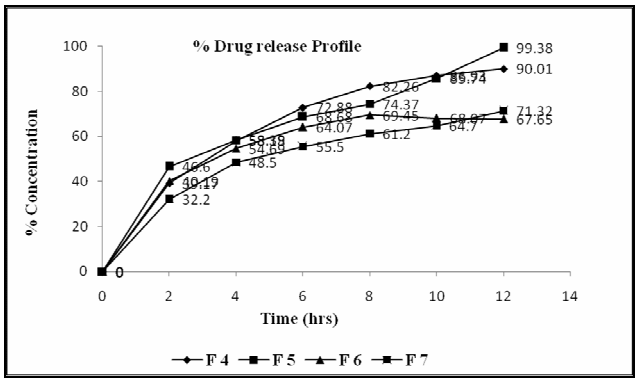

Fig. 6: Dissolution release profile of Eperisone hydrochloride

Release Kinetics

To describe the drug release kinetics of from matrix tablets, release data was analyzed according to different kinetic equations. Such as zero order, first order, Higuchi's model, Korsmeyer-peppas, and Hixson-crowell.The data were analyzed by the regression coefficient method and regression coefficient value (r^2) of all batches are shown in Table 5. The formulations F3, F4 and F5 were followed Korsmeyer –peppas model, F7 was followed Hixson Crowell kinetics whereas remaining all the formulations showed Higuchi's release kinetics. The in vitro release profiles of drug from all these formulations could be best expressed by Higuchi's equation as the plots showed highest linearity (r^2=0.98to 0.99). To confirm the diffusion mechanism, the data were fitted into Korsmeyer-Peppas equation. The formulations showed good linearity (r^2 = 0.965 to 0.98) with slope (n) between 0.470- 0.586, which appears to indicate a coupling of diffusion and erosion mechanisms-so called anomalous diffusion.

Table 5: Different formulations release kinetics data

	Formulations						
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
Zero order							
r^2	0.742	0.865	0.243	0.720	0.744	0.409	0.682
K	5.626	5.732	8.822	9.219	9.296	7.504	7.098
First order							
r^2	0.620	0.588	0.440	0.526	0.515	0.472	0.520
K	4.661	4.496	3.812	3.907	3.886	4.01	4.144
Higuchi							
r^2	0.970	0.986	0.880	0.987	0.986	0.917	0.984
K	0.063	0.058	0.035	0.035	0.035	0.042	0.046
Korsmeyer-peppas							
r^2	0.988	0.975	0.991	0.977	0.993	0.965	0.985
K	16.80	17.12	20.09	19.69	20.84	17.46	18.91
N	0.586	0.470	0.618	0.615	0.677	0.453	0.625
Hixson-crowell							
r^2	0.935	0.954	0.972	0.980	0.991	0.964	0.993
K	0.053	0.041	0.046	0.046	0.051	0.380	0.056

Stability studies

The selected formulation was subjected upto 3 months for stability studies as per ICH guidelines at room temperature (25ºC±2º / 60º±5%RH) and an accelerated stability (40ºC±2º /75%±5%RH) to find out the effect of aging on release pattern. The result of the stability study does not indicate any significant changes in drug content, average weight and *In-vitro* drug release.

The results are shown in Table 6 and 7.

Table 6: Stability study of drug content, average weight and *In-vitro* drug release profile for optimized formulation at room temperature (25ºC±2º /60º±5%RH)*

Test	Specifications	Initial	1 Month	2 Months	3 Months
Appearance	White, circular, biconvex, Coated plain on both side	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Average weight(mg)	300±2.5	300.05±1.0	299±1.23	298±0.88	298±1.80
Hardness (kg/cm^2)	8.5 - 11.50	9.50±0.82	10.25±0.16	9.15±1.08	9.80±0.77
Dissolution	2 hrs.	41.07±1.25%	40.45±1.37%	40.25±1.43%	40.19±0.95%
	4 hrs.	58.39±1.96%	56.81±1.84%	57.50±1.24%	57.25±0.62%
	6 hrs.	68.68±1.75%	67.20±1.07%	68.07±2.55%	67.86±1.30%
	8 hrs.	74.37±1.35%	75.46±2.19%	74.46±1.46%	73.46±2.17%
	10 hrs.	85.74±2.06%	87.37±1.93%	86.93±1.69%	85.38±1.35%
	12 hrs.	99.38±1.58%	99.15±1.20%	98.85±1.71%	98.94±1.18%
Assay	90.0% -110% of The labeled amount	97.75±1.08%	96.25±1.58%	96.10±1.19%	97.12±1.27%

*All values are expressed as mean ± SD

Table 7: Stability study of drug content, average weight and *In-vitro* drug release profile for optimized formulation at Accelerated condition (40°C±2º /75%±5%RH)

Test	Specifications	Initial	1 Month	2 Months	3 Months
Appearance	White, circular, biconvex, Coated plain on both side	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Average Weight(mg)	300 ± 2.5	300±1.06	298±1.80	298±0.88	298±0.72
Hardness (kg/cm^2)	8.5 – 11.50	9.50±0.45	10.50±0.63	9.25±1.05	9.60±0.15
Dissolution	2 hrs.	41.07±1.69%	41.45±1.71%	40.85±1.55%	41.00±1.96%
	4 hrs.	58.39±2.15%	57.28±1.45%	58.05±1.23%	57.92±1.38%
	6 hrs.	68.68±0.97%	68.12±2.31%	67.56±1.66%	67.95±1.12%
	8 hrs.	74.37±1.23%	74.87±0.59%	75.17±0.86%	74.19±2.09%
	10 hrs.	85.74±1.21%	85.24±1.61%	86.01±2.15%	85.12±0.65%
	12 hrs.	99.38±1.74%	99.32±2.03%	98.96±1.87%	98.94±1.39%
Assay	90.0% -110% of the labeled amount	96.01±2.05%	95.48±1.60%	95.10±1.12%	6.71±1.91%

*All values are expressed as mean ± SD

DISCUSSION

Eperisone hydrochloride is a new generation antispasmodic drug for the treatment of relaxing both skeletal muscles and vascular smooth muscles, and demonstrates a variety of effects such as reduction of myotonia, improvement of circulation and suppression of the pain reflex. The extended release dosage form, compared to a conventional dosage form, is the uniform drug plasma concentration and it provides uniform therapeutic effect. Eperisone hydrochloride has a biological half-life of 1 to 4.3 hrs i.e., it requires three-times a day dosing. Multiple daily dosing is inconvenient to the patient and can result in missed doses, made up doses and patient incompliance with the therapeutic regimen. Therefore, there were continued efforts to improve the pharmaceutical formulation of Eperisone hydrochloride in order to achieve an optimal therapy. These efforts mainly focused on to formulate the matrix film-coated extended release tablets to improve the bioavailability. Matrix devices, due to their chemical inertness, drug embedding ability and drug release character, have gained steady popularity for extended release of a drug[12]. The main aim was to control the release of drug up to 12 hrs.

On the basis of preliminary identification test it was concluded that the drug complied the preliminary identification. There was no drug polymer interaction, which was confirmed by the Differential scanning calorimetry of drug and physical mixture. The DSC graph report is shown in figures 2-4. The Eperisone hydrochloride matrix film coated tablets were evaluated for precompression parameters like angle of repose, bulk density, tapped density and compressibility index and physical characters like tablet weight variation, thickness, hardness, friability, drug content and in vitro drug release. The values of preformulation parameters evaluated were within the prescribed limit and indicated that good fine flow property[27], the results of the flow properties were shown in Table 2. The Eperisone hydrochloride matrix film coated tablets prepared by wet granulation method. The physical parameters of formulated tablets showed that all the batches had desirable physical characteristics and it was depicted in Table 3. The performance of extended release formulation has been reported to be greatly affected by physicochemical properties of the polymers. Five different combination of polymer: drug was used to formulate the extended release matrix tablets. The combination of micro crystalline cellulose and hydroxy propyl methyl K4M sustains the drug release for longer time. The varying amount of hydroxy propyl methyl observed that the amount of polymer influences the drug release. The results of dissolution studies of formulations K4M didn't affect the drug release. Higher concentration of MCC exhibit the prolong drug release. Formulations containing combinations of different grades of hydroxy propyl methyl cellulose were evaluated. An addition of Ethyl cellulose was decrease the drug release. The formulations F4 and F5 provide drug release 81.37% and 90.01% respectively.

The release kinetics data was analyzed according to different kinetic equations .The data were analyzed by the regression coefficient method and regression coefficient value (r^2) of all batches are shown in Table 5. Analyze the regression coefficient value for all batches. The formulations F3, F4 and F5 were followed Korsmeyer –peppas model, F7 was followed Hixson Crowell kinetics whereas remaining all the formulations showed Higuchi's release kinetics. The formulations showed good linearity (r^2 = 0.965 to 0.98) with slope (n) between 0.470- 0.586, which appears to indicate a coupling of diffusion and erosion mechanisms-so called anomalous diffusion. The optimized formulation was subjected to stability studies as per ICH guidelines at room temperature (25ºC±2º / 60º±5%RH) and an accelerated stability conditions (40ºC±2º /75%±5%RH). The formulated tablets does not indicates any significance changes in average weight, hardness, *In-vitro* drug release, and drug content all the characters before and after stability studies and these values were represented in table 6 and 7.

CONCLUSION

Eperisone hydrochloride Matrix film coated tablets were formulated for oral extended release delivery. This fabricated tablets showed acceptable parameters like hardness, thickness, friability, percentage weight variation and drug content. The acceptable extended release of the drug was achieved by using different polymers like HPMC and MCC. Batch F3, F4 and F5 formulations

were gave better extended release in comparison to other prepared formulation and these formulations were best fitted to Korsmeyer – peppas model. These results suggested that the fabricated extended release have a potential for extended release dosage forms.

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