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FORMULATION AND *INVITRO* DRUG RELEASE STUDIES OF BACLOFEN CONVENTIONAL TABLETS

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ABSTRACT

The aim of this study was to formulate the baclofen conventional tablet in order to enhance its dissolution characteristics by using different excipients. The conventional tablet formulations of baclofen were formulated by using suitable different diluents and other excipients. The tablets are prepared by using direct compression method. The prepared tablets are evaluated in terms of their Precompression studies such as bulk density, tapped density, angle of repose, carr's Index and hausner's ratio, Postcompression studies such as hardness test, thickness test, weight variation test, friability test and *invitro* study. All the batches showed good to satisfactory of free flowing properties, hardness, thickness, weight variation, friability, and the values are within the pharmacopeia limit. The i*n vitro* dissolution studies showed that the formulation FA-3 gave the maximum percentage of drug release (56.18%) within 60 mints.

KEY WORDS

Baclofen, Conventional tablet, Direct compression method, Evaluation Parameters and *In vitro* study.

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INTRODUCTION[1]

The oral route of drug administration is the most important method of drugs for systematic affects. It can be said that at least 90% of all drugs used to produce systemic effect by oral route of drugs that are administered orally, solid oral dosage forms represents the preferred loss of product because in this form one usual dose of the drug has been accurately placed. Tablets are oral solid dosage forms of medicinal substances usually prepared with the aid of suitable pharmaceuticalexcipients[1].

Baclofen is a chlorophenyl derivative of GABA originally prepared as a lipophilic GABA-like agent in order to assist penetration of the blood-brain barrier, which is impermeable to GABA itself. Baclofen is a selective agonist at GABAβ-receptors. The antispastic action of Baclofen is exerted mainly on the spinal cord, where it inhibits both monosynaptic and polysynaptic activation of motor neurons. It is effective when given by mouth, and is used in the treatment of spasticity associated with multiple sclerosis or spinal injury[2].

MATERIALS AND METHOD

MATERIALS

Baclofen was obtained from Sun pharmaceutical ltd, India. Lactose, Di basic calcium Phosphate, Starch, Mannitol, Sorbitol, Talc and Magnesium stearate were purchased from Loba Chemie Pvt. Ltd., Mumbai, India. All other chemicals and ingredients were used for study are of Analytical grade.

METHOD[3]

Preparation of Baclofen conventional tablets

Baclofen conventional tablet formulations were prepared by direct compression technique. All the powders are passed through 40 mesh sieve. Weigh the required quantity of pure drug and other ingredients were mixed thoroughly. Talc and magnesium stearate were finally added as a glidant and lubricant respectively. The blend was directly compressed using multiple punch tablet compression machine (Table No.1).

EVALUATION PARAMETERS[3-5]

Pre-formulation Studies

Fourier Transform Infrared Spectroscopy

The Fourier transform infra-red analysis was conducted for the structure characterization. FTIR spectra of the pure drug, diluents and formulations were recorded by using BOMEN MB SERIES FTIR instrument. Approximately 5mg of samples were mixed with 50mg of spectroscopic grade KBr, samples were scanned in the IR spectroscopy.

Pre-compression studies of tablet powder

Bulk density

3gm of powder were weighed separately and transferred into 100ml measuring cylinder, initial volume was measured and calculated bulk density according to the formula

Formula

Bulk density = Mass / Volume

The packing properties of the drugs and their formulations widely depend upon bulk density. It has been stated that bulk density values less than 1.2gm/cm^3 indicate good flow and values greater than 1.5 gm/cm^3 indicate poor flow.

Tapped density

Tapped density is determined by placing a graduated cylinder containing a known mass of powder and mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. Using the weight of the powder in the cylinder and this minimum volume, the tapped density may be computed.

Formula

Tapped density = Weight of Powder/ Tapped volume of Powder

Angle of Repose

The manner in which stresses are transmitted through a bead and the beads response to applied stress are reflected in the various angles of friction and response. The most commonly used of this in angle of repose, which may be determined experimentally by number of methods. The method used to find the angle of repose is to pour the powder a conical on a level, flat surface and measure the included angle with the horizontal.

Formula

$$\theta = \mathrm{Tan}^{-1} (h/r)$$

Where,

θ = **Angle of repose,**

h = Height of the powder cone,

r = Radius of the powder cone.

Angle of repose is less than or equal to 40° indicates free flowing properties of the powders. However angle of repose is greater than 40° indicates poor flow of material.

Compressibility Index or Carr's Index

Carr's Index is measured using the values of bulk density and tapped density.

The following equation is used to find the Carr's Index,

$$CI = \frac{(TD-BD)}{TD} \times 100$$

Where, TD = Tapped density

BD = Bulk density.

Carr's Index is less than or equal to <10 indicates free flowing properties of the powders. However Carr's Index is greater than >10 indicates poor flow of material.

Hausner's Ratio

It indicates the flow properties of the powder and ratio of Tapped density to the Bulk density of the powder.

Hausner's Ratio is less than or equal to 1.069 indicates free flowing properties of the powders. However Hausner's Ratio is greater than 1.35 indicates poor flow of material.

Formula

Hausner's Ratio = Tapped density/Bulk density

Post compression studies of Baclofen conventional tablets

Hardness or Crushing strength Test[6]

Hardness of the tablet was determined using the Monsanto hardness tester (The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force. The force required to break the tablet is measured in kilograms and a crushing strength of 4Kg is usually considered to be the minimum for satisfactory tablets. Oral tablets normally have a hardness of 4 to 10 kg; however, hypodermic and chewable tablets have a hardness of 3 kg and some sustained release tablets have a hardness of 10 -20 kg.

Thickness Test

The thickness of the tablet is mostly related to the tablet hardness can be uses as initial control parameter. Ten tablets were randomly selected from each tablet thickness was determined using a Venire caliper and the reading was recorded in millimeters.

Friability Test

The pre-weighed tablets were placed in the friabilator (EF-2, Electro lab, Mumbai) which was then operated for 100rpm, then dusted and reweighed. The Conventional compressed tablets that lose less than 0.5-1.0% of their weight are generally considered acceptable.

$$\text{Friability index} = \frac{I - F}{I} \times 100$$

Where,

I - Initial weight

F - Final weight

Weight variation test

Weights of 20 individual tablets were noted and their mean weight also calculated. The percentage deviation was calculated by using the following formula,

$$\text{Percentage deviation} = [X - X^*/ X] \times 100$$

X - Actual weight of the tablet

X* - Average weight of the tablet.

Estimation of Drug Content

An accurately weighed amount of powdered Baclofen (100 mg) was extracted with water and the solution was filtered through 0.45 µ membrane filter paper. The absorbance was measured at 220 nm after suitable dilution.

Calculation

The amount of Baclofen present in tablet can be calculated using the formula

$$A_t/As \times S_w/100 \times 100$$

Where,

A_t = Absorbance of sample preparation

A_s = Absorbance of Standard preparation

S_w= weight at Baclofen working standard (mg).

***In vitro* drug release studies**

The dissolution was carried out using rotating paddle method; freshly prepared 0.1N Hcl (pH 1.2) (900 ml) was placed in dissolution flask and allowed to obtain temperature at 37±0.5°C. The tablets were placed in beaker and rotated with 50rpm for 1 hrs. 1 ml of sample was withdrawn at different time intervals (0,

15, 30, 45, 60, 75, 90, 105 and 120 mints). After each withdrawal, medium was replaced by equal amount of fresh 0.1N Hcl (pH 1.2). The sample were diluted to 10 ml with dissolution medium and used for measurement of absorbance at 220 nm. The dissolution data obtained were plotted as percentage drug release versus time.

RESULTS AND DISSCUSION

Pre formulation studies

Compatability studies (Fourier Transform Infrared Spectroscopic studies)

The fourier transform infra-red analysis was conducted for the surface structure characterization. FTIR spectrum of the formulated tablets, pure drug and different diluents was recorded. The tablets were taken in a KBr pellet by using BOMEN MB SERIES FTIR instrument. The Fourier Transform Infrared Spectroscopy study reveals that there is no interaction between the different diluents and pure drug. Then all the functional groups are found in the IR spectrum of pure drug and different diluents.

Precompression studies of powders

Bulk density

From the results it can be seen that the bulk density values are less than 1.2gm/cm^3 for all formulations (F-1 to F-5. The values are 0.694 to 0.721gm/cm^3. This indicates good flow characteristics of the powders. Values are showed in Table No.2.

Tapped density

From the results it can be seen that the Tapped density values are within the limits. This indicates good flow characteristics of the powders. Values are showed in Table No.2.

Angle of Repose

It can be observed that the angle of repose for various batches of the powders is found to be less than 40^0, it indicates good flow properties of the powders. Values are showed in Table No.2.

Compressibility Index or Carr's Index

It can be observed that the Carr's Index for various batches of the powders is found to be less than <10; it indicates good flow properties of the powders. Values are showed in Table No.2.

Hausner's Ratio

It can be observed that the Hausner's Ratio for various batches of the powders is found to be less than 1.35; it indicates good flow properties of the powders. Values are showed in Table No.2.

Postcompression studies

Hardness Test

The hardness of the tablet various batches were determined. The various batches of the tablets of hardness values are found within limits and it indicates good strength of the conventional tablets. Values are showed in Table No.3.

Thickness Test

The thickness of the tablet various batches were determined. The thicknesses of tablets were almost uniform in the all formulations and were found to be within the range of 0.3mm. Values are showed in Table No.3.

Friability Test

The conventional tablets of friability values are found to be less than 1% in all formulation and considered to be satisfactory. Values are showed in Table No.3.

Weight variation test

All this conventional tablets are passed weight variation test. As the % of weight variation of all formulation was within the pharmacopoeia limits. The weight of the all tablets was found to be uniform. Values are showed in Table No.3.

Estimation of Drug Content

Drug content of all the batches are within the acceptable range which shows the proper mixing of the drug and excipients. Values are showed in Table No.3.

In vitro drug release studies

Among all the batches FB-5 formulation showed the better *invitro* release of drug. Values are showed in Table No.4 and the *in vitro* drug release graph plotted time in mints Vs % of drug release. The *in vitro* drug release results are showed in Figure No.1.

Table No.1: Formulation of different batches of Baclofen Tablets

S.No	Ingredients	FB-1	FB-2	FB-3	FB-4	FB-5
1	Baclofen	20 mg	20 mg	20 mg	20 mg	20 mg
2	Lactose	125mg	-	-	-	-
3	Di basic calcium Phosphate	-	125mg	-	-	-
4	Starch	-	-	125mg	-	-
5	Mannitol	-	-	-	125mg	-
6	Sorbitol	-	-	-	-	125mg
7	Talc	2.5mg	2.5mg	2.5mg	2.5mg	2.5mg
8	Magnesium stearate	2.5mg	2.5mg	2.5mg	2.5mg	2.5mg

Total weight of the tablet –150mg/tab

Table No.2: Precompression studies of powders

S.No	Formulations	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Angle of Repose (θ)	Carr's Index (%)	Hausner's Ratio
1	FB-1	0.694	0.705	26.12	1.56	1.015
2	FB-2	0.697	0.714	26.24	2.38	1.024
3	FB-3	0.704	0.721	25.32	2.41	1.024
4	FB-4	0.714	0.724	26.21	1.38	1.014
5	FB-5	0.721	0.735	25.46	1.90	1.019

Table No.3: Postcompression studies of Beclofen Tablets

S.No	Formulations	Hardness Test (kg/cm)	Thickness Test (cm)	Friability Test (%)	% of Weight variation test	Estimation of Drug Content
1	FB-1	6.82	0.3	0.533	99.6	99.8
2	FB-2	6.75	0.3	0.6	99.6	99.7
3	FB-3	6.72	0.3	0.666	99.8	99.8
4	FB-4	6.68	0.3	0.533	99.5	99.6
5	FB-5	6.65	0.3	0.8	99.5	99.7

Table No.4: Comparative dissolution study of different formulations of Beclofen tablets

S.No	Time (mints)	% of drug release (FB-1)	% of drug release (FB-2)	% of drug release (FB-3)	% of drug release (FB-4)	% of drug release (FB-5)
1	0	0.00	0.00	0.00	0.00	0.00
2	15	5.32	5.54	5.85	6.14	6.18
3	30	10.23	11.77	9.200	11.39	10.23
4	45	16.53	25.57	16.70	24.46	24.31
5	60	28.63	45.92	32.27	40.97	41.22
6	75	42.42	62.02	45.16	62.02	63.06
7	90	57.65	73.03	62.33	78.42	78.44
8	105	65.12	81.52	74.65	84.27	85.63
9	120	76.34	92.14	85.34	96.82	97.15

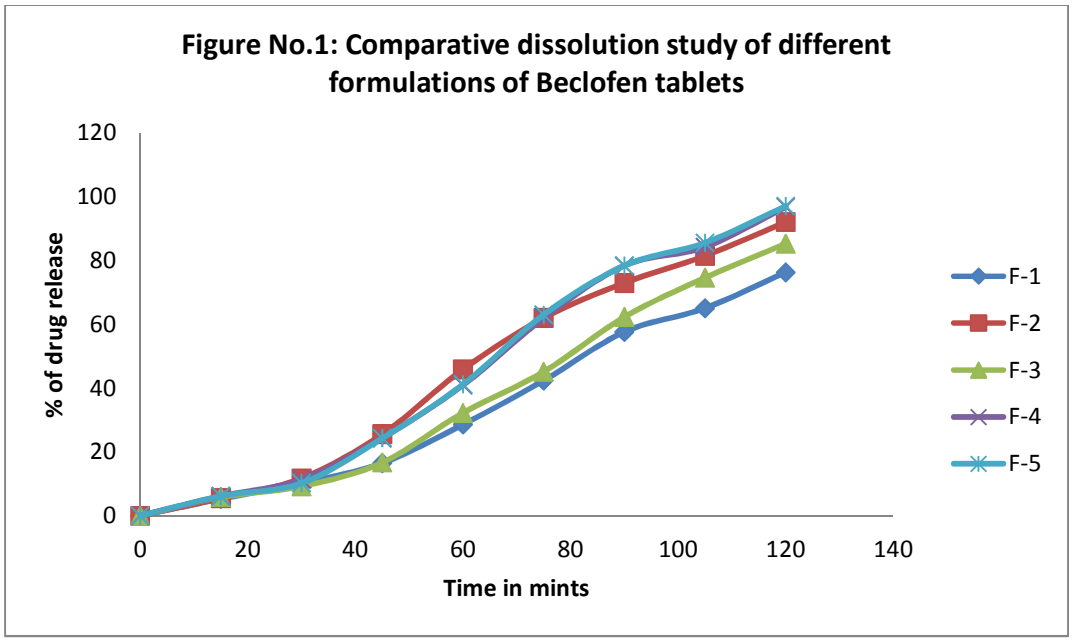

Figure No.1: Comparative dissolution study of different formulations of Beclofen tablets

CONCLUSION

The study was carried out to develop the Beclofen tablets for treatment of spasticity associated with multiple sclerosis or spinal injury. All the batches showed good to satisfactory of free flowing properties, hardness, thickness, weight variation, friability, and the values are within the pharmacopeia limit. The *in vitro* studies showed that this formulation FB-5is given best drug release when compared to other formulations. From the results was concluded that a optimum formulation is combination of Baclofen and Sorbitol (diluent). Hence, this formulation can be making a suitable conventional dosage forms for drug therapy.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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