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FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF BACLOFEN

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ABSTRACT: The aim of this investigation was to prepare orodispersible tablets of baclofen using various concentrations of superdisintegrant agents like Ac-Di-Sol, crospovidone, sodium starch glycolate by direct compression method. Nine formulations having superdisintegrants at different concentration levels were prepared. These tablets were evaluated for drug content, weight variation, friability, hardness, wetting time and invitro disintegration time. Among the formulations tablets of batch F3 containing Ac-Di-Sol showed superior organoleptic properties along with excellent in-vitro disintegration time and drug release as compere to other formulations. It was concluded that superdisintegrants addition technique is a usuful method for preparing orodispersible tablets by direct compression method.

Keywords: Baclofen, Orodispersible tablets, Ac-Di-Sol, Crospovidone, Sodium starch glycolate.

INTRODUCTION AND EXPERIMENTALS

Many patients find it difficult to swallow tablets and hard gelatin capsules and thus not comply with prescription that results in high incidence of non-compliance and ineffective therapy.[1] Orodispersible tablets are gaining prominence as new drug delivery systems.[2] These dosage forms dissolves or disintegrate in oral cavity within a minute without the need of water or chewing. In this study, an effort has been made to formulate orodispersible tablets of baclofen using different disintegrants. Baclofen is structural analog of gamma-aminobutyric acid is a centrally acting skeletal muscle relaxant, which is widely used in the treatment of spasticity resulting from multiple sclerosis, muscle spasms, muscular rigidity and spinal cord injuries,[3] where pain persist predominantly, in such cases the quick onset of action is of prime importance. Baclofen is available in oral and intravenous formulation. Though the conventional oral tablets are widely used, they suffer from a few practical drawbacks such as its nonsuitability when quick onset of action is required. Often time people experience inconvenience using conventional oral dosage forms in mentally ill and uncooperative patients. Some times it may be difficult to swallow conventional products due to unavailability of water.[4, 5] Hence the present work was aimed to formulate the orodispersible tablets of baclofen using Ac-Di-Sol, crospovidone and sodium starch glocolate as a disintegrants. Orodispersible tablets are those when put on tounge disintegrate instateneously, releasing the drug which dissolve or disperses in the saliva.[6] Faster the drug in the solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down in to the stomach. In such cases, bioavailability of a drug is significantly greter than those observed from conventional tablet dosage form. The advantages of mouth dissolving dosage form are increasingly being recognized in both, industry and academia. Their growing importance was underline recently when European pharmacopoeia adopted the term "Orodispersible Tablet" as tablet that is to be place in the mouth where it disperses rapidly before swallowing.[4,7]

MATERIALS AND METHODS

Baclofen was received as a gift sample from Sun Pharma, Baroda India. Ac-Di-Sol, crospovidone, sodium starch glycolate was obtained as gift sample from Signet Chemicals Mumbai. All other materials like aspartame, mannitol, microcrystalline cellulose, magnesium stearate, talc used was of analytical grade and procured from commercial sources.

Preparation of Orodispersible tablets:

Baclofen orodispersible tabletes were prepared by direct compresion method according to formula given in the table 1. A total number of nine formulation were prepared. All the ingridents were passed through 60-mesh sieve seperately and collected. The drug and microcrystalline celullose were mixed in small portion of both at each time and blended to get a uniform mixture and kept aside. Then the ingriedents were weighed and mixed in geometrical order and the tablets were compressed using flat face 9 mm size punch to get a tablets of 200 mg weight using single puch tablet compression machine (Cadmach machinery Limited, Ahmadabad). Before tablets preparetion, the mixture blends of all the formulation were subjected for compatibility studies (IR) and pre-compression parameter like Bulk density, Tapped density, Angle of Repose, percentage compressibility and Hausner ratio.[8]

Evaluation of Tablets: [9, 10, 11, 12]

The prepared tablets were evaluated for various official and nonofficial specifications.

Weight variation:

Twenty tablets were selected at a random and average weight was calculated. Then individual tablets were weighed and the individual weight was compared with an average weight.

Hardness, Friability and content uniformity Tests:

Tablets were evaluated for hardness and friability test using Monsanto hardness tester and Roche friabilator respectively. Content uniformity test were done as per procedure given below:

Twenty tablets from each batch were powdered and weighed accurately equivalent to 100 mg of Baclofen. Weighed quantity of powder was dissolved into 100 ml of 0.1 N NaOH solution by stirring it for 15 min. 1 ml of solution was pipette out into 10 ml volumetric flask, to it 1 ml of 5% Ninhydrin solution was added and the solution was boiled for 3 min, cooled it and the volume was made up with distilled water. The sample was then immediately analyzed by taking absorbance at 403 nm using UV-visible spectrophotometer[13] (Shimadzu 1601, Shimadzu Corporation, Kyoto, Japan).

Wetting Time: [5, 14]

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A piece of tissue paper folded double was placed in a Petri plate containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds.

In-vitro Disintegration time:

The in-vitro disintegration time was determined using disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

In vitro drug release study: [15]

An in-Vitro drug release study was carried out using tablet dissolution test apparatus USP XXIII at 100 rpm (Electrolab, TDT-06T, Mumbai). The dissolution medium consisted of 900 ml phosphate buffer pH 7.2, maintained at temperature 37 ± 0.5^0C. The sample of 5ml was withdrawn at predetermined time intervals and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. From that 5 ml sample, 1 ml sample was withdraw and placed in a 10 ml volumetric flask, to it 1 ml of 5 % ninhydrin solution and 1 ml of 0.1 N NaOH solution was added. The solution was then boiled for 3 min at water bath, cooled it at room temperature and the volume was made up with distilled water. The absorbance of diluted sample was measured spectrophotometrically at 403 nm using UV-visible spectrophotometer[13] (Shimadzu 1601, Shimadzu Corporation, Kyoto, Japan).

RESULTS AND DISCUSSION

In the present study Baclofen orodispersible tablets were prepared by using Ac-Di-Sol, crospovidone and Sodium starch glycolate as a disintegrants (Table 1). Total numbers of nine formulations were prepared by direct compression technique. The values of pre-compression parameters evaluated were within prescribed limit and indicated good free flowing property (Table 2). IR spectroscopy was used as means of studying drug-excipient compatibility and confirmed undisturbed structure of Baclofen, which indicate no drug-excipient interaction. The data obtained of post-compression parameters such as hardness, friability, weight variation, amount of drug content, in-vitro wetting time and in-vitro disintegration time are shown in table 4. The hardness was found to be in the range of 3.4±0.41 to 3.6±0.87 kg/cm^2 for all the formulations indicating good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. In all the formulations the friability values are less than 1% and meet the IP limits. All the tablets passed weight variation test as the percentage weight variation was within the pharmacopoeial limits. The weight of all the tablets was found to be uniform with low standard deviation values indicating efficient mixing of drug, disintegrants and excipients. The percentages drug contents of all the tablets were found to be between 98.14±1.66% to 101.05±0.28% of baclofen, which was within the acceptable limits. The results of in-vitro wetting time and in-vitro disintegration time of all the tablets were found to be within the prescribe limits and satisfy the criteria of orodispersible tablets. The in-vitro wetting time was found to be in the range of 20.4±1.15 to 46.8±0.35 seconds while the in-vitro disintegration time was founds in the range of 28.6±1.22 to 51.7±2.46 seconds respectively. It was observed that when Ac-Di-Sol is used as disintegrant, the tablets disintegrates rapidly within less time due to easy swelling ability of Ac-Di-Sol when compared to other tablets prepared by using crospovidone and Sodium starch glycolate. Among the formulation tablets of batch F3 containing Ac-Di-Sol 15

mg was found to be the best as compare to other formulations as this formulation showed good hardness, low friability and least wetting time (20.4±1.15 sec.) and disintegration time of (28.6±1.22 sec.), which is an ideal characteristic of an dispersible type tablet.[16] The cumulative percentage of the drug released for formulation batch F3 found by the dissolution test shows the better drug release of 100.51±0.30% at the end of 6 min. indicates good bioavailability of the drug from these formulations. Ac-Di-Sol when comes in contact with water gets inflated immediately burst out there by releasing the drug in the short duration of time. It was concluded that orodispersible tablets of baclofen can be prepared successfully as it satisfies all the criteria as an orodispersible tablet and would be alternative to the currently available conventional tablets.

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Table No. 1- Formulation Design

Ingredient	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
Baclofen	10	10	10	10	10	10	10	10	10
Ac-Di-Sol	05	10	15		-	-	-	-	-
Crospovidone	-	-	-	05	10	15	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	05	10	15
Avicel 102	25	25	25	25	25	25	25	25	25
Aspartame	2	2	2	2	2	2	2	2	2
Talc	4	4	4	4	4	4	4	4	4
Mg. stearate	2	2	2	2	2	2	2	2	2
Mannitol	152	147	142	152	147	142	152	147	142
Total	200	200	200	200	200	200	200	200	200

Table No. 2 - Micromeritic properties of power blend

Formulation Code	Bulk density (gm/ml)	Tapped density (gm/ml)	Angle of repose (θ)	Percentage compressibility	Hausner ratio
F1	0.58	0.68	25.61	14.71	1.172
F2	0.56	0.67	25.07	16.42	1.196
F3	0.55	0.64	24.68	14.06	1.164
F4	0.53	0.62	24.50	14.52	1.170
F5	0.52	0.59	23.82	11.86	1.135
F6	0.50	0.57	23.49	12.28	1.140
F7	0.58	0.70	30.05	17.14	1.207
F8	0.58	0.71	30.64	18.31	1.224
F9	0.59	0.73	31.45	19.18	1.237

Table No. 3 – Evaluation of Tablets

Formulation code	Weight* variation	Hardness* (kg/cm^2)	Friability* (%)	Wetting* Time (sec)	In-vitro* disintegration Time (sec)	Amount of drug content (%)
F1	Passes	3.5±0.47	0.73±0.01	40.8 ±1.04	45.3 ±1.53	98.14 ±1.66
F2	Passes	3.4±0.83	0.76±0.14	32.0 ±0.95	34.0 ±1.00	99.02 ±0.50
F3	Passes	3.5±0.84	0.79±0.11	20.4 ±1.15	28.6 ±1.22	100.51 ±0.30
F4	Passes	3.5±0.50	0.74±0.02	42.0 ±0.85	48.4 ±2.42	98.91 ±0.61
F5	Passes	3.5±0.65	0.78±0.07	35.0 ±1.35	36.6 ±2.12	100.04 ±0.57
F6	Passes	3.4±0.43	0.80±0.09	29.4 ±1.48	32.6 ±1.25	99.86 ±0.84
F7	Passes	3.4±0.41	0.69±0.10	46.8 ±0.35	51.7 ±2.46	98.92 ±0.33
F8	Passes	3.6±0.87	0.65±0.04	34.7 ±1.45	35.5 ±0.50	101.05 ±0.28
F9	Passes	3.5±0.86	0.66±0.08	29.1 ±1.05	30.3 ±0.58	100.34 ±0.57

- All values are expressed as mean ± SD, n=3

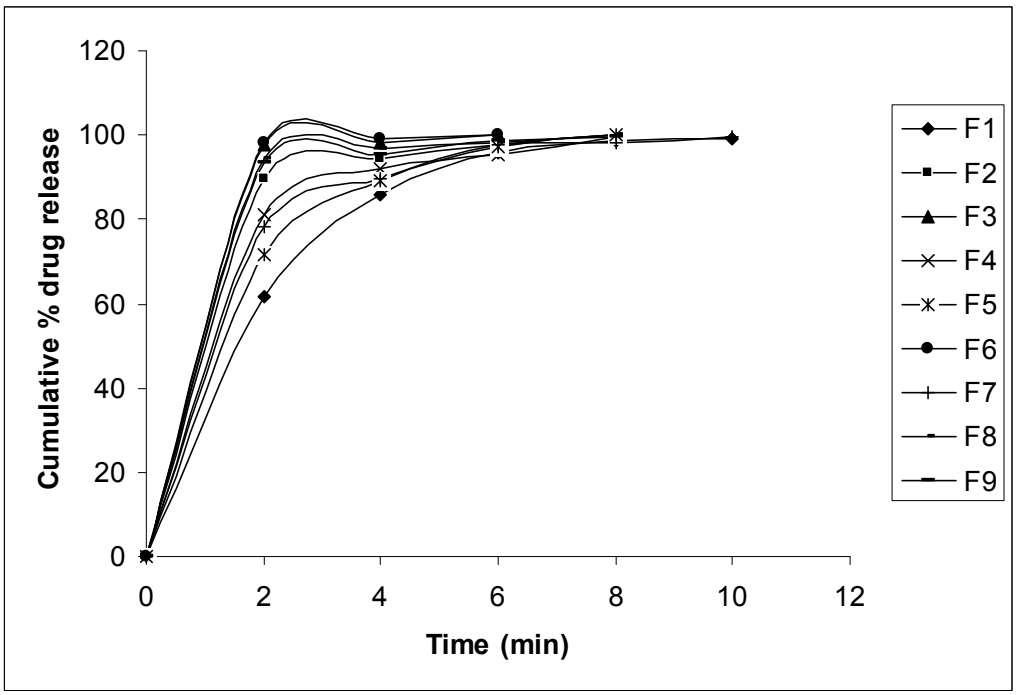

Fig.1- In-Vitro Dissolution profile of prepared formulations

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