ISSN: 0975-5772

Biresh Kumar Sarkar et al / Journal of Pharmaceutical Science and Technology Vol. 3 (10), 2011,717 - 724

Formulation And Evaluation Of Flurbiprofen Matrix Tablets For Colon Targeting

Biresh Kumar Sarkar*[1], Devananda Jain[1], Mamta Parwal[2]

1. **Bhagwant University, Dept.of Pharmaceutical Tech and Sciences, Ajmer, Rajasthan**
2. **Chemind Diagnosis & Biosolutions, Jaipur**

Abstract

The present study is the development of colon targeted matrix tablets of the drug flurbiprofen, a NSAIDS of the class of Ibuprofen designed to prolonged the release for sustained effect. Different formulation (F1 TO F9) batches were made with the help of different polymers and their different proportions (Guar Gum ,Eudragit RL, Eudragit RS) with the help of Wet granulation techniques. The prepared matrix tablets were evaluated in terms of their pre-compression parameters, physical characteristics like hardness, friability, uniformity of weight, uniformity of drug content, invitro drug release. From this study we concluded that the batch F7 shows good results then the other batches. The batch F7 shows maximum prolong release upto 12 hrs.

Keywords: Flurbiprofen, Colon, Sustained release, Guar gum, Eudragit RL, Eudragit RS.

Introduction

Colonic delivery refers to targeted delivery of drugs into the lower GI tract, which occurs primarily in the large intestine (i.e., colon). The site-specific delivery of drugs to lower parts of the GI tract is advantageous for localized treatment of several colonic diseases, mainly inflammatory bowel diseases (Crohn's disease and ulcerative colitis), irritable bowel syndrome, and colon cancer. Other potential applications of colonic delivery include chronotherapy, prophylaxis of colon cancer and treatment of nicotine addiction [1].

Targeting of drugs to the colon by the oral route could be achieved by different approaches including matrix and coated systems, for which the drug release is controlled by the gastrointestinal pH, transit times or intestinal flora. The method by which the drug release will be triggered by the colonic flora appears to be more interesting with regard to the selectivity. A number of synthetic azo polymers and natural or modified polysaccharides (chondroitin sulphate, guar gum, xanthan gum, locust gum, inulin, dextrans, starch, amylose,pectins) degraded by the human colonic flora, have thus been investigated as colonic drug delivery carriers.[2] The human colon has over 400 distinct species of bacteria as resident flora, a possible population of up to 1010 bacteria per gram of colonic contents. Among the reactions carried out by these gut flora are azoreduction and enzymatic cleavage i.e. glycosides.8 These metabolic processes may be responsible for the metabolism of many drugs and may also be applied to colon-targeted delivery of peptide based macromolecules such as insulin by oral administration.[3]

MATERIAL AND METHOD:

Material: - The drug Flurbiprofen was obtained as a gift sample from Panacia Biotech. Guar Gum, Eudragit RL, Eudragit RS used in the preparation are of Analytical grade.

Preparation of granules

Powdered ingredients were weighed, mixed and granulated with the binder solution/paste prepared as above. This mixture was thoroughly blended manually and passed through a sieve with a nominal aperture of 1 mm. The granules prepared were dried in a tray drier at a temperature between 30 and 40 °C for 4 h. The dried granules were screened, mixed with lubricants and stored for tableting**. [4]**

Preparation of Flurbiprofen matrix tablets

Matrix tablets of Flurbiprofen were prepared by wet granulation technique using 10% PVP paste as binder. Microcrystalline cellulose was used as diluent and mixture of talc and magnesium stearate at 2:1 ratio was used as lubricant. Flurbiprofen matrix tablets containing Guar gum,Eudragit RS-100, Eudragit RL-100 were prepared. The composition of different formulations used in the study containing 100 mg of Flurbiprofen in each case is shown in table Polymers were sieved through a mesh (250 µm) and mixed with Flurbiprofen (149 µm) and MCC (250 µm). The powders were blended and granulated with 10% PVP paste. The wet mass was passed through a mesh (1190 µm) and the wet granules were dried at 50 °C for 2 h. The dried granules were passed through a mesh (1000 µm) and were lubricated with a mixture of talc and magnesium stearate (2:1). The lubricated granules were compressed with a maximum force of compression (4000–5000 kg) using 11 mm round, flat and plain punches on single station tableting machine.[5**]**

Formulation of Flurbiprofen tablets.

S.No	Ingredients (mg/tab)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Flurbiprofen	100	100	100	100	100	100	100	100	100
2	Eudragit RL 100	50	---	---	100	----	---	50	50	---
3	Eudragit RS 100	---	50	---	---	100	---	50	---	50
4	Guar gum	---	---	50	---	---	100	---	50	50
5	PVP K 30	3	3	3	3	3	3	3	3	3
6	MCC	138	138	138	88	88	88	88	88	88
7	Magnesium stearate	3	3	3	3	3	3	3	3	3
8	Talc	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**	**6**
	Total	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**

Evaluation Studies

EVALUATION OF GRANULES

Determination of bulk density and tapped density

An accurately weighed quantity of the powder (W) was carefully poured into the graduated cylinder and the volume (vo) was measured. then the graduated cylinder was closed with lid, set into the density determination apparatus (bulk density apparatus, electrolab, Mumbai). The density apparatus was set for 500 taps and after

that ,the volume (Vf) was measured and continued operation till the two consecutive readings were equal. The bulk density, and tapped density were calculated using the following formulas.
Bulk density = W/V_o
Tapped density = W/V_f
Where,
V_o = initial volume
V_f = final volume.

Compressibility index

The *Compressibility index* and *Hausner ratio* are measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the *Compressibility Index* and the *Hausner Ratio.*

The compressibility index and Hausner ratio may be calculated using measured values for bulk density ***(ρ bulk***) and tapped density ***(ρ tapped***) as follows:

$$\text{compressibility index} = \frac{\rho_{tapped} - \rho_{bulk}}{\rho_{tapped}} \times 100$$

$$\text{Hausner ratio} = \frac{\rho_{tapped}}{\rho_{Bulk}}.$$

Loss on drying

Determination of loss on drying of granules are important drying time during granulation was optimized depending LOD value. LOD of each batches were tested at 105oc for 2.5 minutes by using “Sartorius” electronic LOD apparatus.

Angle of repose

The flow characteristics are measured by angle of repose. Improper flow of powder is due to frictional forces between the particles. These frictional forces are quantified by angle of repose.

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane.

$\tan\theta = h/r$

$\theta = \tan^{-1} h/r$

Where *h* = height of pile

r = radius of the base of the pile

ɵ = angle of repose

EVALUATION OF TABLET

All the prepared Sustained release tablets were evaluated for following official and unofficial parameters.

Weight Variation

Thickness

Hardness Test

Friability Test

Drug content

Dissolution Study

WEIGHT VARIATION:

Twenty tablets were randomly selected form each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more then two of the individual tablet weight deviate from the average weight by more than the percentage shown in **Table** and none deviate by more than twice the percentage shown.

Table- Percentage deviation allowed under weight variation

Percentage deviation allowed under weight variation test.

Average weight of tablet (X mg)	**Section 1.01 Percentage deviation**
X < 80 mg	10
80 < X < 250 mg	7.5
X > 250 mg	5

.

Thickness

Twenty tablets were randomly selected form each batch and there thickness and diameter was measured by using digital vernier caliper.

FRIABILITY:

Method:

Twenty tablets were weighed and placed in the Electrolab friabilator and apparatus was rotated at 25 rpm for 4 minutes. After revolutions the tablets were dedusted and weighed again. The percentage friability was measured using the formula,

$\% F = \{1-(Wt/W)\} \times 100$

Where, % F = friability in percentage
W = Initial weight of tablet
Wt = weight of tablets after revolution

Tablet Hardness

The crushing strength Kg/cm2 of prepared tablets was determined for 10 tablets of each batch by using Monsanto tablet hardness tester. The average hardness and standard deviation was determined.[6] The results are shown in Table.

Uniformity of Weight

Twenty tablets were individually weighed and the average weight was calculated. From the average weight of the prepared tablets, the standard deviation was determined. The results are shown in Table.

In vitro Dissolution studies

In Vitro dissolution study was carried out using USP II apparatus in 900 ml of 0.1 N HCl (pH 1.2), pH6.8 & pH7.4 for 12 hours. The temperature of the dissolution medium was kept at 37± 0.5oC and the basket was set at 50 rpm. 10 ml of sample solution was withdrawn at specified interval of time and filtered through Whatman filter paper. The absorbance of the withdrawn samples was measured at λmax 247 nm using UV visible spectrophotometer. The concentration was determined from the standard curve of Flurbiprofen prepared in 0.1N HCl (pH 1.2), pH6.8 & ph 7.4 at λ max 247 nm.

The pharmacokinetic parameters of Flurbiprofen were used to calculate a theoretical drug release profile for 12 hr oral dosage form. The immediate release part for sustained release Flurbiprofen was calculated.

Results and discussion:- In the present study flurbiprofen matrix tablets were prepared with the help of different polymers by wet granulation method**.**After preparation of the matrix tablets Evaluation studies were done with different parameters and the results were shown below.

Study of preformulation studies

Parameters> Batch	Bulk Density	Tapped Density	Carrs Index	Hausners Ratio	Angle Of Repose(degree)
F 1	0.488	0.526	7.22	1.08	22.14±0.03
F 2	0.512	0.574	10.80	1.12	19.16±0.06
F 3	0.486	0.526	7.22	1.08	24.18±0.057
F 4	0.502	0.581	13.60	1.16	18.16±0.042
F 5	0.523	0.602	13.12	1.15	19.14±0.02
F 6	0.543	0.592	8.47	1.09	21.14±0.026
F 7	0.499	0.564	11.52	1.13	20.42±0.01
F 8	0.544	0.601	9.48	1.10	18.21±0.02
F 9	0.561	0.611	8.19	1.08	24.14±0.042

Physico-chemical evaluation of matrix tablets

Thickness

The results of the thickness of tablet are shown in Table. The mean tablet thickness was found to vary from. 3.0 to 3.5

Parameter Batch	Thickness*	Hardness (Kg/cm3)*	Friability (%)	Disintigration Time(sec)*
F 1	3.3	5.0±	0.52	190±
F 2	3.1	6.1	0.58	210
F 3	3.3.	6.8	0.62	145
F 4	3.3	5.5	0.55	205
F 5	3.2	5.9	0.64	250
F 6	3.3	6.3	0.59	197
F 7	3.1	6.6	0.67	240
F 8	3.2	5.8	0.70	300
F 9	3.2	5.3	0.66	243

Mean weight variation

The results of the weight variation of tablets are shown in Table

Parameter Batch	Weight Variation	Hardness (Kg/cm3)*	Friability (%)	Disintigration Time(sec)*
F 1	200.1	5.0±	0.52	190±
F 2	198.9	6.1±	0.58	210±
F 3	202.1	6.8±	0.62	145±
F 4	201.4	5.5±	0.55	205±
F 5	199.3	5.9±	0.64	250±
F 6	198.4	6.3±	0.59	197±
F 7	200.7	6.6±	0.67	240±
F 8	201.5	5.8±	0.70	300±
F 9	199.3	5.3±	0.66	243±

Drug content uniformity

The results of drug content of ocular tablets are shown in Table. The drug content of ocular tablet was found to vary between 97.2% to 99.9% .

*Values are Mean ± SD (n=3)

Parameter Batch	Hardness (Kg/cm3)*	Drug Content(%)
F 1	5.0±	99.50
F 2	6.1±	92.89
F 3	6.8±	100.02
F 4	5.5±	99.59
F 5	5.9±	99.38
F 6	6.3±	97.05
F 7	6.6±	99.60
F 8	5.8±	91.69
F 9	5.3±	95.62

In Vitro studies

Time	Abs	Con µg	Amount release	Cumulative amount release	%Cumulative release
10	0.0009	0.107143	0.096429	0.096429	2.410714
20	0.0015	0.178571	0.160714	0.16125	4.03125
30	0.0023	0.27381	0.246429	0.247857	6.196429
60	0.0041	0.488095	0.439286	0.442083	11.05208
90	0.0059	0.702381	0.632143	0.636488	15.9122
120	0.0082	0.97619	0.878571	0.887321	22.18304
150	0.0017	0.314815	0.283333	1.161905	29.04762
180	0.0029	0.537037	0.483333	1.363479	34.08697
210	0.0049	0.907407	0.816667	1.699497	42.48743
240	0.0061	1.12963	1.016667	1.904034	47.60086
300	0.0012	0.272727	0.245455	2.149489	53.73722
360	0.002	0.454545	0.409091	2.314489	57.86222
420	0.0036	0.818182	0.736364	2.644034	66.10086
480	0.0058	1.318182	1.186364	3.098125	77.45313
540	0.0074	1.681818	1.513636	3.431989	85.79972
600	0.0089	2.022727	1.820455	3.747216	93.68041

Conclusion: - From this study we concluded that Flurbiprofen matrix tablets with the help of ph dependent polymers prove to be a better drug delivery for colon targeting drug delivery.

References:

[1] Brahma N. Singh*Modified-Release Solid Formulations for Colonic Delivery,Recent Patents on Drug Delivery & Formulation 2007, 1, 53-63

[2] A. D. Kajale et al, colon targeted drug delivery using natural polymers, ijprd/2010/pub/arti/vov-2/issue-2/apr/003.

[3] Chien YW. Oral drug delivery and delivery systems. In: Chien YW, editor. Novel drug delivery systems. New York: Marcel Dekker Inc; 1992; 139-196.

[4] V. R. Sinha et al, Binders for colon specific drug delivery: an in vitro evaluation,International journal of pharmaceutics Volume 249, Issues 1-2, 5 December 2002, Pages 23-31.

[5] Y. S. R. Krishnaiah et al, Studies on the development of oral colon targeted drug delivery systems for metronidazole in the treatment of amoebiasis, International Journal of pharmaceutics, Volume 236, Issues 1-2, 2 April 2002, Pages 43-55.

[6] Hosseinali Tabandeh et al Preparation of Sustained-Release Matrix Tablets of Aspirin with Ethylcellulose, Eudragit RS100 and Eudragit S100 and Studying the Release Profiles and their Sensitivity to Tablet Hardness, Iranian Journal of Pharmaceutical Research (2003) 201-206