International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol.2, No.2, pp 1250-1255, April-June 2010

Formulation and Evaluation of Bilayered Tablets of Ibuprofen and Methocarbamol

Remya P.N.[1]*, Damodharan N.[2], Sulakshan Kumar C.V.[3]

Department of Pharmaceutics,

SRM College of Pharmacy, SRM Nagar, Kattankulathur-603203,

Kanchipuram District, Tamil Nadu., India

Corres.author: mathu_2004@yahoo.co.in
Mobile no-09840871992

ABSTRACT: The aim of present work was to develop a robust formulation of Bi-layer tablets of Ibuprofen and methocarbamol using povidone k-30 as binder. The basic aim of any Bi-layer tablet formulation is to separate physically or chemically incompatible ingredients and to produce repeat action or prolonged action tablet. The drug products may be developed to reduce Low back pain. The mechanism of methocarbamol is a skeletal muscle relaxant which acting centrally through inhibiting inter neuronal activity and blocking polysynaptic reflex pathway at spinal card. Ibuprofen is a pain relieving agent which inhibits the activity of Cyclooxygenase an enzyme crucial for synthesis of prostaglandins. A total number of nine formulations have been taken to optimize and develop a robust and stable formulation. Wet granulation process was used for the formulation of both layers and the final film coated tablets were evaluated for the thickness, weight variation, hardness, friability, disintegration time, dissolution study. Among the formulations tablets of formulation -8 was taken as optimized formula due to its higher rate of dissolution and compiled all the other parameters with the official specifications.
Keywords: Ibuprofen and methocarbamol, Bi-layered tablets, Povidone K-30, Wetgranulation process.

INTRODUCTION

Now a day's various developed and developing countries move towards combination therapy for treatment of various diseases and disorders requiring long term therapy such as hypertension and diabetes. Combination therapy have various advantages over monotherapy such as problem of dose dependent side effects minimized. A low-dose combination of two different agent reduces the dose-related risk, the addition of one agent may counteract some deleterious effects of the other. Using low dosage of two different agents minimizes the clinical and metabolic effects that occur with maximal dosage of individual component of the combined tablet and thus dosage of the single component can be reduced.[1]

The term Bi-layered tablets refers to tablet containing subunits that may be either the same or different. Bi-layered tablets allows for designing and modulating the dissolution and release characteristics and they are prepared with one layer of drug for immediate release while second layer designed to release drug latter, either as second dose or in an extended release manner.[1]

This study shows how to formulate the Bi-layered tablets of Ibuprofen and Methocarbamol by using povidone k-30 as a binder. Ibuprofen, one of the first propionicacid derivatives of non-anti inflammatory drugs, is a centrally and pheripherally acting analgesic. It is used in the treatment of Osteoarthritis, Rheumatoid arthritis, Juvenile chronic arthritis, musculoskeletal pain of all type including spot injury.[2]

Second drug, methocarbamol, is a central muscle relaxant for skeletal muscles. Used to treat spasm, it is structurally related to guaifenesin. It will not directly relax contracted skeletal muscles. The drug has secondary sedative effect. The use of two drugs in same formulation shows synergism effect to reduce back pain.[2]

The object of this study was to formulate the Bi-layered tablets of Ibuprofen and Methocarbomal using

povidone k-30 as binder. Bi-layer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substances. Bi-layer tablets are preferred when the release profiles of the drugs are different from one another. Bi-layer compression is becoming more prevalent across the pharmaceutical industry as the number of FDC'S increases.[1]

MATERIALS AND METHODS

Ibuprofen and Methocarbomal was received as a gift sample from Rexer pharma, India. Also Providone k-30, Maize starch, Pregelatinised starch was obtained as a gift sample from Rexer pharma, Hyderabad, India. All other materials like microcrystalline cellose-101, Sodium lauryl sulphate, Sodium starch glycolate, Colloidal silicon dioxide, Magnesium sterate, Stearic acid used was of analytical grade and procured from commercial sources.

Preparation of Bi-layer tablets:

Ibuprofen and methocarbamol Bi-layer tablets were prepared by wet granulation process according to the formula given in the table-1 and 2. Up to nine formulations are prepared. First Methocarbomal layer is prepared by sifting the materials shown in table-1, through the sieve separately. Then binding agent is prepared by dissolving Povodine k-30 in specified quantity of purified water. Load the sifted Methocarbamol, Pregelatinized starch, microcrystalline cellulose in a rapid mixer granulator. Add the binding agent which is previously prepared.[3]Similarly Ibuprofen layer is prepared by using maize starch, along with ingredients shown in table-2.[4] then the tablets were compressed by using the double-sided tablet press has been specifically designed and developed for the production of quality Bi-layer tablets. Methocarbamol layer blend is initially pre-compressed with low hardness and Ibuprofen layer blend is compressed over it, till the desired hardness is achieved. This technology is called Bi-layered technology. Bi-layered tablets are coated using Neocota coating machine using Advantia prime clear film coat material.[5,6] Before tablet preparation the mixture blend of all formulations are subjected to pre-formulation studies like bulk density, tapped density, compressibility index(%), hausners ratio, angle of repose.[7]

Evaluation of tablets: [7, 8, 9]

The prepared tablets can be evaluated for various official and non official specifications.

Thickness:

The thickness of the tablet is measured by vernier calipers scale. Thickness of the tablet related to the tablet hardness and can be used an initial control parameter.

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:

Tablets were evaluated for hardness and friability test using Monsanto hardness tester and Roche friabilator respectively.

In-vitro Disintegration time:

A tablet was placed in each of the six tubes of the basket. Suspend the assembly in water maintained at a temperature of 37^0c ± 2^0c and operate the apparatus, simultaneously note the time taken taken to disintegrate completely by using stop watch.

In-vitro drug release study:

An in-vitro drug release study was carried out using tablet dissolution test apparatus USP type-2(paddle) at 50rpm.The dissolution medium consisted of 900ml phosphate buffer pH7.2, maintained at a temperature 37±0.5^0c. A sample of 5ml was withdrawn at predetermined time intervals and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced, and then measure absorbance by HPLC technique.

RESULTS AND DISCUSSIONS

In the present study Ibuprofen and Methocarbamol Bi-layered were prepared by wet granulation process by using ingredients shown in (table-1, and table-2). A total number of nine formulations were prepared. The values of preformulation parameters evaluated were within prescribed limit and indicated good fine flow property (table-3). The data of evaluated tablets such as thickness, weight variation, hardness, friability, and In-vitro disintegration time, are shown in (table-4). The hardness was found to be in the range of 13kp to 17kp, the normal acceptance criteria for hardness are not more than 25.00kp. The formulation F6, F9 has got hardness in the acceptable range and was consider acceptable upon comparing with the innovator product. All the formulations indicate good thickness except F4 and F6. The normal acceptable criterion for friability is not more than 1.0%. The formulation F1, F2, F5, F7, F8 and F9 has got friability within the acceptable range. All the tablets passed weight variation test as the percentage weight variation was within the pharmacopoeial limits. The percentage drug release of Bi-layer tablets in F8 when compare with Ibuprofen innovator was found to be between 70.4 to 97.2%. The percentage drug release of Bi-layer tablets in F8 when compare with Methocarbamol innovator was found to be between 68.7 to 95.1% and the results are shown in the table-5 along with figures 1, 2. While the in-vitro disintegration time was found in the range of 3.23 to 7.34 min. sec. Formulation F1, F2, F5, F8, F9 are nearly matched with the disintegration time of

innovator product. Among the formulation tablets of batch F8 containing Ibuprofen 200mg and Methocarbamol 500mg per tablet is similar and equal to the innovator product in respect of all tablets properties and dissolution rate and showed good hardness, low friability, and disintegration time of 4.16min/sec. The percentage drug release for formulation F8 shows the better drug release between 95.1 to 97.2%. It was concluded that Ibuprofen, Methocarbamol Bi-layer tablets can be prepared successfully as it satisfies all the criteria as a Bi-layered tablet and would be alternative to the currently available conventional tablets.

Table No.1- Comparative data of various formulations: Methocarbamol

	Ingredient	**Trials**								
		PF1	PF2	PF3	PF4	PF5	PF6	PF7	PF8	PF9
1	Methocarbamol	83	83	83	83	83	83	83	83	83
2	Pregelatinisedmaizestarch	4.025	3.925	3.67	3.5	3.65	3.6	3.55	3.45	3.45
3	Microcrystallinecellulose	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
4	PVP K-30	0.4	0.5	0.4	0.4	0.4	0.4	0.4	0.4	0.4
5	FD&C Blue No.2	0.075	0.075	0.18	0.25	0.25	0.25	0.25	0.25	0.25
6	Ferric Oxide Red	0.1	0.1	0.35	0.45	0.3	0.3	0.3	0.3	0.3
7	Sodium Lauryl Sulphate	_	_	_	_	_	0.05	0.1	0.2	0.2
8	Microcrystallinecellulose	3.68	3.68	3.68	3.68	3.68	3.68	3.68	3.68	3.68
9	Sodium starch glycolate	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
10	Colloidal silicon dioxide	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
11	Megnesium Sterate	0.60	0.60	0.60	0.60	0.60	0.60	0.60	0.60	0.60
	Total% Composition	100	100	100	100	100	100	100	100	100

Table No. 2- Comparative Data of various formulations: Ibuprofen

S.NO	**Ingredient**	**Trials**								
		PF1	**PF2**	**PF3**	**PF4**	**PF5**	**PF6**	**PF7**	**PF8**	**PF9**
1	Ibuprofen	66	66	66	66	66	66	66	66	66
2	Pregelatinised starch	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0	8.0
3	Microcrystallinecellulose	5.4	5.3	_	_	_	5	5	_	_
4	Maize starch	17.0	15.0	19.40	19.20	19.80	16.29	14.40	14.80	14.8
5	Sodium starch glycolate	_	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
6	PVP K-30	1.5	1.2	1.0	1.2	0.6	0.6	1.0	0.6	0.6
7	Sodium starch glycolate	_	1.4	2.5	2.5	2.5	2.5	2.5	2.5	2.5
8	Colloidal silicon dioxide	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
9	Stearic acid	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
	Total% Composition	100	100	100	100	100	100	100	100	100

TableNo.3-Micromeritic properties of powder blend

Formulation	Drugs	Bulkdensity (gm/cc)	Tapped density (gm/ml)	Angle of repose (θ)	Compressibility index (%)	Hausner Ratio
F1	Metho	0.45	0.56	46.66	28.64	1.39
	Ibu	o.44	0.55	50.12	27.0	1.44
F2	Metho	0.44	0.57	48.20	31.80	1.38
	Ibu	0.41	0.51	47.32	28.33	1.42
F3	Metho	0.41	0.59	50.56	30.50	1.40
	Ibu	0.43	0.52	48.26	27.30	1.382
F4	Metho	0.44	0.57	46.99	32.80	1.383
	Ibu	0.41	0.51	46.56	29.61	1.255
F5	Metho	0.44	0.56	47.30	24.42	1.382
	Ibu	0.42	0.54	42.21	32.22	1.383
F6	Metho	0.43	0.54	42.21	20.37	1.255
	Ibu	0.49	0.50	38.65	20.0	1.222
F7	Metho	0.47	0.59	34.56	18.64	1.208
	Ibu	0.48	0.55	36.23	18.15	1.25
F8	Metho	0.48	0.58	30.12	17.24	1.124
	Ibu	0.48	0.51	28.13	15.69	1.146
F9	Metho	0.45	0.55	31.63	18.18	1.125
	Ibu	0.47	0.55	30.23	20	1.25

Table No.4 Evaluation of Tablets

Formulation	Thickness* (mm)	Weight* variation (mg)	Hardness* (kg/cm^2)	Friability* (%)	In-vitro* Disintegration Time(sec)
F1	6.72	900	17.1	0.008	3.23
F2	6.66	896	16.8	0.068	4.09
F3	6.74	887	16.3	1.062	7.34
F4	6.84	885	15.5	1.076	5.12
F5	6.63	903	16.5	0.089	3.97
F6	6.88	895	14.3	1.174	6.25
F7	6.71	903	13.0	0.041	5.12
F8	6.75	905	13.7	0.055	4.16
F9	6.72	901	13.3	0.050	4.05

Table No.5 In-Vitro dissolution profile of various formulations

Time	Innovator-(Ibuprofen)	Innovator-(Methocarbamol)	%Drug release					
			Ibu F6	Metho F6	Ibu F7	Metho F7	Ibu F8	Metho F8
10	72.4	70.7	85.8	59.3	90.2	60.5	70.4	68.7
15	84.2	82.6	90.1	70.6	93.4	73.6	83.1	80.5
30	93.2	91.3	92.5	83.2	95.5	85.6	91.7	89.4
45	96.8	94.9	95.2	86.4	97.3	89.7	95.2	93.2
60	98.2	96.4	96.7	90.2	96.6	91.5	97.2	95.1

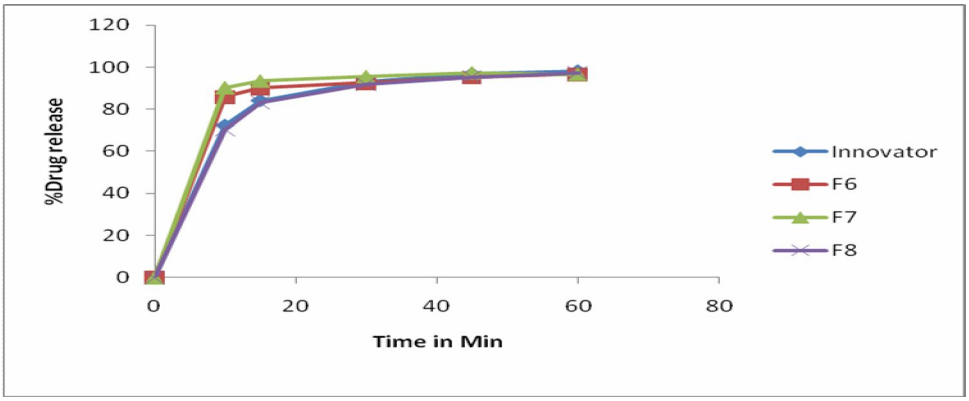

Figure.1-Comparision of dissolution profile of Innovator Drug (Ibuprofen) and F6, F7, F8 (Ibuprofen) in pH 7.2 phosphate buffer

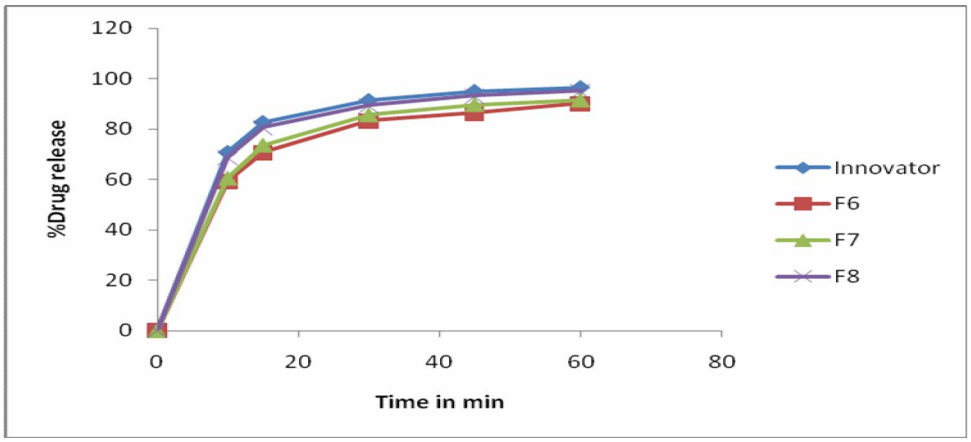

Figure.2-Comparison of dissolution profile of Innovator drug (Methocarbamol) and F6, F7, F8 (Methocarbamol) in pH7.2 phosphate buffer.

ACKNOWLEDGMENTS

The authors are thankful to Rexer pharma, Hyderabad for providing gift sample of Ibuprofen, Methocarbamol and other disintegrants.

REFERENCES

1. Podczeck F., Drake K.R., Neton J.M., and Harian I., The strength of bi layered tablet. Europian Journal of Pharmaceutical Sciences 2008, 1-14.

2. USP NF., The official compendia of standards, 30th Edition, Volume-II and III, 2325, 2610.

3. Erk N., Ozkan Y., Banoglu E., Ozkan S.A., and Senturk Z., Simultaneous determination of Paracetamol and Methocarbamol in tablets by ratio spectra derivative spectroscopy and LC, Journal of Pharmaceutical Biomedical Analysis, 2001, 469-475.

4. Morteza R.T., and Sadegh-Shobeiri N., Effect of Various Polymers on formulation of controlled release Ibuprofen tablets by fluid bed technique, Drug Development and Industrial Pharmacy, 21, (1995), 1193-1202.

5. Mohamed K.G., and Moji C.A., High Shear Mixing Granulation of Ibuprofen and β-cyclodextrin: Effect of process variables on Ibuprofen dissolution AAPS Pharm Scitech 2007, 84.

6. Birringer N., Shoemaker s., Gilman C., Haynes M., and Plank R., Measurement and optimization of layer adhesion in Bi-layer tablets. Pharmaceutical Development, Merck &Co.

7. Rahman Z., and Ali M., Design and evaluation of Bi-layered tablets of captopril. Acta Pharm, 56 (2006) 49-57.

8. Chinam N.P., Kumar A.B., Pandit H.K., Singh S.P., and Devi M.V., Design and Evaluation of Sustained Release Bilayer Tablets of Propranolol Hydrochloride. Acta Pharm. 57 (2007) 479-489.

9. Bushra R., Muhammad H.S., Aslam N., Hashmat D., and Rehman M., Formulation Development and Optimization of Ibuprofen Tablets by Direct

Compression Method. Pakistan journal of Pharmaceutical Science, Vol.21, 2008, 113-120.

10. Chowdary K.P.R., and Hemavathi R., Formulation and Dissolution Rate Studies on Dispersible Tablets of Ibuprofen .Indian journal of Pharmaceutical Sciences, 2000, 213-6.

11. Kishor S.S., Kulkarni M.V., Formulation and In-vitro evaluation of Dextrin matrix tablet of Ibuprofen for colon specific drug delivery. Pakistan Journal of Pharmaceutical Sciences, Vol.21, 2008, 17-20.

12. Costa P., An Alternative Method to the Evaluation of Similarity Factor in Dissolution Testing .Int.J.Pharm.2000,220,77-83.

*****