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FORMULATION AND IN-VITRO EVALUATION OF TABLET CONTAINING IBUPROFEN AND COATED OMEPRAZOLE

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ABSTRACT
The present study was carried out for development of fixed dose combination of ibuprofen and omeprazole in a single tablet. Ibuprofen and the omeprazole (coated with the Eudragit L100) are combined in a single tablet. The omeprazole was coated with Eudragit L 100 by solid dispersion method. Ibuprofen granules were prepared by wet granulation method. The formulation blends were subjected to various pre-formultion studies and were found to be good. The tablets were compressed and subjected to dissolution studies. The batch F3 shows better results and good dissolution.

KEYWORDS: Ibuprofen, Omeprazole, Eudragit L 100, Solid dispersion, Tablet.

INTRODUCTION
Many patients especially children and elderly have difficulty in swallowing tablets and capsules and consequently unable to take medicine as prescribed. Almost 50% of the population is affected by such problem, resulting in the high incidence of non-compliance and ineffective therapy. OTC analgesics like NSAID are widely used, are frequently taken inappropriately and potentially dangerously, and users are generally unaware of the potential for adverse side effects.

Now a day's various developed and developing countries move towards combination therapy for treatment of various diseases and disorders requiring long term therapy. Combination therapy has various advantages over monotherapy such as problem of dose dependent side effects minimized. A low-dose combination of two different agents 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. The goal of any drug delivery system is to provide a therapeutic amount of the drug to the proper site in the body to achieve promptly, and then maintain the desired drug concentration. Combination products-also known as fixed dose combinations are combinations of two or more active drugs produced in a single dosage form. They provide the advantages of combination therapy while reducing the number of prescriptions and the attendant administrative costs and improving patient compliance.

Ibuprofen is a propionic acid derivative and belongs to non-steroidal anti-inflammatory drugs commonly known as (NSAIDS). Omeprazole belongs to the class of antisecretory compounds that neither exhibit anticholinergic nor histamine H-2 receptor antagonistic properties, but suppress gastric acid secretion by inhibiting gastric H+ K+ ATPase at the secretory surface of the gastric parietal cell. Hence both the drugs are used for the study.

Most pharmaceutical forms for oral administration are formulated for direct ingestion, or for chewing, or for prior dispersion and/or dissolution in water; some of them are absorbed in the mouth (sublingual or buccal tablets). To obviate the problems associated with conventional dosage forms, orally fast disintegrating tablets have been developed, which combine hardness, dosage uniformity, stability and other parameters, with extremely easy administration, since no water is required for swallowing the tablets and they are thus suitable for geriatric, pediatric and traveling patients. FDTs can be prepared by different methods as direct compression, freeze-drying, spray drying, sublimation and wet granulation method. The aim of this study was to formulate FDTs with sufficient mechanical integrity and to achieve faster disintegration in the oral cavity without water. Attempts were made to enhance dissolution rate

along with faster disintegration using superdisintegrants like micro crystalline cellulose.

MATERIALS AND METHOD

Materials

Ibuprofen was obtained as a gift sample from (Sanofi,Goa), Omeprazole was obtained as a gift sample from (Murali Krushna, Ranjangaon), Eudragit L 100 was obtained as a gift sample from (BASF,Navi Mumbai), working solution was prepared immediately before experiment by appropriate dilution.

Method

Coating of Omeprazole

Omeprazole-Eudragit L 100 (1:2) solid dispersion was prepared by solvent evaporation technique. Omeprazole was dissolved in ethanol to get clear solution. Then, Eudragit L 100 was dispersed as fine particles and the solvent was removed by evaporation on a water bath at 50^0C. The dried mass was stored in desicator until constant mass was obtained, pulvarised and passed through sieve no. 22.

Preparation of ibuprofen granules

Ibuprofen powder was mixed with starch paste (5%) to form a damp mass. The mass was then passed from sieve no.40. The formed granules were dried in hot air oven at 60^0C until a constant mass was obtained.

Characterization of granules

Angle of repose

Static angle of repose was determined according to the fixed funnel where by accurately weighed granules (3g) were carefully poured through the funnel with its tip at 2 cm height (H) until the apex of the conical heap so formed just reached the tip of the funnel. The mean diameter of the base for the powder cone was measured and the angle of repose (θ) was calculated using the following equation.

$$\tan\theta = h/r$$

Bulk density and Tapped density

Again the bulk density and tapped density was determined where by a quantity (3g) of pure drug and granules from each formula, previously light shaken to break any agglomerates formed, was introduced into a 10-ml measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 second intervals. The tapping was continued until no further change in volume was noted.

Housner's ratio

Housner found that the ratio of tapped density to bulk density was related to interparticle friction and as such, could be used to predict powder flow properties.

Compressibility index

Compressibility index of granules was calculated from the following formula.

$$Compressibility\ \% = \frac{Dt-Db}{Dt} * 100$$

Where Dt is tapped density and Db is bulk density

Preparation of tablet

All excipients used to formulate tablets were passed through sieve # 40 and mixed in geometric dilution. All excipients and drug were compressed on Cadmach rotary 10 station to form flat faced tablets of diameter 12mm and weight 300mg.

Characterization of ibuprofen and omeprazole tablets.

Sr.No	INGREDIENT	F1(mg)	F2(mg)	F3(mg)	F4(mg)
1	OMEPRAZOLE	10	10	10	10
2	IBUPROFEN	200	200	200	200
3	MCC	15	30	45	60
4	EUDRAGITL100	60	45	30	15
5	STARCH	15	15	15	15

Description

Formed tablets were evaluated for shape, surface, and morphology, color of tablet, hardness, weight variation, friability, thickness, and disintegration time.

Weight variation test

Twenty tablets were selected randomly and weighed. The average weight were compared with individual tablet weight. The percentage weight variation was calculated. As per Indian pharmacopoeia specification, tablets with an average weight between >250 mg, the percentage deviation should not be more than 5 %.

Hardness determination

The hardness of three tablets from each batch was measured by using hardness tester (Monsanto hardness tester).

Friability test

Weighed amount of 20 de-dusted tablets were subjected to rotating drum of friability test apparatus. The drum was rotated at a speed of 25 rpm for 4 minutes and reweighed the tablets. % friability was calculated b the following formula.

$$\% \text{ friability} = \frac{\text{Initial weight} - \text{Final weight} \times 100}{\text{Initial weight}}$$

Disintegration test

Disintegration was evaluated to ensure that the drug substance is fully available for dissolution and absorption from the gastrointestinal tract. In disintegration test, measured using USP tablet disintegration test apparatus (ED2L, Electrolab, India) using 900 ml of distilled water without disk at room temperature (37±2^0 C).

Wetting Time

A piece of tissue paper (12 cm X10.75 cm) folded twice was placed in a small petridish containing 6 ml of distilled water. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch were determined.

In-vitro dissolution studies

Dissolution test of the tablets was performed using USP dissolution testing apparatus 2 (Paddle method; Electrolab TDT-08L). The dissolution test was performed using 900 ml of 0.01N HCL and 7.2 pH buffer at 37 ± 0.5°C and 100 rpm, using a Shimadzu UV/Vis double beam spectrophotometer. Test sample (5 ml) was withdrawn at particular time interval (15 minutes) and replaced with fresh dissolution media as used maintained at 37 ± 0.5 ^{0}C. The test sample was filtered (membrane filter, 0.45 µm) and the concentration of drug determined using UV spectrophotometer at λ-max 264 & 276 nm respectively. This test was performed on 6 tablets and mean ± SD calculated for the tablets.

RESULTS AND DISCUSSION

Pre-compression evaluation results of granules

Since, the flow properties of the powder mixture are important for the uniformity of mass of the tablets, the flow of the powder mixture was analyzed before compression to tablets. Low Hausner`s ratio (≤1.29), compressibility index (≤21.68) and angle of repose (≤22.13) values indicated a fairly good flowability of powder mixture. As the tablet powder mixture was free flowing, tablets produced were of uniform weight with acceptable weight variation due to uniform die fill. All results are shown in Table 1.

Table 1: Pre-compression study of granules.

Evaluation parameter	F1	F2	F3	F4
Bulk density (gm/ml)	0.330 ±1.2	0.278±1.9	0.264±0.5	0.263±1.3
Tapped density (gm/ml)	0.385±0.7	0.322±1.3	0.310±0.6	0.312±1.1
Angle of repose(^{0})	20.11±0.2	18.38±0.4	20.75±0.8	24.21±0.9
% compressibility	14.28±0.2	13.66±1.3	14.84±0.6	15.70±0.9
Hausner's Ratio	1.16±0.6	1.158±0.3	1.17±0.4	1.18±0.6

Post-compression evaluation of prepared tablet

Hardness (2.63-3.41 kg/cm^2) and friability loss (0.37-0.83 %) indicated that tablets had a good mechanical resistance. All result shown in Table 2.

Table 2: Post-compression study of tablet.

Batch Code	Average Weight (mg)	Hardness (kg/cm2)	Friability (%)	Disintegration Time (min)	Wetting Time (sec)
F1	302.5±0.5	3.36±0.09	0.42±0.03	2.3±0.41	62±1
F2	304.8±0.23	2.94±0.19	0.39±0.54	2.8±0.34	68±5
F3	301.9±0.11	3.63±0.15	0.37±0.12	1.8±0.24	54±4
F4	302.2±0.30	3.43±0.12	0.44±0.32	2.1±0.34	58±4

Table 3: In vitro dissolution study data for release of Omeprazole from prepared tablets.

Time (sec)	Cumulative % release			
	F1	F2	F3	F4
0	0	0	0	0
15	13.43	12.22	23.44	20.67
30	26.44	28.88	43.45	42.66
45	49.88	51.99	67.11	65.77
75	61.56	64.11	78.98	74.76
90	79.34	83.56	89.23	85.78
120	88.91	89.11	90.22	90.03

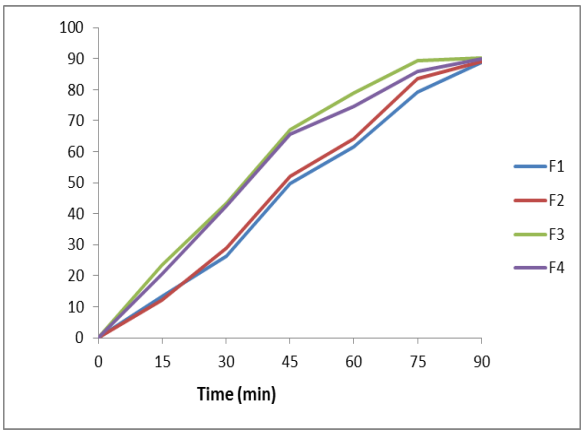

Fig 1. *In-vitro* dissolution profile showing release of Omeprazole from tablet.

In vitro dissolution study data for release of Ibuprofen from prepared tablets

Time (sec)	Cumulative % release			
	F1	F2	F3	F4
0	0	0	0	0
15	11.01	13.43	14.56	10.33
30	32.45	39.44	45.32	21.34
45	47.98	53.3	58.88	43.32
75	61.01	70.33	78.95	58.21
90	81.88	87.23	88.91	68.22
120	89	91.01	94.12	81.23

In vitro dissolution study data for release of Ibuprofen from prepared tablets

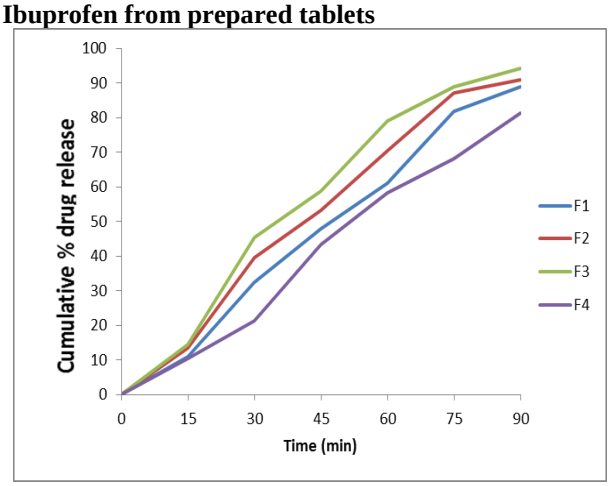

Fig 2: *In-vitro* dissolution profile showing release of Ibuprofen from tablet.

CONCLUSION

The drug release of both the drugs is studied. The maximum drug release of 90.22 and 94.12 Omeprazole and Ibuprofen respectively. By the study we can conclude that the batch F3 shows better results and good dissolution and hence this batch can be further used for further work.

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