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FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLET OF CELECOXIB

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ABSTRACT

Orodispersible tablets are useful in patients, such as pediatric, geriatric, bedridden or developmentally disabled, who may face difficulty in swallowing conventional tablets or capsules and liquids orals or syrup, leading to ineffective therapy, with persistent nausea, sudden episodes of allergic attack or coughing for those who have an active life style. Fast onset of action- dispersible tablet has major advantage that the drug product is already in solution at that time it is consumed. Thus the absorption is faster and more complete than with conventional tablet. Celecoxib is a selective COX-2 inhibitor used in the treatment of acute pain, inflamation.arthrhitis. Three super disintegrating agents were used at lower medium and higher concentration. Six formulations were designed. All the superdisintegrants such as crosscarmellose, crosspovidone, sodium starch glycolate were maintained 2-3 % in all the formulations. Microcrystalline cellulose and mannitol were used as diluents. Here microcrystalline cellulose was also a superdisintegrant, Each formulation was composed of drug and excipients in various proportions. This design techniques was used to optimized and obtain better formulation with respect to in vitro dispersion time , Drug release (%), Disintegration time. In vitro drug release showed that formula Batch F4 (Crosspovidone) had better % drug release as compare to other formulations. The faster disintegration of Batch F4 (Crosspovidone) tablets may attribute to its rapid capillary activity and pronounce hydration with little tendency to gel formation. Thus these results can suggest that the disintegration time can be decreased by using wicking type of disintegrants.

Keywords: Orodispersible tablets, disintegration time, Crosspovidone, superdisintegrant.

INTRODUCTION

Orodispersible tablets are uncoated tablets intended to be oral administration, giving a homogenous dispersion in mouth. The tablets produced must have the ability to form adequate dispersion which is uniform and stable. The chief advantage is quicker absorption and onset of clinical effects. They are generally prepared for geriatric or pediatric patients or for those who are having difficulty in swallowing tablets. They comprise of totally water soluble excipients and components. Of all the orally

administered dosage forms, tablet is most preferred because of ease of administration, compactness and flexibility in manufacturing. Because of changes in various physiological functions associated with aging including difficulty in swallowing, Administration of intact tablet may lead to poor patient compliance and ineffective therapy. The paediatric and geriatrics patients are of particular concern. To overcome this, orodispersible tablets have been developed. Sweeteners and flavors were used to enhance the organoleptic properties of tablet. Tablets were prepared by direct compression technique. Three types of super disintegrants was used and six batches was prepared and evaluated for thickness, uniformity of weight, hardness, friability, wetting time, in-vitro disintegration time and in vitro drug release. All the formulations were evaluated for the influence of disintegrants and their concentrations on the characteristics of fast dissolving tablets mainly in terms of disintegration time and dissolution studies. Crosspovidone showed less disintegration time, dispersion time, wetting time as compare to other super disintegrants. In terms of most of the official specifications prepared tablets was better than those from various conventional tablets at the same drug dosage.

MATERIALS AND METHODS

Celecoxib procured by MODERN Lab., Indore (M.P.), Cross carmellose sodium, Sodium starch glycolate, Micro crystalline cellulose are gifted by Signet chemical corporation,Mumbai, Magnesium stearate, Talc, Lactose procured by Loba chemie,cochin.

FORMULATION OF ORODISPERSIBLE TABLETS OF CELECOXIB

Table No.:1 Standard formulas for preliminary trials

INGREDIENTS	BATCH NO					
	QUANTITY PER TABLET INGREDIENT (MG)					
	F1	F2	F3	F4	F5	F6
Celecoxib	100	100	100	100	100	100
Microcrystalline cellulose	109.5	106	109.5	106	109.6	106
Starch	117.5	117.5	117.5	117.5	117.5	117.5
Sodium starch glycolate	7	10.5	-	-	-	-
Crosspovidone	-	-	7	10.5	-	-
cross carmellose Sodium	-	-	-	-	7	10.5
Aspartame	2	2	2	2	2	2
Mint flavors	2	2	2	2	2	2
Talc	5	5	5	5	5	5
Aerosil	2	2	2	2	2	2
Magnesium stearate	5	5	5	5	5	5
Total Wt	350					

All quantities are in mg

EVALUATION OF ORODISPERSIBLE TABLETS

Evaluation parameters of tablets mentioned in the pharmacopoeia need to be assessed, but some, which require special concern or need to be modified, are discussed here.

Mechanical Strength:

Tablets should possess adequate strength to withstand mechanical shocks of handling in manufacturing, packaging and shipping. Crushing strength and friability are two important parameter to evaluate a tablet for its mechanical strength.

a. Crushing Strength:

It is the force required to break a tablet by compression in the radial direction, it was an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time. In the present study the crushing strength of the tablet was measured using Pfizer hardness testers. An average of three observations was reported.

b. Friability testing:

The crushing test may not be the best measure of potential behavior during handling and packaging. The resistance to surface abrasion may be a more relevant parameter. Friability of each batch was measure in "Electro lab friabilator". Ten preweighed tablets were rotated at 25 rpm for 4 min, the tablets were then re weighed and the percentage of weight loss was calculated**.**

$$F = (1 - W/Wo)\ 100$$

Weight variation:

20 tablets were selected randomly from the lot and weighted individually to check for weight variation.

Table No. 4: Weight Variation Specification as per IP

Average Weight of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

Thickness:

Three tablets were selected randomly from each batch and thickness was measured by using vernier calipers.

Rapidly Disintegrating Property:

To evaluate the tablets for their rapid disintegration properties, following tests were carried out.

- **Wetting time:**

Five circular tissue papers of 10 cm diameter are placed in a Petridis with a 10 cm diameter. Ten millimeters of water-containing Eosin, a water-soluble dye, is added to Petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to

reach upper surface of the tablet is noted as a wetting time.

- **Modified disintegration test:**

The standard procedure of performing disintegration test for these dosage forms has several limitations and they do not suffice the measurement of very short disintegration times. The disintegration time for ODT needs to be modified as disintegration is required without water, thus the test should mimic disintegration in salivary contents. The tablet was carefully put in the center of petridish and the time for the tablet to completely disintegrate into fine particles was noted.

- **Water absorption Ratio:**

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using following equation

R = 100 (Wb-Wa/Wa)

Where, wb is weight of tablet before water absorption wa is weight of tablet after water absorption.

- **In-vitro dispersion time:**

Tablet was added to 10 ml of .01N HCL, (pH 1.2) at 37+0.5ºc. Time required for complete dispersion of a Tablet was measured.

In-Vitro drug release

Release of the drug *in vitro*, was determined by estimating the dissolution profile**.**

Dissolution test:

USP 2 Paddle apparatus was used and paddle was allowed to rotate at 50 rpm. 0.1 N HCl (900 ml) was used as a dissolution medium. Determination of amount of drug dissolved form tablets was carried by Schimadzu UV 1700 spectrophotometer at 252 nm.

RESULTS

EVALUATION OF FORMULATIONS (DIRECT COMPRESSION)

Physical Characterization of Formulation Blends

Table no.5:-Physical characterization of formulation blends

FORMULATION PARAMETER	F1	F2	F3	F4	F5	F6
Angle of repose (^{0})	41.86	42.08	43.01	41.86	42.86	40.59
Bulk density (gm/ml)	0.526	0.540	0.549	0.510	0.492	0.543
Tap density (gm/ml)	0.667	0.714	0.666	0.689	0.680	0.641
Carr's index(%)	21.13	22.12	18.91	23.65	18.38	24.92
Hausner's ratio	1.26	1.28	1.23	1.30	1.225	1.282

EVALUATION OF FORMULATED PARAMETER

Table no: 6 Evaluation of formulated Tablets.

FORMULATION PARAMETERS	F-1	F-2	F-3	F-4	F-5	F-6
Uniformity of mass	350 mg ± 3 %	350 mg ± 3 %	350 mg ± 4 %	350 mg ± 3 %	350 mg ± 2 %	350 mg ± 3 %
Hardness (Kp)	3-4	3-4	3-4	3-4	3-4	3-4
Thickness (mm)	3.42	3.37	3.39	3.39	3.41	3.47
Friability (%)	0.8	0.95	1.3	0.85	0.9	0.71
Disintegration time (sec)	40-50	40-42	30-40	20-25	40-42	30-35
Dispersion time (sec)	45-60	40	30-40	40-50	30-40	35-40
Drug content (%)	97.56	98.44	96.16	99.47	99.88	97.54
Wetting time (sec)	19	52	21	15	53	43

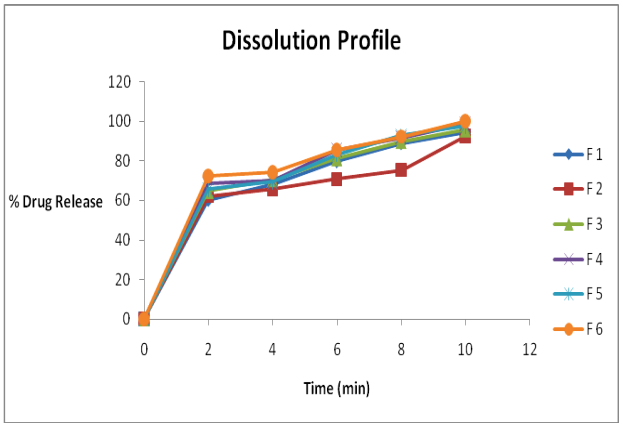

Figure No.1 Comparative dissolution profile of formulations (F1-F6)

CONCLUSION

The flow properties of the powdered blend for all the batches were found to be good and free flowing. The weight variation, hardness and friability of all the formulated tablets within the specified requirements. The disintegration time for the formulated tablets was with in the limit. Here disintegration time of formulation containing crosspovidone was less as compared to sodium starch glycolate and crosscarmellose sodium. The wetting time was found to be less in formulation containing crosspovidone. The friability percentage of all formulation was found to be in the limit. In vitro drug release showed that formula Batch F4 (Crosspovidone) had better % drug release as compare to other formulations. The faster disintegration of Batch F4 (Crosspovidone) tablets may attribute to its rapid capillary activity and pronounce hydration with little tendency to gel formation. Thus these results can suggest that the disintegration time can be decreased by using wicking type of disintegrants.

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