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PREPARATION AND EVALUATION OF ORODISPERSIBLE TABLET OF ANTI-INFLAMMATORY DRUG CELECOXIB

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ABSTRACT

The present investigation an effort was made to formulate and evaluate or dispersible Tablets of Celecoxib which is a anti-inflammatory drug. Preparation of the tablet was done by taking super disintegrating agent in different concentration in order to get better and fast release of drug from the formulation. Sodium starch glycolate is used as a superdisinigrant in different concentration as it has been using in tablet formulations as superdisintegrants. The optimized formulation was further evaluated for tablet evaluation parameters like weight variation, wetting time, hardness, friability, thickness, in vitro release and disintegration time. Formulation Batch F3 revealed fast release of drug and and promising results for all the evaluation

KEYWORDS: Celecoxib, Orodispersible Tablet, Disintegrant.

INTRODUCTION

The US Food and Drug Administration , Center for Drug Evaluation and Research defines, an orally disintegrating tablets as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue"[1]

Mouth dissolving tablets have many advantages of ease of administration and rapid onset of action, rapid disintegration without use of water in oral cavity. When the mouth dissolving tablet is kept in oral cavity then saliva starts penetrating on to the tablet pores and this will ultimately causes rapid disintegration of tablet formulation. [2-3] Oral dispersible tablets can be used where there is difficulty in swallowing which is also known as Dysphagia and it is common in all age groups. Dysphagia is seen in about 35% of the general population. The preparation of Orally Disintegrating tablets also improve patient's compliance and thus reduce the Difficulty of swallowing conventional tablets and capsules is usually seen in all age groups, mostly in elderly and dysphasic patient.[4]

Oral route are always considered as best route and for that Orodispersible tablet is the best formulation.[5]

Celecoxib is a non-steroidal, anti-inflammatory drug that acts by inhibiting the activity of the enzyme cyclooxygenase-2 (COX-2). It is used mainly for osteoarthritis, rheumatoid arthritis, and dysmenorrhea. Celecoxib is practically insoluble in water (0.003 mg/ml), and its peak blood levels are reached between 2 and 3 h after oral.

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It has potential bioavailability problems due to its extremely hydrophobic property (aqueous solubility less than 0.1 mg/ml at 37 °C) which leads to erratic or incomplete absorption from the GIT. So in the present studyan attempt has been made to develop and evaluated mouth dissolving tablet of Celecoxib to improve its bioavailability .[6-8]

MATERIAL AND METHOD

Celecoxib was obtained as gift sample from Kekul Pharma ltd. Ahemdabad (India) Mannitol, Sodium Starch Glycolate, PVP, Saccharine Sodium, Magnesium Sterate and Menthol were purchased from Central drug house New Delhi.

PREPARATION OF TABLET

Preparation of tablet -Power were shifter and compressed by single station compression machine by using direct compression methods, Different batches were further prepared by varying the concentration ration of polymer and effect on response was studied .

Table 1.Formulation of orodispersible tablets having different concentration of superdisintegrants

Formulation code	F1	F2	F3
Drug	26.8	26.8	26.8
Mannitol	93.8	92.55	90.2
Sodium Starch Glycolate	4	6	8
PVP	0.89	0.89	0.89
Saccharine Sodium	0.53	0.53	0.53
Magnesium Sterate	0.26	0.26	0.26
Menthol	0.26	0.26	0.26

Table 2.Preparation of the optimized formulation

S no	Ingredient	Quantity %w/w
1	Celecoxib	26.8
2	Mannitol	63.4
3	Sodium Starch Glycolate	8
4	PVP	0.89
5	Saccharine Sodium	0.26
6	Magnesium Sterate	0.53
7	Menthol	0.26

PRE-COMPRESSION PARAMETERS

Angle of repose- The angle of repose (a) was determined using funnel method. The blend was poured through a funnel that can be raised vertically to a maximum cone height (h) was obtained. The radius of the heap (r) was measured and angle of repose was calculated.

$$= \tan^{-1}\frac{h}{r}$$

BULK DENSITY (BD)

The bulk density was determined by transferring the accurately weighed blend sample into the 100 ml graduated cylinder by keeping it in a slanting position. The initial volume and weight were noted. The ratio of weight of the sample to the volume it occupied was calculated.

TAPPED DENSITY (TD)

Tapped density was determined by transferring the accurately weighed blend sample into 100 ml

measuring cylinder which was placed in Electrolab Tapped Density Apparatus. Initial volume (V0) of the cylinder was noted and then the cylinder was tapped for 10 times and the volume was measured. Further additional 500 tapings were made and the volume was noted. .

COMPRESSIBILITY INDEX (CI)

Compressibility index (CI) is a measure of the propensity of a powder to be compressed. It is a direct measurement of potential powder arch or the bridge strength and stability. It was calculated according to the equation given:

$$CI = \frac{Tapped\ \ Density - Bulk\ \ Density}{Tapped\ \ Density} \times 100$$

HAUSNER RATIO

Hausner ratio is an indirect index of ease of powder flow. It was calculated by the following formula:

$$Hausners\ \ \ Ratio = \frac{Tapped\ \ \ Density}{Bulk\ \ \ Density}$$

Table 3.Evaluation results of Precompression Parameters

Formulation code	Angle of repose	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index %	Hauseners ratio
F3	25.6	0.42	0.71	10	1.54

POST COMPRESSION EVALUATION

The mixture of powder was evaluated for bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose. The tablets were evaluated for thickness, hardness, friability, weight variation test, drug content and In-Vitro release rate studies

GENERAL APPEARANCE

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance and tablet's size, shape, colour, presence or absence of an odour, Taste, surface texture, physical flaws and consistency and legibility of any identifying marking. Size and Shape. The size and shape of the tablet can be dimensionally described, monitored and controlled.

TABLET THICKNESS

Tablet thickness can be measured using a simple procedure. Five tablets are taken and their thickness is measured using Vernier Caliper.

WEIGHT VARIATION

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

HARDNESS

The fracture strength, which is defined as the force required to breaking a tablet by radial compression is measured with a tablet hardness tester (Monsanto hardness tester). It is expressed in kg/cm^2.

FRIABILITY

The friability of sample of six tablets is measured using a Roche Friabilator. This device subject the tablets to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Six pre-weight tablets are rotated at 25 rpm for 4 minutes. The tablets are then reweighed after removal of fines using 60 mesh screens and the percentage of weight loss is calculated.

$$\%Friability = \frac{Loss\ \ in\ \ weight}{Initial\ \ Weight} \times 100$$

WETTING TIME

Wetting time of dosage form is related to the contact angle. It needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. For this purpose, a tablet is placed on a piece of tissue paper folded twice and kept in a small Petri dish (ID = 6.5 cm) containing 6 ml of water, and the time for complete wetting is measured .

DISSOLUTION TEST

The development of dissolution methods for ODTs is comparable to the approach taken for conventional tablets, and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent ODT. Other media such as 0.1 M HCl and buffer (pH 4.5 and 6.8) should be evaluated for ODT much in the same way as their ordinary tablet counterparts. It has been suggested that USP Type - 2 paddle apparatus is the most suitable and common choice for orally disintegrating tablets, with a paddle speed of 50 rpm commonly used.

Table 4.Evaluation results of Post compression Parameters

Formulation code	Weight variation	Friability %	Hardness (kg)	Wetting time(min)	Thickness
FF	Passed	0.9	3.2	2	0.3 cm

RESULT AND DISCUSSION

Evaluation of Precompression parameters of the Powder blend-Powder for compression of Orordispersible tablets were evaluated for their flow properties .Angle of repose was 25.6, cars index was 10 and Hausners ration was 1.54 for different formulation these valued indicate that showed flow property, the angle of repose of the formulation comes under range of 25-30 which is the range of good flow property hence it passed the parameters of angle of repose.

The range of cars index for excellent flow of the powder is 5-15 since the prepared formulation comes under this range ,it also passes the parameter of cars index, since the Hausner's ration of the formulation comes under the range 1.25 -1.5 which is the range for good flow properties.

Evaluation parameters of Post compression Parameters revealed that the final formulation Batch F3 which possess maximum concentration of Superdisintegrants shows fast disintegration of Formulation .It is again prepared and it passed weight variation test, wetting time was 2 minutes and friability test showed within 1% limit. Thickness was also found to be in the range.

The formulation of Celecoxib were used to calculate a percent drug release profile for 3 minutes .The in vitro release study of optimized formulation revealed that formulation F showed release of 35.9 at 3 minutes .

CONCLUSION

In this study, the concentration of superdisintegrants was observed to have a profound and interactive effect on the dispersion time. The data observed showed this experimental design was successfully applied to optimize the concentration of superdisintegrants to formulate Orodispersible tablets of Celecoxib with desirable properties of low dispersion time and high drug release. It can be concluded that the development of Celecoxib Orodispersible tablets with fewer numbers of trials and better quality attributes.

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