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Formulation and evaluation of fast dissolving tablet of aceclofenac

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Abstract

Fast disintegrating drug delivery system offers a solution for these patients having difficulty in swallowing tablets/ capsules etc. Aceclofenac (anti-inflammatory and analgesic) was selected as the model drug. The poor aqueous solubility of the drug results in variable dissolution rate and hence poor bioavailability. In the present study, an attempt had been made to prepare fast dissolving tablets of the drug using various super disintegrates sodium starch glycolate following by direct compression technique. The tablets were evaluated for hardness, friability, weight variation, disintegration time, water absorption ratio and wetting time, in vitro dissolution studies. All the formulation showed disintegration time in range of 12.2 to 27.5 second along with rapid in vitro dissolution. It was concluded that the fast dissolving tablets of the poor soluble drug can be made by direct compression technique using selective super disintegrantes showing enhanced dissolution, taste masking and hence better patient compliance and effective therapy.

Keywords: Aceclofenac; Fast disintegrating; Superdisintegrants; Taste masking

Introduction

Aceclofenac is a non- steroidal agent with marked anti-inflammatory and analgesic properties. The mode of action of Aceclofenac is largely based on the inhibition of prostaglandin synthesis. Aceclofenac is a potent inhibitor of the enzyme cyclo-oxygenase, which is involved in the production of prostaglandins. Aceclofenac can be administered twice daily as 100mg orally in the treatment of rheumatoid arthritis. Geriatric patients may have difficulty in swallowing and chewing the tablets resulting in patient non compliance and ineffective therapy.

To overcome these problems mouth dissolving tablets are good option. Since, they disintegrate and dissolve rapidly in saliva without need for drinking water. The development of a fast dissolving tablet also provides an opportunity for a line extension in the market place.

Thus the present drug is chosen as a suitable candidate for the formulation of fast disintegrating tablet using three super disintegrants in different ratio [1-3].

Materials and Methods

Aceclofenac were received as a gift sample from Intas Pharmaceuticals, Ahemdabad. Sodium starch glycolate, mannitol, microcrystalline cellulose was obtained from commercial sources. All other reagents were of analytical grade.

Preparation of taste masked granules of Aceclofenac

The bitter drug Aceclofenac was thoroughly mixed with different amount powered EudragitE100. Then 10% ethanol was added to this mixture in a glass

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beaker and a gel was prepared. The prepared gel was manually pressed out using a syringe. After extrusion of the gel, ethanol was removed by evaporation overnight at room temperature.

Subsequently the solidified gel was crushed into granules using a pestle mortar. The prepared granules were subjected to percent drug content, flow properties and for evaluation of taste [4].

Table1. Preformulation Studies of Granules

Formulation Code	Drug: Eudragit E100	Drug Content (%)	Angle of repose (^{0})	Carr's Index	Bulk Density	Taste
A_1	1 :0.5	56.62 ±1.22	18.66±0.102	8.56±0.214	0.552±0.051	Bitter
A_2	1:1	70.71±0.61	19.24±0.884	10.24±1.22	0.549±0.077	Slightly Bitter
A_3	1:1.15	89.54±2.42	27.14±0.536	19.52±0.541	0.502±0.41	Slightly Bitter
A_4	1:2	95.55±1.16	26.47±0.258	22.49±0.475	0.486±0.087	Slightly Bitter
A_5	:2.5	98.71±1.02	30.85±0.334	24.27±0.98	0.425±0.015	Tasteless
Pure Drug		100	18.24±0.265	8.22±0.574	0.5574±0.051	Bitter

Formulation of tablet

Rapidly disintegrating tablets were prepared using super disintegrants addition. Different ratio of microcrystalline cellulose and sodium starch glycolate were used. The ratio giving the best disintegration time along with optimum hardness was chosen and tablets prepared by direct compression. The final formulae for preparation of RDT are given in table-2. Accurately weighed taste masked granules were mixed with Microcrystalline Cellulose, Sodium starch glycolate, Mannitol and Sucrose for about 10-15 minutes. Then menthol and magnesium state was added and mixed for further 2 minutes and Compressed into tablets using double concave punches. The tablet prepared was evaluated for weight variation, friability, disintegration time as procedure given in Indian pharmacopoeia in triplicate [5, 6].

Water absorption ratio and wetting time

A piece of tissue paper folded twice was placed in a Petridish containing 5ml of water. A pre weighed tablet was placed on the paper and the time for complete wetting was measured which is characterized by coloring of tablet (Figure 1). The wetted tablet was then weighed. Water absorption ration R was determined according to the following formula [7].

$$R = (Wa- Wb/ Wb) 100$$

Wa = weight of tablet after absorption of water
Wb= weight of tablet before absorption of water

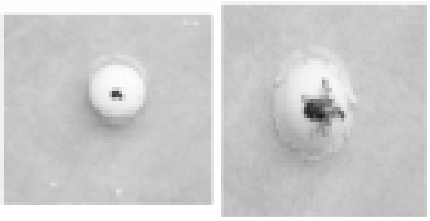

Figure 1. *In vitro* wetting property

***In vitro* Dispersion Time**

Tablet was added to 10ml of phosphate buffer pH 6.8 and time required for complete dispersion was measured (Figure 2). Three tablets from each

formulation were randomly selected and in vitro dispersion time was performed (8).

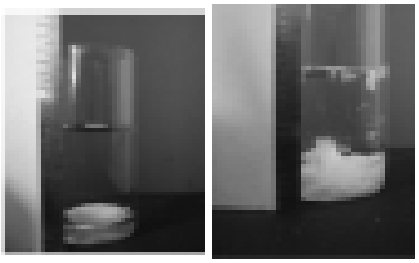

Figure 2. *In vitro* disintegration property

Dissolution Studies

In vitro dissolution studies for all the fabricated tablets was carried out using USP paddle method at 100 rpm in 900 ml of phosphate buffer pH 6.8 as dissolution media, maintained at 37±0.5°C. 5 ml aliquot was withdrawn at the specified time intervals, filtered through whattman filter paper and assayed spector-photometrically at 275 nm. An equal volume of fresh medium, which was pre-warmed at 37°C was replaced into the dissolution media after each sampling to maintain the constant volume throughout the test [9].

Table 2. Formulation Composition

Formulation Code	RDT_1	RDT_2	RDT_3	RDT_4	RDT_5	RDT_6
Granules	350	350	350	350	350	350
Ac- Di- Sol	10	15	20	-	-	-
Explo Tab	-	-	-	10	15	20
Mannitol	25	25	25	25	25	25
Sucrose	102	97	92	102	97	92
Mg. Sterate	13	13	13	13	13	13
Total Weight	500	500	500	500	500	500

Result and Discussion

Taste masked granules of Aceclofenac: EudragitE100 (1:0.5 to 1:2.5) was prepared by gel extrusion method to mask the bitter taste of Aceclofenac. The ratio of drug: Eudragit E100 was optimized to 1:2.5. The EudragitE100 was selected as taste masking agent because it has both taste masking and super disintegrants properties. The optimized Aceclofenac: EudragitE100 (1:2.5) granules was evaluated for drug content, bulk density, Carr's index and angle of repose. The results are given in table-1. The taste masked granules of Aceclofenac: EudragitE100 were compressed with super disintegrants at different concentration level (2-4%) to assist disintegration. The prepared tablets were then evaluated for weight variation, hardness, friability, disintegration time, water absorption ratio. The results are given in table-3. The prepared tablets in all formulation possessed good mechanical strength with sufficient hardness. Percent friability was less than 1% in the entire six formulations.

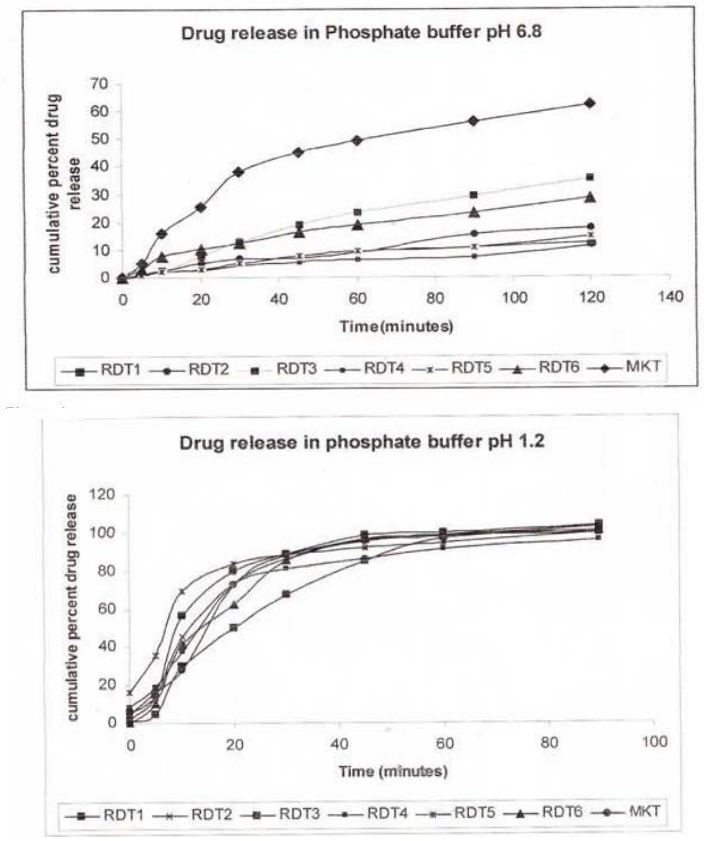

Figure 3. In vitro dissolution studies of various formulations In phosphate buffer pH 6.8 (a) and pH 1.2 (b).

In vitro dissolution studies of various formulations at different time interval are reported in (Figure 3a) and (Figure 3b). In phosphate buffer pH 6.8 (Figure 3a) and pH 1.2 (Figure 3b), a cumulative percent drug release of less than 55.50% was obtained even after 2 hours of dissolution for RDTs of Aceclofenac. The results are much in agreement with the pH-sensitive nature of EudragitE100. This value suggests that sufficient taste

masking has been achieved and that the bitter taste of drug will not perceived while the tablet is in mouth after oral intake. (Figure 3b) shows that almost 99% of drug was found to be released after 60 minutes of dissolution. It is therefore implied that the drug will be released from the taste masked granules in the acidic pH of the stomach Ac-di sol formulation showed maximum dissolution rates with more than 99% of drug release in 90min. Explotab formulation released more than 97% of drugs in 90 minute. Stability studies were conducted for the promising formulation.

Table 3. Comparative evaluation of different formulation

Formulation Code	RDT1	RDT2	RDT3	RDT4	RDT5	RDT6
Uniformity of Weight	Passes	Passes	Passes	Passes	Passes	Passes
Uniformity of Content (%)	99.35±1.263	100.25±1.74	99.84±2.35	100.11±2.14	99.86±3.25	100.01±0.958
In – vitro Disintegration Time (sec)	27.5±1.2	18.2±2.3	12.2±2.1	31.7±1.1	24.8±4.1	18.8±1.3
Hardness(Kg/cm^2)	3.5±0.5	3.3±0.2	3.4±0.9	3.8±0.2	3.6±0.7	3.5±0.9
Friability (%)	0.67±.03	0.69±.04	0.72±.05	0.69±.08	0.72±.02	0.77±.08
%Water Absorption	125.26±1.36	167.25±2.36	184.36±3.27	98.52±3.56	102.55±5.21	118.24±2.65

RDT-3 and RDT-6. The tablets were analyzed for hardness, uniformity of drug content, in-vitro disintegration time and friability. Both the formulations showed no significant variations in all the parameters and were found to be stable. Results are given in table 4.

Table 4. Effect of temperature on tablet characters

Code		Temperatures														
		40^{0}C Time period (in Weeks)					50^{0}C Time period (in Weeks)					45^{0}C / 75% RH Time period (in Weeks)				
		0	1	2	3	4	0	1	2	3	4	0	1	2	3	4
Uniformity of Content (%)	RDT3	99.84	99.68	99.75	99.67	99.65	99.84	99.58	99.54	99.32	99.16	99.84	99.52	98.79	97.45	96.84
	RDT6	100.01	99.87	99.72	99.68	99.64	100.01	99.41	99.31	99.02	98.56	100.01	99.25	98.71	97.84	96.83
In- Vitro Disintegration Time (sec)	RDT3	12.2	12.0	11.7	11.2	10.9	12.2	11.7	11.3	11.11	10.6	12.2	14.1	14.7	15.2	15.9
	RDT6	18.8	18.2	18.00	17.6	17.1	18.8	18.0	17.2	16.8	16.1	18.8	19.2	19.6	19.8	19.9
Hardness(kg/cm^2)	RDT3	3.4	3.6	3.7	3.9	4.1	3.4	3.6	3.8	4.0	4.2	3.4	3.4	3.2	3.1	2.9
	RDT6	3.5	3.7	3.9	4.0	4.0	3.5	3.7	3.9	4.1	4.3	3.5	3.3	3.1	3.0	2.8
Friability (%)	RDT3	0.72	0.70	0.68	0.64	0.62	0.72	0.69	0.67	0.64	0.61	0.72	0.77	0.79	0.83	0.85
	RDT6	0.77	0.75	0.74	0.73	0.70	0.77	0.73	0.68	0.64	0.61	0.77	0.81	0.84	0.87	0.91

Conclusion

From the present studies, it may be concluded that the fast disintegrating Aceclofenac tablets can be prepared by direct compression using superdisintegrants. Ac di sol was found to be best among the two super disintegrants. At 4% concentration level it showed the least disintegration time of 12.2 sec and the highest release of more than 99% of drug in 60 minute.

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