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Formulation of Diclofenac tablets for rapid pain relief

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ABSTRACT

Objective: To develop fast dissolving tablets of diclofenac in order to get fast relief from pain. **Methods:** Fast dissolving tablets of diclofenac potassium were prepared by direct compression method using Indion 214, Indion 234, Indion 244 and croscarmellose as superdisintegrants. Microcrystalline cellulose was used as diluents and mannitol, as sweetening agent. Tablets were evaluated for weight variation; weight variation of all the formulations was observed which were within the acceptable limit for uncoated tablets as per United States Pharmacopoeia. **Results:** Mechanical strength, the hardness of tablets was determined and was found to be in the range of 6.4 to 7.13 Kg/cm^2. *In vitro* disintegration time, the formulation containing indion214, indion234 andindion244 showed 34,31and 39 seconds value for *in vitro* disintegration respectively. Wetting time for all the formulations was found to be (4.425±0.25) to (5.75±2.25) seconds and the cumulative percentage drug release of formulations FD1– FD5. It was observed that in first 10 minutes, only 12.89% of drug was release from formulation FD5 without using superdisintegrants and while it was 88.56% in the case of formulation FD2. At the end of 24 minutes only 85.42 % of drug was released from the control tablet formulation FD5 whereas the cumulative release from other formulations FD1 and FD4 at the end of 12 minutes was 89.52 %and 79.29%, respectively. The results of in vitro disintegration time show that formulation containing Indion 244, showed the disintegration time of 29.66 seconds. **Conclusions:** Indion 244 was found to have super disintegrant property the addition technique is a best method for preparing fast dissolving tablets for rapid pain mangment.

1. Introduction

Pain is a feeling triggered in the nervous system. Pain may be sharp, stabbing, burning and bumping. Acute pain is usually managed with medications such as analgesics.Elderly people and children sometimes have difficulties in swallowing these dosage forms. Such problem is more serious for bed-ridden patients. Recent advances in novel drug delivery system aims to provide rational drug therapy by enhanced safety and efficacy of drug molecule by formulating a convenient dosage form for administration and also by ensuring better patient compliance[1].

Fast disintegrating tablets are dosage form, which disintegrate in patient's mouth within a few seconds without the need of water, or chewing, providing best remedy for the patient suffering from dysphasia[2]. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down the stomach. In such cases the bioavailability is greater than those observed for conventional dosage form. The advantages of mouth dissolving dosage form are increasingly being recognized in both industry and academia[3].

More than 50% of pharmaceutical products are orally administered for several reasons[4]. This route of administration is considered as the most widely used route as it offers advantages like ease of administration, versatility, patient compliance and accurate dosing. Undesirable taste is one of the important formulation problems that are encountered with such oral products. Difficulty in swallowing is also a common problem of all age groups, especially the elderly and pediatrics, because of physiological changes associated with these groups[5].Fast disintegrating drug delivery systems have started gaining popularity and acceptance as new drug delivery systems which aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance[6]. The bioavailability of drug is significantly greater than those observed from conventional tablet dosage form.

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In the present study it was proposed to formulate an oral delivery device, in the form of fast disintegrating tablets by using direct compression technology[7],with the aim of reaching a high serum concentration in a short period of time[8].In this study, effort has been made to formulate fast disintegrating tablet of diclofenac potassium using super disintegrants, like Croscarmellose sodium and ion exchange resin was investigated for the super disintegrating property. The disintegrating property was compared with the Croscarmellose at fixed concentration.

2. Material sand methods

2.1. Materials

Diclofenac potassium (Amoli Organics Ltd), Indion 214, Indion 234, Indion 244 (Colorcon pvt.Ltd.), Cros carmellose (Mapple biotech pvt. Ltd.), Micro crystalline cellulose (Reliance Cellulose Products Pvt Ltd) the above were the gift samples. Magnesium stearate(Ozone international), Mannitol (Ozone international) were purchased.

2.2. Methods

2.2.1. Preparation blends and tablets

Fast disintegrating tablets containing 50 mg diclofenac potassium were prepared by direct compression method and the formulae used in the study are shown in Table 1. Different super disintegrants such as Indion 214, Indion 234, Indion 244 and croscarmellose were used. Microcrystalline cellulose was used as diluents and mannitol as sweetening agent. Diclofenac potassium was mixed in geometric proportions with sweeteners, diluents, and lubricants. Blend was screened and compressed on rotary punching machine.

2.2.2. Evaluation of tablets

All the tablets were evaluated for different parameters as weight variation, hardness, friability, uniformity of weight, disintegration time, wetting time, drug content and *in vitro* dissolution study[9,10].

2.2.3. Weight variation

Twenty tablets were selected randomly from the lot and weighted individually to check for weight variation and then the average weight was determined and compared with average weight the positive and negative deviation. The tablets meets USP specifications if no more than 2 tablets are outside the percentage limit and if no tablets differs by more than 2 than the percentage limit.

2.2.4. Hardness and friability

The hardness of the prepared tablets was determined using a monsanto hardness tester, which also measures the tablet diameter. Ten tablets were tested for hardness from each batch and the mean and SD were calculated. Pre-weighed 20 tablets were placed in a plastic chambered friabilator (Roche) attached to a motor revolving at a speed of 25 rpm for 4 min. The tabletswere then de-dusted, reweighed and percentage mass loss (friability) was calculated.

2.2.5. Wetting time

A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6 mL of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in minutes.

2.2.6. Disintegration time

In vitro disintegration time of the prepared tablets was carried out at (37 ± 2) ℃ in 900 mL of distilled water. using a disintegration test apparatus. Disintegration time of 6 individual tablets was recorded. was carried out at (37±2) ℃in 900 mL of distilled water.

2.2.7. Drug content

Twenty tablets were weighed and powdered. An amount of the powder equivalent to 50mg of diclofenac potassium was dissolved in 100 mL of pH 6.8 phosphate buffer, filtered, diluted suitably and analyzed for drug content at 265nm using UV-Visible spectrophotometer.

2.2.8. In vitro drug release studies

In vitro drug release studies of all the formulations were carried out using tablet dissolution test apparatus (USP XXII type) at 50 rpm. Phosphate buffer pH6.8 was used as the dissolution media with temperature maintained at (37.0±0.5) ℃. Samples were withdrawn at different intervals, diluted suitably and analyzed at 265 nm for cumulative drug release using Shimadzu UV-Visible spectrophotometer (Figure 1).

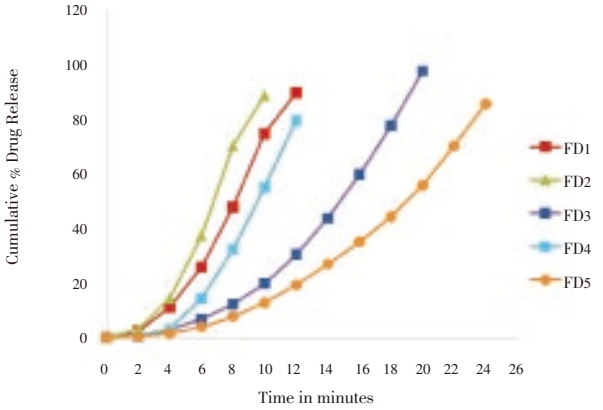

Figure 1. *In vitro* Drug Release Profile of The Formulations

2.2.9. FT-IR study

The pure drug diclofenac potassium and the solid admixture of drug and various excipients used in the preparation of fast dispersible tablet formulations were characterized by FT-IR spectroscopy to know the compatibility, The FT-IR study did not show any possibility of interaction between

Table 1
Formula of different formulations of Diclofenac potassium fast disintegrating tablets (mg).

Ingredients	Formulation code				
	FD1	FD2	FD3	FD4	FD5
Diclofenac	50	50	50	50	50
Indion 214	10	–	–	–	–
Indion 234	–	10	–	–	–
Indion 244	–	–	10	–	–
Cros carmellose	–	–	–	10	–
Microcrystalline cellulose	100	100	100	100	100
Talc	10	10	10	10	10
Magnesium state	5	5	5	5	5
Mannitol	95	95	95	95	105

Table 2
Characeterization of fast dissolving tablets.

Formulation Code	Thickness(mm)	Weight Variation		Hardness(kg/cm^2)	Percentage Friability (%)	Wetting Time(sec)	Drug content (mg)	Disintegration Time(sec)
FD1	12	+0.0594	−0.0453	7.33±0.11	0.73	5.75± 2.25	98.0	34.67
FD2	12	+0.0397	−0.0369	7.06±0.23	2.29	4.75±0.25	99.8	32.00
FD3	12	+0.0312	−0.0312	6.93±0.30	1.03	4.53±0.03	96.5	29.66
FD4	12	+0.0370	−0.0398	6.40±0.52	3.16	4.43±0.03	100.0	25.33
FD5	12	+0.0418	−0.0698	7.06±0.30	2.24	5.10±0.10	97.2	106.33

Diclofenac potassium and superdisintegrants used in the fast disintegration tablets.

3. Results

The different batches of Diclofenac potassium fast disintegrating tablets were prepared by direct compression method using various super disintegrants like cros carmellose, Indion 214, Indion 234 and Indion 244. Total number of four formulations with fixed concentration of different super disintegrants and one control formulation without the addition of super disintegrants were prepared and evaluated. Results were shown in Table 2.

4. Discussion

Weight variation of all the formulations was observed which were within the acceptable limit for uncoated tablets as per United States Pharmacopoeia. One of the primary requirements of immediate release preparation is faster disintegration[11]. It is well known to formulation scientists that the tablets with higher crushing strength show longer disintegration time. Since mechanical integrity is of paramount importance in successful formulation of fast disintegrating tablets.

The hardness of tablets was determined and was found to be in the range of 6.4 to 7.13 kg/cm^2. But Friability was observed between 0.7 to 2%, which was not within the acceptable limit.

The wetting time for all the formulations was found to be (4.43±0.03) to (5.75±2.25) seconds. The tablets were subjected for evaluation of *in vitro* disintegration time. *In vitro* disintegration time for formulations FD1 to FD4 was 25.33 to 34.66 seconds. The formulations containing cros carmellose showed rapid disintegrating time of 25 seconds this is due to rapid uptake of water from the medium swelling and burst effect, there was the direct correlation between wetting time and disintegration time. It was found that the formulation containing cros carmellose showed rapid wetting time and disintegration time compared to other super disintegrants. The formulation containing indion 214, indion 234 andindion 244 showed 34, 31 and 39 seconds value for *in vitro* disintegration respectively. The formulation FD4 containing 10 mg of cros carmellose shows the disintegration time of 25.33 seconds. Hence the cros carmellose was considered as optimum disintegrant.

Percentage drug content of all the formulations was found to be 97.48 to 108.16 of diclofenac potassium which was within the acceptable limits.

It was observed that in first 10 minutes, only 12.89 % of drug was release from formulation FD5 without using superdisintegrants and while it was 88.56 % in the case of formulation FD2. At the end of 24 minutes only 85.42 % of drug was released from the control tablet formulation FD5 whereas the cumulative release from other formulations FD1 and FD4 at the end of 12 minutes was 89.52% and 79.29% respectively. Thus the release rate of diclofenac potassium fast disintegrating tablet was significantly enhanced by superdisintegrants Indion 214, indion234 and cros carmellose. But the formulation containing Indion 244 does not shows much significant effect in the drug release rate, as it release only 30.44% drug at the end of 12 minutes. By comparing the drug release profile of all formulations FD1 to FD4 , the formulation FD2 containing Indion 214 super disintegrant was considered as best formulation.

The FT-IR study did not show any possibility of interaction

between diclofenac potassium and superdisintegrants used in the fast disintegration tablets.

In the present work an attempt was made to study the disintegrating property of the ion exchange resin Indion 214, Indion 234 and Indion 244. These ion exchange resins are well known and employed as taste masking agent they have not been used as disintegrating agent. The formulations were developed with the aim to develop fast disintegrating tablets of diclofenac potassium. Different formulations of Fast Disintegrating tablets of diclofenac potassium were prepared by direct compression method using Indion 214, Indion234, Indion 244 to study the disintegrating property and Cros carmellose sodium is used as Super disintegrating agent as standard. *In vitro* drug release from the tablets shows significantly improved drug dissolution. The dissolution parameters were consistent with disintegration time of the formulation containing Indion 214 and Indion 234. However the disintegration time value of formulation containing cros carmellose was not correlating with dissolution profiles. The results of *in vitro* disintegration time shows that formulation containing Indion 244, showed the disintegration time of 29.66 seconds , this reveals its superdisintegrant property and it was found to be suitable for preparing fast disintegrating tablets . The Indion 244 was found to have super disintegrant property as compared to Indion 214 and Indion 234 and had acceptable hardness and friability. Hence it could be concluded that the super disintegrant based fast disintegrating tablets of diclofenac potassium would be quite effective, providing quick relif from form pain without need for water for swallowing or administration.

Conflict of interest statement

We declare that we have no conflict of interest.

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References

[1] Uday S Rangole, PS Kawtikwar, DM Sakarkar. Formulation and *In vitro* evaluation of rapidly disintegrating tablets using hydrochlorothiazide as a model drug. *Res J Pharm Tech* 2008;**1**(4):349-352.

[2] Gedam Shweta S, Tapar KK, Borse MD, Ghuge RA. Taste masking and characterization of diphenhydramine hydrochloride by spray drying technique. *Int J Pharma Res Dev* 2010 ;**1**(12):1-7.

[3] Anupama Kalia, Shelly Khurana, Neena Bedi. Formulation and evaluation of mouth dissolving tablets of oxcarbazepine. *Intl J Pharm Pharm Sci* 2009;**1**(Suppl 1):12-23.

[4] Sunita Kumari, Sharad Visht, Pramod Kumar Sharma, Rakesh Kumar Yadav. Fast dissolving drug delivery system. *J Pharm Res* 2010;**3**(6):1444-1449.

[5] Kanakadurga DN, Prameela Rani A, Sai Mrudula B. Formulation and evaluation of oral disintegrating tablets of montelukast sodium: effect of functionality of superdisintegrants. *J Pharm. Res* 2010; **3**(4):803-808.

[6] Gandhi1 CK, Patel1 MR, Patel1 KR, Patel1 NM. A review: Taste masking in pharmaceuticals. *Int J Pharm Res Dev* 2011;**3**(3):19 -26.

[7] Rajnibala, Shailesh S, Neelam S, Ghanshyam DG. Development of non-bitter zolpidem tartrate mouth dissolving tablet. *J Pharm Res* 2009; **2**(9): 1530-1535.

[8] Mukesh P Ratnaparkhi, Mohanta GP, Lokesh U. Review on: Fast dissolving tablet. *J Pharm Res* 2009; **2**(1):5-12.

[9] Margret Chandira R, Venkataeswarlu BS, Kumudhavalli MV, Debjitbhowmik Jayakar B. Formulation and evaluation of mouth dissolving tabletsOf the etoricoxib. *Pak J Pharm Sci* 2010 ;**23**(2):178-181.

[10] Dandag P, Halakatti P, Mastiholimath V, Patil M, Manvi F. Rapidly disintegrating domperidone tablets. *Indian Drugs* 2006; **43**(7): 594-597.

[11] Yunxia B, Sunada H, Yonezawa Y, Danjo K. Evaluation of rapid disintegrating tablets prepared by direct compression method. *Drug Dev Ind Pharm* 2006; **25**:571.