Research Article

Formulation and Evaluation of Fast Dissolving Tablets of Diclofenac Sodium Using PVP

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ABSTRACT

In this research work, we are formulating a batch of tablets using Diclofenac sodium which is used as an NSAID's in the treatment of Arthritis, inflammation and pain. We made different blends of super disintegrants with different ratio in fixed concentration were taken and tablets were formulated and evaluated with a view to optimize a formula and concentration blends of super disintegrants for Fast Disintegrating Tablets (FDT). In this research work three super disintegrants, viz. Cross carmellose, PVP were used. Six blends were prepared and 3 batches of tablets of each formulation code blend were formulated and evaluated for pre-compression parameters like Compressibility, Bulk density, Tapped density and post-compression parameters like Hardness, Weight variation, Disintegration time, Friability. Based on results it revealed that the formulation code blend A3 which had Cross carmellose, PVP in ratio 1:2 (4%w/w) emerged as best blend of super disintegrants for FDT formulation. To optimize the formula of A3 blend, Diclofenac sodium FDT was formulated and evaluated using the concentration blend of A3; three batches were formulated and evaluated for all above parameters and *in-vitro* drug release (pH7.4 phosphate buffer) and disintegration time was found between 34-37 seconds and release was more than 70% in 30 minute. We can conclude that a good FDT can be formulated using the above A3 blend concentration. All formulations are rapidly disintegrated in oral cavity as well as all formulations possess good NSAID's properties.

Keywords: Introduction with characteristics of FDT's, profile of diclofenac sodium, super disintegrants (HPMC, PVP), direct compression method, bioavailability.

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INTRODUCTION

Recent developments in technology have presented viable dosage alternatives for patients specially who may have difficulty swallowing tablets, capsules, liquid dosage forms. However, some patients, particularly pediatric and geriatric patients, who are in their old age, have difficulty swallowing or chewing solid dosage forms [1]. Many pediatric and geriatric patients are not comfortable, unwilling to take these solid preparations due to fear of choking [2]. For example, a very elderly patient may not be able to take or swallow a daily dose of antidepressant.

Solid dosage forms like tablets, capsules are the most popular form among all the other dosage forms and liquids, existing today because of its convenience of compactness, easy manufacturing and self administration. It is difficult to swallow tablets as well as hard gelatin capsules and also when water is not available in the case of motion sickness, allergic attacks of coughing during the common cold and bronchitis. For these reasons tablets which rapidly dissolve or disintegrate in the oral cavity play an important role and are called fast dissolving tablets. These fast dispersible/dissolving tablets disintegrate instantaneously when put on tongue, releasing the drug, which dissolve or disperses within 60 seconds in the saliva in the absence of water. FDTs are not formulated for people who have swallowing difficulties, but also are ideal for active people.

Fast dissolving tablets are also called as mouth dissolving tablets, melt-in-mouth

tablets, orodispersible tablets, rapimelts, porous tablets, quick dissolving tablets etc. some drugs are absorbed from the mouth, and pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly in greater amount than those observed from conventional tablet dosage form. The faster the drug into the solution, quicker the absorption and onset of clinical effect. The use of super disintegrants like cross carmellose, sodium starch glycolate polyvinyl pyrollidone, crosspovidone etc which provide rapid disintegration of tablet and release drug in saliva is the basic approach in development of FDTs. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablet. Patients for whom chewing is difficult and painful can use FDTs easily. Fast dissolving tablets can also be used easily by children who have lost their teeth but do not have full use of their permanent teeth. The various technologies which are used for manufacturing fast- dissolving tablets are as lyophilization also called as freeze-drying, tablet molding, spray-drying, sugar-based excipients, sublimation, tablet compression, disintegration addition and many other patented technologies.

Fast-dissolving tablets (FDDTs) are a perfect fit for all of these patients [3]. Fast-dissolving drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. There are multiple fast-dissolving OTC and Rx products on the market worldwide, most of which have been launched in the past 3 to 4 years. There have also been significant increases in the number of new chemical entities under development using a fast-dissolving drug delivery technology.

Advantages of Fast Dissolving Drug Delivery Systems (FDDT'S) [4]

Fast dissolving technology offers:

1. Ease of administration for those patients who have difficulty in swallowing tablet.
2. No need of water to swallow the dosage form.
3. These tablets are useful for paediatric, geriatric and psychiatric patients.
4. Have acceptable taste masking property.
5. Achieve increased bioavailability through absorption of drugs from mouth, pharynx and oesophagus as saliva passes down.
6. Have a pleasant mouth feel and leave minimal or no residue in the mouth after drug administration.
7. Have rapid dissolution and absorption of the drug which will produce quick onset of action.
8. It combines advantages of solid dosage form in terms of stability and liquid dosage form in term of bioavailability.
9. Cost effective

Characteristics of Fast Dissolving Delivery Systems [4]

1. EASE OF Administrations:

Fast Dissolving Delivery Systems are easy to administer and handle hence, leads to better patient compliance. Usually, elderly people experience difficulty in swallowing the conventional dosage forms (tablets, capsules, solutions and suspensions) because of tremors of extremities and dysphasia. Fast Dissolving Delivery Systems may offer a solution for these problems.

2. Taste of the Medicament:

As most drugs are unpalatable, mouth dissolving delivery systems usually contain the medicament in taste masked form. Delivery systems dissolve or disintegrate in patient's mouth, thus releasing the active ingredients which come in contact with the taste buds and hence, taste masking of the drugs becomes critical to patient compliance.

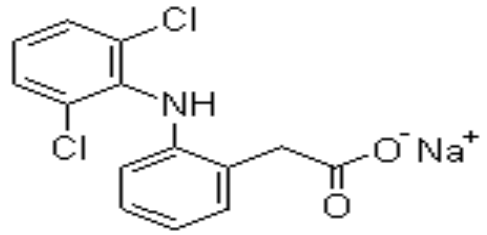
3. Hygroscopicity:

Several fast dissolving dosage forms are hygroscopic and cannot maintain physical Integrity under normal condition from humidity which calls for specialized product packaging.

4. Friability:

In order to allow fast dissolving tablets to dissolve or disperse in the mouth, they are made things either of very porous and moulded matrices or of compressed into tablets with very low compression force, which makes the tablets friable and/ or brittle which are difficult to handle, often requiring specialized peel-off blister packaging. To overcome this problem, some companies introduced more robust forms of FDT's.

PROFILE OF DICLOFENAC SODIUM [21]



Formula	$C_{14}H_{10}Cl_2NNaO_2$
Molecular Mass	318.13
Melting point	284°C (543.2°F)
Bioavailability	49-73%
Protein binding	99.5%
Metabolism	Hepatic
Half life	1.2-2 hrs
Excretion	Billiary

MATERIALS AND METHODS.

MATERIAL USED:

The drug diclofenac sodium which is a (NSAID's), (Sigma Pharmaceutics, Delhi), HPMC (lobachemie Pvt. Ltd.) and other chemicals like crosspovidone, aerosil, talc, mag- stearate was used from institute itself.

OTHER EXCIPIENTS USED IN THE FORMULATION:

Mannitol
Citric Acid
Lactose
Sodium Saccharin
Magnesium Stearate
Menthol

EQUIPMENTS [8]

Dissolution apparatus - Lab India DS - 8000

UV spectrophotometer - Pharma spec - 1700, UV – Spectrophotometer Shimadzu

Hot air oven - SHIVAKI 701

Hardness tester – breaking force tester USP (1217), digital force gauge model EL – 500, capacity – 500 N

Friabilator – Electolab EF-2 Friabilator USP

Punching Machine- Cadmach, 16station punching machine Ahmadabad, India.

METHODS 1

Direct Compression Technique [11]

The vast majority of medicinal agents are rarely so easy to tablet, however in addition the compression of a single substance may produced that do not dissolve or disintegrate. If disintegration is the main problem here, then other components are needed, which intern may interfere with the compressibility of the active ingredient and thus minimize the usefulness of method. Most material posses relatively weak intermolecular attraction or are covered with films of adsorbed gases or tend to hinder compaction. Thus, most large dose do not lend themselves to this process with many other drugs having small doses , uniform blends of the drugs and coarser direct compression diluents cannot be achieved, which ultimately makes this process impractical. However, the uses of compressible diluents with many moderate dose drugs make this process the most streamlined method of tablet manufacture.

Conventional equipment which are easily and commonly available excipients and a limited number of processing steps are involved in the direct compression method. Disintegrant efficiency is strongly affected by tablets size and hardness. Large and hard tablets have disintegration time more than that of it usually required. As a consequence, the product with optimal disintegration properties manufactured often have medium to small size or high friability and low hardness. Disintegrants have major role in disintegration and dissolution of mouth dissolving tablets made by direct compression method. Disintegration efficiency is based on force equivalent concept, which is combined measurement of the swelling force development and high amount of water absorption. The simultaneous presence of disintegrant with high swelling force called disintegrating agent and substance with low swelling agent are claimed to be key factor for rapid disintegration of tablets, which also offer physical resistance.

Method 2:

Preparation of Standard Calibration curve of diclofenac sodium.

Take 100 mg powder of Diclofenac sodium and dissolve in 100 ml of pH 6.8 Phosphate buffer this is stock solution. Pipette out 10 ml from this solution and dilute up to 100 ml using pH 6.8 Phosphate buffer. Now pipette out 1, 2,3,4,5 ml from above solution and dilute up to 10m. Measure the absorbance at 283 nm using UV/Visible spectrophotometer and plot the graph of concentration (microgram / ml) versus absorbance.

Characterization and Evaluation of the Formulation [10]

Pre compression parameter:

The compatibility of the drug and polymers under experimental conditions is important prerequisite before formulations .it is therefore necessary to confirm that the drug does not react with the polymer and excipients under experimental condition and should not affect the shelf life of product. This is confirmed by Fourier Transform Infrared spectroscopy (FTIR).It is a powerful technique for functional group identification of the drug molecules hence the chemical interaction of drug with the other excipients. In the present study, the potassium bromide disc (pellet) of drug and excipients were prepared for prepared for recording the FTIR spectra. The spectra were taken in the transmittance range of 4000-450 cm-1.The pure drug Diclofenac and their formulations were subjected to IR studies.

(ii) Angle of repose:

The frictional force is a loose powder or granules can be measured by the angle of repose Angle of repose is indicative of the flow behavior of the powders, which is very important parameter to have good content uniformity within the developed batches and formulations. Angle of repose is the maximum angle possible between the surface of the pile of powder or granules and the horizontal plane. It is calculated from the following equation

Tan 0 = h/r

0 = 1/tan * (h/r)

Where, 0= angle of repose,

h = height and r = radius

The fixed weight of granules was allowed to flow through the funnel fixed to a stand at definite height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

(iii) Bulk density:

The accurate weighed amounts of granules were taken in 25 ml measuring cylinder. Volume of granule packing was recorded before doing tapping thereafter measuring cylinder containing granule was tapped 100 times on a plane hard wooden surface and tapped volume of packing recorded. Both loose bulk density (LBD) and tapped bulk density (TBD) were calculated by the following formula:

LBD (Loose bulk density) = Mass of Powder/Volume of Packing

TBD (Tapped bulk density) = Mass of Powder/ Tapped Volume of Packing

(iv) Compressibility index:

Percent compressibility of powder mix was determined by Carr's compressibility index calculated by the formula.

Carr's index % =TBD-LBD/TBD*100

Dissolution test for Diclofenac sodium dispersible formulations.

The following procedure was employed throughout the study to determine the in vitro dissolution rate for all the formulations.

Dissolution medium: 900 ml of Phosphate buffer 6.8 for 60 min

Temperature: 37 ± 1ºC

Stirring speed: 100 rpm

Tablet taken: One tablet in each basket

Volume withdrawn: 10 ml every 2 min

Volume made up to: 10 ml

Absorbance: 261 nm

Dilution factor: 10 ml

FORMULATIONS DEVELOPMENT:

Different batches of tablets prepared by direct compression methods .Four different batches of tablets prepared by taking super disintegrant (sodium starch glycolate) concentration of 10,20,30,40 mg ,of each with HPMC and compare with four different batches of tablet prepared by taking another polymer (corn starch)as same as concentration with HPMC. Thus the total eight batches were prepared (different combinations shown in table). Different content were taken accordingly to need (for 20 tablets). Properly weighed amount was mixed together .The mixture triturated mildly. Powder is then subjected to different testing & then after satisfactory result,

RESULT AND DISCUSSION:

The tablets were formed in white colour, odorless, smooth surface with zero defects. Granules powder was evaluated for angle of repose, hardness, friability, compressibility index and drug content. The results of angle of repose indicated good flow properties of the granules. This was further supported by lower compressibility index values.

Table 1: Formulation Table of Diclofenac Tablets

INGREDIENTS	F1	F2	F3	F4
Diclofenac sodium	25.0	25.0	25.0	25.0
Mannitol	30	30	30	30
HPMC	122.7	120.7	120.9	118.3
Lactose	58.0	58.0	58.0	58.0
PVP	7.0	_	3.1	4.4
Citric acid	1.7	1.7	1.7	1.7
Sodium saccharin	6.0	6.0	6.0	6.0
Crosscarmellos sodium	_	9.5	5.72	7.0
Aerosil	3.4	3.4	3.4	3.4
Talc	1.7	1.7	1.7	1.7
Magnesium stearate	2.4	2.4	2.4	2.4
Menthol	2.0	2.0	2.0	2.0

Generally, compressibility index values up to 15% result in good to excellent flow properties. In addition, Bulk density may influence compressibility, dissolution and other properties. The result of angle of repose was found to be in the 24.82. Both formulations showed angle of repose within 30° which indicates good flow of powder mixture. Angle of repose little higher above 30° is indicative of fair flow behavior of powder. The loose bulk density and tapped bulk density for both formulations varied from 0.80 gm/cm3 and 0.98 gm/cm3 respectively. The values obtained lies within the acceptable range and not large differences found between loose bulk density and tapped bulk density. All formulations showed good compressibility hence these tablets can directly compressed.

Table 2: Evaluation of Pre Compression Parameter of Granules Powder

Bulk density (gm/cm3)	Tapped density (gm/cm3)	Bulkiness	Angle of repose	Compressibility index (%)	Swelling index
0.80	0.98	1.21	24.82	24.37	21

The post compression parameter have also evaluated .the friability of all the formulation was found to be less than 1.0%.The result shows resistance to loss of weight indicates the tablets ability to withstand abrasion in handling, packaging and shipment. The disintegration time of tablets was varied 60 to 110.The average weight of the prepared tablet was found 266 to 396 mg. A tablet requires certain amount of hardness to withstand the mechanical shocks in handling packaging and at time of application. The hardness of the tablet varied from 4.2-4.8 kg/cm 2 which have satisfactory strength to withstand the mechanical shocks.

Evaluation parameter of fast dissolving tablet of diclofenac sodium.

(**Table 3**). depicts the physical parameters (hardness, weight variation, thickness, drug content and friability) and drug content of all fabricated tablets.

Table 3: Evaluation of Post Compression Parameters of Tablets

PARAMETER	A 1	A 2	A 3	A 4
Diameter (mm)	9.78	9.23	9.17	9.26
Thickness(mm)	2.56	2.43	2.51	2.48
Wetting time(sec)	28	15	27	24
Wt.variation(mg)	266	266	268	396
Hardness (kg/cm2)	4.4	4.8	5.3	4.8
Friability (%)	0.88	0.76	0.82	0.79
Disintegration time (sec)	68	34	54	43
Drug content	198.2	197.4	198.6	198.2

(**Table 4**) reflects the cumulative release studies data of these tablets. All the tablet formulation showed acceptable pharmaco-technical properties and complied with pharmacopoeial specification for weight variation, drug content (%), friability, disintegration and uniformity of dispersion (UOD). Hardness was maintained to be within 4.48 kg/cm2 to 4.63 kg/cm2. Since fast disintegrating tablets are less hard then conventional ones, which is due to the lower compression employed (Hardness is usually 3KPa.), these tablets can therefore be fragile and need individual packaging. The lower standard deviation values indicated that the hardness of all the formulations were almost uniform in specific method and possess good mechanical strength along with sufficient hardness.

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To obviate the difference in the hardness super disintegrants are added in the formulations. In fact, a fast disaggregating tablet must disintegrate in the saliva; harder tablets need a de-aggregating agent of a superior ability. In this case Ac-Di-sol and polyplastadone XL were employed. Tablet disintegration was affected by the wicking and swelling of the disintegrant, and the wicking property would be closely related to the porosity. Both the porosity and average pore size of tablets in all formulation decreased with increase of the tablet hardness.

The wicking property may also correlate to the wetting behaviour of the tablet. Rapid dispersion within seconds has been observed in all the formulations. On the basis of the de-aggregation time of the tablets, according to the EP IV Ed. almost all the formulations developed can be defined "Fast dispersible" the limit for de-aggregation is in fact suggested as within 3 min. These direct compressed (FDT's) tablets consumes less wetting time and all formulation passes test for dispersion.

All formulated dispersible tablets gave faster and rapid dissolution of Diclofenac. The results are reported in (**Table 3**) and formulations follow zero order release kinetics. The graphs were plotted as time Vs percentage (**Figure 1**) drug release for all the formulations. We have made a Standard calibration curve of Diclofenac sodium to which the R^2 value is found to be 0.991.

The % Drug release has been shown in fig 1 due to which it is showing different formulations in cylinders type chart format in which F4 shows the highest release profile as per the readings. Thus we can concluded that Diclofenac sodium shows the best formulations of Fast dissolving tablets to increase the bioavailability by using the different Super disintegration like PVP, Crosscarmellos etc. Thus, the different formulating parameters are discussed here after.

CONCLUSION

Besides delivering drug to the body, a drug delivery system aim to improve patient compliance and convenience, and fast dissolving tablets are no exception. The introduction of fast dissolving dosage forms has solved some of the problems encountered in administration of drugs to the pediatric and elderly patient, which constitutes a large proportion of the world's population. Hence, patient demand and the availability of various technologies have increased the market share of Fast dissolving tablets, which in turn prolongs the patent life of a drug. Keeping in view of the advantages of the delivery system, rapidly disintegrating dosage forms have been successfully commercialized, and because of increased patient demand, these dosage forms are expected to become more popular.

The fast disintegrating tablets of diclofenac sodium was found to be formulated by the

use of super disintegrants like cross carmellose and PVP .The use of this two super disintegrants at concentration of 3.7 and 2.7 % respectively was found to be the best formulation of Fast disintegrating tablets of diclofenac sodium.

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Table 4: Cumulative release studies of diclofenac tablets

Time	Cumulative release		
	F 1	F 2	F 3
0	0	0	0
5	29.2	32.8	36.7
10	49.3	53.1	61.4
15	65.2	71.4	75.2
20	78.6	79.8	86.5
25	85.9	87.1	90.2
30	92.3	93.5	94.8

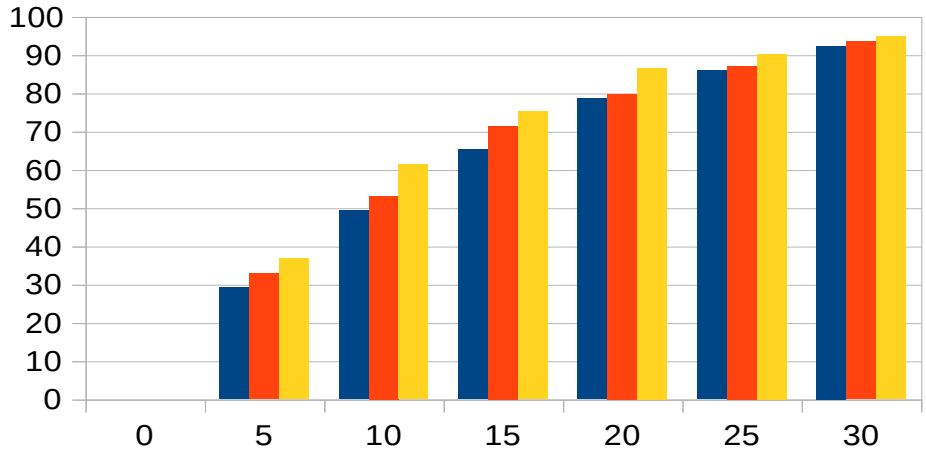

Figure 1: Cumulative release studies of diclofenac tablets

Table 5: The absorbance data for standard curve

Concentration (microgram/ml)	Absorbance
10	0.34
20	0.6
30	1.1
40	1.55
50	1.99

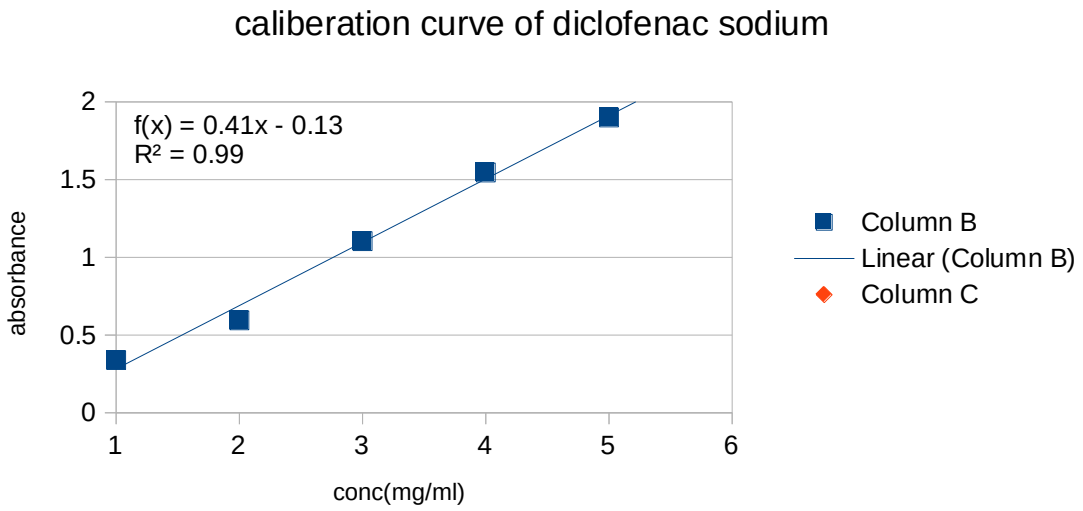

Figure 2: The absorbance data for standard curve

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