Research Article

In Vitro Evaluation of Three Different Tablet Formulations of Diclofenac

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ABSTRACT

The objective of the study was to perform the in vitro evaluation tests of three chemically equivalent tablet formulations of diclofenac sodium. The study was made by conducting study of quality control parameters like weight variation, friability (roche friabilator), hardness (monsanto hardness tester), disintegration and dissolution (paddle type) on enteric coated, film coated and dispersible tablet form of diclofenac sodium. All the formulation complied with the official specifications for uniformity of weight, disintegration and dissolution tests.

Keywords: Diclofenac, enteric, film, dispersible.

INTRODUCTION

Pharmaceuticals play an important role in improving human health and promoting well- being. However, to produce the desired effect, they have to be safe, efficacious and of acceptable quality, and have to be used rationally. The use of ineffective and poor quality drugs will endanger therapeutic treatment and may lead to treatment failures. Thus, the production, storage, and distribution of drugs in each country need to be regulated by the government drug regulatory authority. . Quality assessment studies on some of the marketed drug products could give an insight into the quality of the pharmaceutical products marketed within the distribution chain and Consumed[1]. The focus of this research is to conduct all the in process quality tests of three chemically equivalent tablet formulations of diclofenac sodium[2]. Diclofenac sodium, 2-[2,6-dichlorophenyl)-amino] benzene acetic acid monosodium salt, is a nonsteroidal anti-inflammatory drug with potent activity[3]. Diclofenac is used to relieve pain, tenderness, swelling, and stiffness caused by osteoarthritis (arthritis caused by a breakdown of the lining of the joints), rheumatoid arthritis (arthritis caused by swelling of the lining of the joints), and ankylosing spondylitis (arthritis that mainly affects the spine)[4-8]. Diclofenac immediate-release (short-acting) tablets are also used to treat painful menstrual periods and pain from other causes[9]. This phenyl acetic acid derivative acts as an inhibitor of hyaluronidase, prostaglandins synthesis and platelet aggregation[10-11]. Diclofenac is presented as tablets (enteric coated, controlled release), creams and injectables. As long-term use of diclofenac and similar NSAIDs predisposes for peptic ulcer[12].

Materials

Diclofenac sodium (50 mg) of three different formulations such as film coated, enteric coated and dispersible was purchased. The products were coded as A, B, and C. The study was performed within product expiration dates. The reagents used were Potassium dihydrogen phosphate, sodium dihydrogen phosphate, perhydrochloric acid, acetic anhydride, perchloric acid, and freshly distilled water. All solvents and reagents used were of analytical grade.

Methods

Uniformity of Weight

Sample tablets (20) of each brand were weighed together and average weight was

determined. Each tablet was weighed individually on mettler toledo analytical balance and the percentage (%) deviation was determined[13].

HardnessTest

Sample tablets (10) of each brand were taken, a tablet was placed between the spindle of the Erwerka hardness tester machine and pressure was applied by turning the knurled knot just sufficiently to hold the tablet in position. The pressure was then increased as uniformly as possible until the tablet breaks and the pressure required to break the tablet was then read off the machine and recorded[14].

Friability Test

Sample tablets (10) of each formulation were taken and weighed, these tablet were then put in the automated Roche Friabilator and this test for the tendency to crumble by allowing it to roll and fall within the rotating apparatus, after 100 revolutions the tablets were weighed and recorded[15]. The friability of the tablets were then calculated using the following expression

% Friability = [(Initial weight – Final weight)/Initial weight]×100

Disintegration Test

Six film coated and six enteric coated tablets were taken in separate basket racks, which were positioned in a 1litre beaker of 0.1NHCl for 2 hr. (simulated gastric fluid) at 37°C+ 2°C without disks. Then same tablets were put in 1litre beaker of pH 7.8 phosphate buffer with disks and operated for 2hr. and 15 minutes**.** The disintegration time was taken to be the time no granule of any tablet was left on the mesh[16].

Dissolution studies[17]

Preparation of standard solutions

A stock solution was prepared using an analytical balance (1mg/ml) that is 100 mg of pure diclofenac was dissolved in 1000ml of phosphate buffer pH 6.8. Different working standard namely 5µg/ml , 10 µg/ml, 15 µg/ml, 20µg/ml and 25µg/ml was prepared by appropriate dilutions. Absorbance of those solutions at the λ max 283 nm was measured.

Sample A-(film coated)

Dissolution studies on film coated tablets of diclofenac sodium were conducted using Apparatus I (paddle method). The dissolution medium was 900 mL of pH 1 hydrochloric acid aqueous solution, or pH 6.8 phosphate buffer at 37 ± 0.5 ˚C and stirred at 50 rpm. The dissolution test was performed after maintaining conditions. In the experiments, 5 ml sample aliquots were withdrawn at 5, 10, 15, 20, 25 and 30 minutes and replaced with an equal volume of the fresh medium to maintain a constant total volume. Samples were assayed by the previously mentioned spectrophotometric method. Cumulative percentages of the drug dissolved from the products were calculated and plotted vs. time.

Sample B-(enteric coated)

Initially the tablet was kept in 0.1N HCl for 2 hr. After 2 hours, the tablet was transferred to pH 6.8 phosphate buffer medium and the dissolution was carried out for 45minutes at 50 rpm and the samples were withdrawn at 5 minutes intervals. Bath volume was maintained at 900 ml. The absorbance of each sample was observed in UV Visible spectrophotometer at 283 nm against blank reagent. Cumulative percentages of the drug dissolved from the products were calculated and plotted vs. time.

Sample C-(dispersible)

For the dissolution of dispersible tablet USP Apparatus 2 is used. Simple distilled water is taken as dissolution medium at 37 ± 0.5 o C and stirred at 50 rpm. In the experiment, 5 ml of sample were withdrawn at 1,2,3,4 and 5 minutes and replaced with equal amount of dissolution media the samples were assayed by U.V. spectrophotometer and Cumulative percentages of the drug dissolved from the products were calculated and plotted vs. Time.

RESULTS AND DISCUSSIONS

Three different formulations of diclofenac tablets were subjected to a number of pharmacopoeial tests in order to assess

their biopharmaceutical equivalence. The assessments involved the evaluation of uniformity of weight, friability, hardness, disintegration and dissolution tests as well as chemical content determination. The uniformity of weight determination for all the formulations gave values that complied with official book specifications for weight uniformity as none of the formulations deviated by up to ±5% from the mean value (Table 1). For A upper and lower limit is found to be 0.22 and 0.19, for B 0.23 and 0.19 and for C 0.30 and 0.27 respectively (Table 2).

The result of tablet friability test showed that all formulations (A, B and C) tested had impressive friability values ranging from 0.01% to 0.1%w/w. According to Indian Pharmacopoeia, no batch should have a friability value greater than 1.0%w/w.

Crushing strength test shows the ability of tablets to withstand pressure or stress during handling, packaging and transportation. It is a property of a tablet that is measured to assess its resistance to permanent deformation. The hardness of sample A and B is found to be same i.e.5.4, and 3.5 for sample C (Table 3).

Disintegration is a crucial step in release of drugs from immediate release dosage forms. The rate of disintegration is directly proportional to the rate of dissolution. The rate of disintegration is influenced by the rate of influx of water into the tablets, which is also dependent on the porosity of the tablets. The disintegration time of samples A, B and C was found to be 3min, 40min and 30 sec respectively. The results showed that all the formulations passed the disintegration test according to Indian pharmacopeia (IP 2007) (Table 4).

According to the monographs in Indian Pharmacopoeia, for each of the tablets tested for dissolution, the amount of active ingredient in solution is not less than 70% of the prescribed or stated amount. The results obtained from the study revealed that all the formulation passed the IP general specifications standard for dissolution rate test for film, enteric coated and for dispersible tablets (Table5-8). The percentage drug release for sample A, B and C was found to be 93, 91 and 98.47 respectively. The results obtained from the assessment of the percentage content of active ingredient in the three formulations of diclofenac tablets showed that all formulations gave values within the monograph specifications (90-105%).

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Table 1: Weights of tablets of all formulations of Diclofenac

Sl. No.	Wt. Of A (g)	Wt. Of B(g)	Wt. Of C(g)
1.	0.20	0.22	0.29
2.	0.21	0.22	0.30
3.	0.20	0.21	0.30
4.	0.21	0.21	0.30
5.	0.20	0.22	0.29
6.	0.21	0.22	0.29
7.	0.21	0.21	0.30
8.	0.22	0.21	0.29
9.	0.22	0.22	0.29
10.	0.21	0.22	0.29
11.	0.20	0.22	0.29
12.	0.22	0.21	0.29
13.	0.21	0.21	0.30
14.	0.22	0.22	0.29
15.	0.21	0.21	0.29
16.	0.22	0.22	0.30
17.	0.21	0.20	0.29
18.	0.21	0.22	0.30
19.	0.21	0.22	0.30
20.	0.21	0.21	0.28
Total wt. (g)	4.21	4.30	5.87
Average wt.(mg)	210.5	215.0	293.5

Table 2: Weight variation of all formulation of Diclofenac

Tablet sample	Percentage weight variation limit	Upper limit (g)	Lower limit (g)
A	7.5	0.22	0.19
B	7.5	0.23	0.19
C	5	0.30	0.27

Table 3: Hardness of all formulations of Diclofenac tablets

S. No.	A(kg/cm)	B(kg/cm)	C(kg/cm)
1.	5.5	6.5	3.5
2.	6.0	6.0	3.0
3.	5.5	5.0	4.0
4.	4.5	4.5	3.5
5.	5.5	5.0	3.5
Total	27	27	17.5
Average.	5.4	5.4	3.5

Table 4: Disintegration test of all formulations of Diclofenac tablets

Sample	Temperature	Rotation per minute	Disintegration time
A	36.5-37.5^{0}C	28-32 rpm	3minutes.
B	36.5-37.5^{0}C	28-32 rpm	40minutes.
C	36.5-37.5^{0}C	28-32 rpm	30 seconds.

Table 5: Standard curve of Diclofenac

Concentration	Absorbance
5	0.2142
10	0.4321
15	0.6231
20	0.8184
25	0.9874

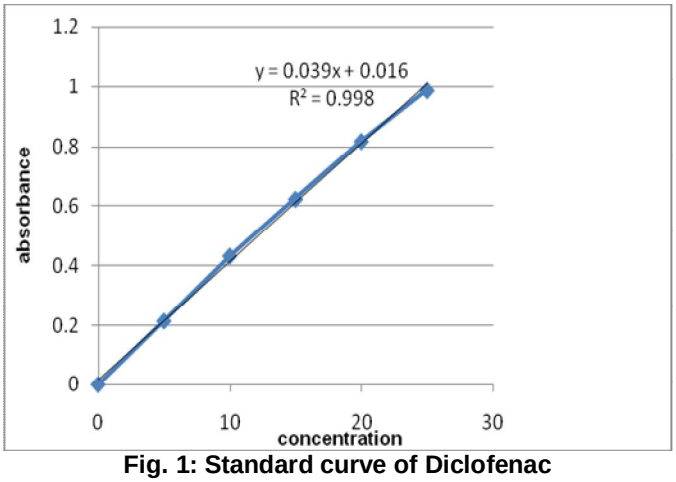

Fig. 1: Standard curve of Diclofenac

For A

Table 6: Observation data of dissolution rate of sample A

S. No.	Time (min)	absorbance	Conc. Of drug per ml(x) (x=y-c/m)	Conc. Of drug per 900ml (x*9)	% drug release ((x*9)/50*100)
1.	0	0	0	0	0
2.	5	0.0611	0.8639	7.7758	15.537
3.	10	0.1140	2.4486	22.0347	44.0694
4.	15	0.1336	2.9420	26.4780	52.956
5.	20	0.1936	4.4534	40.0806	80.1612
6.	25	0.2230	5.1939	46.7455	93.0000

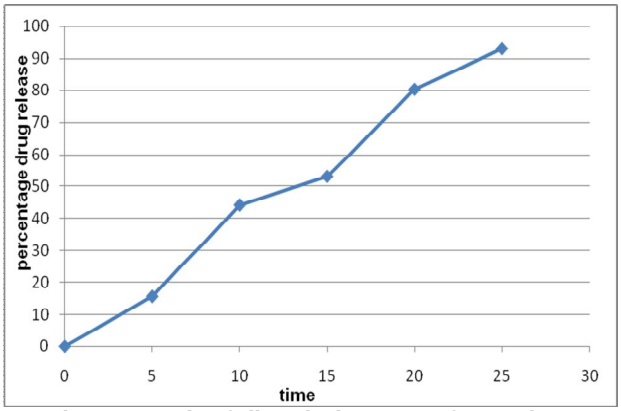

Fig. 2: Graph of dissolution rate of sample A

For B

Table 7: Observation data of dissolution rate of sample B

S. No.	Time (min)	absorbance	Conc. Of drug per ml(x) (x=y-c/m)	Conc. Of drug per 900ml (x*9)	% drug release ((x*9)/50*100)
1.	0	0	0	0	0
2.	5	0.0781	1.5440	13.8967	27.79
3.	10	0.1238	2.6952	24.2568	48.5136
4.	15	0.1434	3.1889	28.7002	57.4004
5.	20	0.1986	4.4534	41.2141	82.42
6.	25	0.2186	5.0831	45.7481	91.00

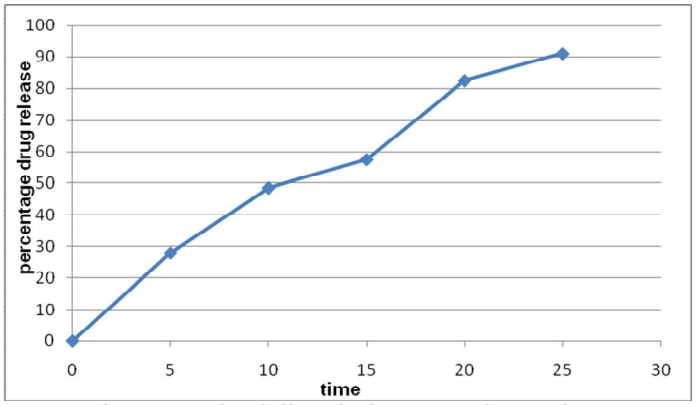

Fig 3: Graph of dissolution rate of sample B

For C

Table 8: Observation data of dissolution rate of sample C

S. No.	Time (min)	absorbance	Conc. Of drug per ml(x) (x=y-c/m)	Conc. Of drug per 900ml (x*9)	% drug release ((x*9)/50*100)
1.	0	0	0	0	0
2.	1	0.1082	2.3022	20.7204	41.4408
3.	2	0.1454	3.2392	29.1536	58.3073
4.	3	0.1684	3.8186	34.3677	68.7355
5.	4	0.2102	4.8715	43.8438	87.6876
6.	5	0.1340	5.4710	49.239	98.47

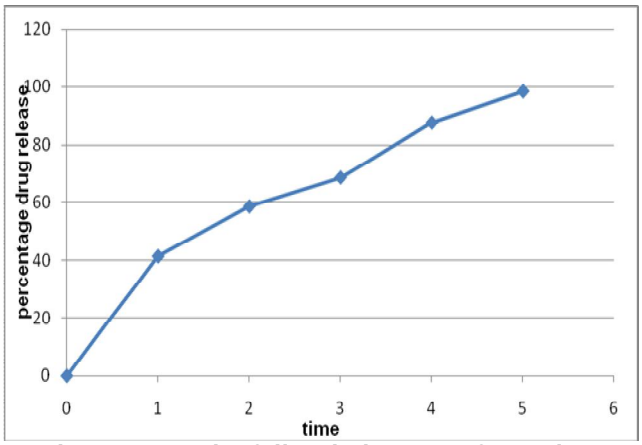

Figure 4: Graph of dissolution rate of sample C

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