# Release Rate of Diclofenac Sodium from Different Polymers

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**Diclofenac sodium (DS) tablets were formulated employing different polymers such as cellulose acetate (5% and 10%) eudragit RS 100 (10 and 20%) in different concentrations. These formulations were evaluated for thickness, hardness, friability, weight variation, drug content uniformity and *in vitro* dissolution rate testing. The *in vitro* dissolution rate studies of DS from different polymers were compared with marketed formulations. The drug release pattern of these DS tablets was slow compared to commercial brands.**

Diclofenac sodium (DS), chemically sodium [o-(2,6-dichlorophenyl)amino] phenyl acetate, is a non-steroidal antiinflammatory analgesic drug (NSAID). It is widely used in painful and inflammatory rheumatic and non-rheumatic conditions. It possesses analgesic, antipyretic and antiinflammatory activities. Tablets and injections of DS are available commercially. In this study, DS tablets were formulated using different polymers and their drug release pattern were evaluated and compared with those of marketed products.

DS was obtained from Sumac Pharma, Hyderabad and cellulose acetate was procured from FMC Inc., New York, USA. Eudragit RS 100 was obtained from Dr. Reddy's Laboratories, Hyderabad and diclacium phosphate was obtained from Acto Laboratories, Warangal. Microcrystalline cellulose was obtained from APT Labs, Guntur and other materials used in tablet formulations were of pharmacopoeial grade and obtained from commercial sources. Ultraviolet spectral measurements were preformed on a Shimadzu UV double beam spectrophotometer. A USP XXI dissolution apparatus of Campbell Electronics was used for dissolution studies. Tablet punching was done using a single punch tablet machine (Cadmach, Ahmedabad).

Hardness testing was carried out using a Monsanto hardness tester, friability was tested using a Roche friabilator and drying was achieved using a fluidized bed dryer.

Wet granulation process was adopted to prepare DS matrix tablets[1-5]. Accurately weighed quantity of DS was mixed with required quantity of either dicalcium phosphate or microcrystalline cellulose in a mortar. To this, sufficient quantity of a binder either cellulose acetate (10%) in acetone or Eudragit RS 100 (10 and 20%) in isopropyl alcohol/acetone (6:4) mixture was added and mixed thoroughly. The wet mass was passed through # 16 mesh sieve. Later the granules were dried in a fluidized bed dryer at minimum flow capacity and 50-60° inlet temperature. The granules were lubricated with 10% talc and 1% magnesium stearate. The granules were compressed into tablets on a single punch tablet machine using 9 mm diameter punches. Eight different formulations were prepared using formulae as listed in Table 1. Drug content of the tablets were determined spectrophotometerically at 276 nm[6].

Thickness and diameter of tablets was measured using a Vernier Caliperse. Friability was related to tablet's ability to with stand both shock and abrasion during the process of manufacture, packing, transport and consumer use. The apparatus used was a Roche Friabilator. A loss of less than 0.5 to 1% in weight is acceptable. Average weight of a tablet was calculated by weighing ten tablets individually and all together. Percentage weight deviation of each tablet was determined as per official method[7]. IP official limit of percentage deviation for 150-300 mg tablet is±7.5%.

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TABLE 1 : FORMULAE OF DICLOFENAC SODIUM TABLETS

| Ingredients (g) | 5% Cellulose Acetate | | 10% Cellulose Acetate | | 10% ERS 100 | | 20% ERS 100 | |
|---|---|---|---|---|---|---|---|---|
| | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ | $F_7$ | $F_8$ |
| Diclofenac sodium | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| Dicalcium phosphate | 170 | - | 170 | - | 170 | - | 170 | - |
| Microcrystalline cellulose | - | 170 | - | 170 | - | 170 | - | 170 |
| Talc | 28 | 28 | 28 | 28 | 28 | 28 | 28 | 28 |
| Magnesium stearate | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |

$F_1$-$F_8$ are various formulations of diclofenac sodium matrix tablets. In each formulation 100 mg diclofenac sodium was taken. Dicalcium phosphate or microcrystalline cellulose (170 mg) was mixed with 28 mg of talk and 2 mg of magnesium stearate.

To determine uniformity of drug content, 5 tablets were taken in each formulation and powdered in mortar. About 300 mg of powder representing 100 mg of drug was taken into a 100 ml volumetric flask and dissolved in methanol (30 ml) for about 30-45 min. The final volume was made up to 100 ml using phosphate buffer pH 7.4 From this, 1 ml was taken and diluted upto 100 ml with phosphate buffer. The absorbance of this solution was measured at 276 nm against blank spectrophotometrically. The results are shown in Table 2.

Release of DS from various tablet formulations was studied employing USP XXI dissolution rate test apparatus (Campbell Electronics). The assembly consists of the following. A 100 ml cylindrical vessel with hemispherical bottom made of glass; a variable speed drive and a cylindrical basket. The vessel is immersed in a water bath maintaining the temperature at 37±1° during the test and keeping the bath fluid in constant, smooth motion. Its sides are flagged near the top. A fitted cover is used to retard evaporation of fluids. The distance between the

TABLE 2 : EVALUATION DATA OF DICLOFENAC SODIUM TABLETS

| Formulation | Thickness (mm) | Diameter (mm) | Hardness ($kg/cm^2$) | Friability | Weight variation Average | Weight variation % deviation | Drug Content |
|---|---|---|---|---|---|---|---|
| $F_1$ | 3.2 | 9 | 4-7 | 0.5-1% | 301.8 | ±3.84 | 92.08 |
| $F_2$ | 3.2 | 9 | 4-7 | 0.5-1% | 307.3 | ±4.48 | 91.46 |
| $F_3$ | 3.2 | 9 | 4-7 | 0.5-1% | 301.3 | ±4.49 | 93.86 |
| $F_4$ | 3.2 | 9 | 4-7 | 0.5-1% | 299.7 | ±4.32 | 93.50 |
| $F_5$ | 3.2 | 9 | 4-7 | 0.5-1% | 301.6 | ±4.47 | 93.68 |
| $F_6$ | 3.2 | 9 | 4-7 | 0.5-1% | 300.2 | ±3.81 | 91.20 |
| $F_7$ | 3.2 | 9 | 4-7 | 0.5-1% | 302.1 | ±4.71 | 92.53 |
| $F_8$ | 3.2 | 9 | 4-7 | 0.5-1% | 300.7 | ±3.97 | 90.66 |

$F_1$-$F_8$ are various formulations of diclofenac sodium matrix tablets. For each formulation, the thickness was found to be 3.2 mm, diameter 9 mm, hardness 4-7 $kg/cm^2$ and friability was 0.5-1%. Weight variation and drug content were different in each formulation.

TABLE 3 : RELEASE RATE OF DICLOFENAC SODIUM FROM VARIOUS FORMULATIONS

| Time | Cumulative amount of drug release in mg | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| (hr) | $F_1$ | $F_2$ | $F_3$ | $F_4$ | $F_5$ | $F_6$ | $F_7$ | $F_8$ | M |
| 0.5 | 19.20 | 11.46 | 13.33 | 7.46 | 23.46 | 17.06 | 14.40 | 8.80 | 19.32 |
| 1 | 29.06 | 23.73 | 17.60 | 13.86 | 38.93 | 25.33 | 22.13 | 16.80 | 33.33 |
| 2 | 37.33 | 27.20 | 26.66 | 21.86 | 49.06 | 33.33 | 28.80 | 21.86 | 38.37 |
| 3 | 46.40 | 29.86 | 29.06 | 27.73 | 56.00 | 39.73 | 29.86 | 28.83 | 42.57 |
| 4 | 49.33 | 39.73 | 34.93 | 31.73 | 62.40 | 47.20 | 32.80 | 31.20 | 48.74 |
| 5 | 55.46 | 45.86 | 38.40 | 34.40 | 65.60 | 51.73 | 37.60 | 35.46 | 60.78 |
| 6 | 58.13 | 51.73 | 40.80 | 38.66 | 67.73 | 55.20 | 40.26 | 37.33 | 66.66 |
| 7 | 62.40 | 56.26 | 44.53 | 40.53 | 69.06 | 57.86 | 42.40 | 40.26 | 71.70 |
| 8 | 64.26 | 59.73 | 49.60 | 42.13 | 71.46 | 61.33 | 45.60 | 42.66 | 75.91 |
| 9 | 74.93 | 72.53 | 60.26 | 44.00 | 74.46 | 68.00 | 54.40 | 44.53 | 83.20 |
| 10 | 77.33 | 74.66 | 64.26 | 49.00 | 76.53 | 70.13 | 60.26 | 49.33 | 88.51 |
| 11 | 80.26 | 78.13 | 67.20 | 50.40 | 79.46 | 72.53 | 64.00 | 51.20 | 94.40 |
| 12 | 82.66 | 80.53 | 70.66 | 53.06 | 82.66 | 76.53 | 66.40 | 53.86 | 98.88 |

*In vitro* dissolution studies were carried out for 12 h to study the drug release profiles of the prepared matrix tablets. In all formulations, the drug release was slow when compared to market product (M).

inside bottom of the vessel and the basket was maintained at 2.5±0.26 cm during the test. The tablets of each formulation was subjected to dissolution testing using rotating basket apparatus used with a speed of 50 rpm in 900 ml of distilled water as dissolution fluid. One tablet was used in each test. A temperature of 37±1° was maintained through out the experiment.

Dissolution study was carried out for a period of 12 h in distilled water. Samples of 5 ml were taken at 30 min, 1 h and for the following period of 12 h at 1 h intervals. After collecting each sample, the dissolution medium was replenished with the same volume of fresh distilled water. The samples were suitably diluted and analyzed for diclofenac content spectrophotometrically at 276 nm. Drug released at various intervals of time was shown in Table 3.

It was observed that the tablet prepared have smooth surface and uniform physical characteristics like hardness, friability and weight variation. The drug content in the matrix tablets was found to be quite uniform in all formulations. Sustained release of the drug could be achieved over a period of 12 h. An average of about 80-85% of the drug was released during this period. DCP (diluent) enhanced the rate of drug release when compared to microcrystalline cellulose. The drug release was appreciably retarded when cellulose acetate and Eudragit RS 100 were used as binders in different concentrations. The concentration of the binder was found to be directly related to the percentage of drug release. The release was faster with cellulose acetate when compared with Eudragit RS 100.

The drug release pattern of these sustained release tablets were found to be better than those of commercial brands. An overview of the above results suggests that in formulations $F_7$ and $F_8$ maximum retardation in drug release was observed. This may be due to high concentration of binder used (20% Eudragit RS 100). Formulations $F_4$, $F_5$ and $F_6$ gave good drug dissolution profiles and were effective in sustaining the release rate by maintaining the drug concentration within the therapeutic range up to 12 h. The drug release pattern from these formulations was found to be better and well controlled when compared to the commercial brands.

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# Spectrophotometric Method for the Determination of Nimodipine in Pharmaceutical Dosage Forms

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**A simple and sensitive spectrophotometric method for the determination of nimodipine in bulk and pharmaceutical dosage forms is described. The method is based on diazotisation of reduced nimodipine with nitrous acid followed by its coupling with α-naphthylamine to form a pink colored chromogen with an absorption maximum of 550 nm. The color obeyed Beer's law in the concentration range of 2-12 μg/ml.**

Nimodipine[1,2] is chemically 1,4-dihydro-3,6-dimethyl-4-(3-nitrophenyl)-3,5-pyridine dicarboxylic acid 2-methoxyethyl-1-methylethylester. It is relatively a new antianginal drug. It is not yet official in any pharmacopoeia. Survey of literature reveals that nimodipine is estimated in pharmaceuticals and in biological fluids by spectrophotometry[3-6], GC[7], HPLC[8-11], HPTLC[11] and polarography[12]. In the present work a simple and sensitive spectrophotometric method was developed for the determination of nimodipine after converting it to its reduced form by zinc dust and hydrochloric acid. The presence of primary aromatic amino group in reduced nimodipine enable the use of diazocoupling reaction with α-naphthylamine. Spectrophotometric parameters are established for standardization of the method including statistical analysis of the data. This method has been successfully extended for the analysis of nimodipine in the pharmaceutical preparations.

An ELICO UV-VIS spectrophotometer model SL-150 with 1 cm matched quartz cells was used for all absorbance measurements. All the chemicals used were of AnalaR grade. Aqueous solutions of hydrochloric acid (5 N), sodium nitrite (0.1% w/v), ammonium sulphamate

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