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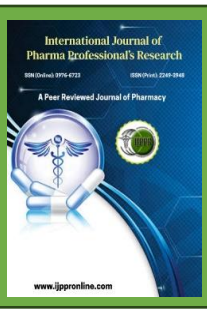

In-Vitro Dissolution Study and Assay of Diclofenac Sodium

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ABSTRACT

This study aims to determine the potency of drug available in our market in Diclofenac Sodium is a potent Non-Steroidal Anti-Inflammatory Drug (NSAID) and that are widely used and it is an Over the Counter (OTC) drug in India. Potency determination was performed to evaluate that the marketed sample comply with the declared specification or not. In vitro Dissolution study was performed to see that if potency is high but the drug is not bioavailable. Hardness is also checked to see that whether it interfere with the dissolution which ultimately effect the bioavailability. In this present study a simple, cost effective and spectrophotometric method for the potency determination of marketed Diclofenac Sodium tablets is used. Four samples were randomly collected from the market and coded as M1, M2, M3 and M4 and the potency determined are 99.30%, 103.38%, 98.22% and 102.16% respectively. Hardness and in vitro dissolution of the above four brands of Diclofenac Sodium tablets were also studied and reported in the paper. After 1 h Dissolution release of M1, M2, M3 and M4 are 94.16%, 93.97%, 96.94% and 98.5% respectively. From all of the studies it seems that the samples were collected complies with the BP and USP requirements.

Keywords: *Invitro; NSAID; Diclofenac sodium*

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1. Introduction

Diclofenac Sodium is sodium salt of [o-(2, 6-dichloro aniline) phenyl] acetate and is a potent Non-Steroidal Anti-Inflammatory Drug (NSAID).[1] DS or sodium 2-[(2,6-

dichlorophenyl)amino]phenyl- acetate, is a broadly used non-steroidal anti-inflammatory drug for the treatment of inflammatory conditions such as rheumatoid arthritis, osteoarthritis and ankylosingspondylitis.[2] NSAIDs are agents having anti-inflammatory, analgesic and antipyretic effects. These drugs are used frequently and commonly in humans as well as in animals to manage pain, fever and inflammation for the treatment of different clinical conditions such as rheumatic disorders, musculoskeletal disorders, sports injuries, muscular cramps and other syndromes involving pain and inflammation. Its pharmacological effects are believed to be due to blocking the conversion of arachidonic acid to prostaglandins by inhibiting cyclo-oxygenase enzymes. Diclofenac Sodium is almost completely absorbed after oral administration. However, due to its first pass metabolism, only about 50% of the absorbed dose is systematically available. The half-life of Diclofenac Sodium in plasma varies from1-3h,with mean peak plasma levels of approximately 0.5µg/ml and 1.0µg/ml occurring after about 2 h after a single dose of 25 mg and 50 mg of enteric coated tablets respectively. About 99% of the drug is bound to human plasma proteins, mainly albumin.[3] It is 99% bound to human serum proteins. It diffuses into and out of synovial fluid. It is eliminated through urinary and biliary excretion of the glucuronide and the sulphate conjugates of the metabolite. Diclofenac Sodium has littleanti-microbial activity and is under investigation for the treatment of tuberculosis. This is also used to treat chronic pain associated with cancer. It may prevent the development of Alzheimer disease if given daily in small doses for many years. Diclofenac Sodium also acts asanti- uricosuric agent. Dosage form testing, development of the improved dosage form and determination of drug in biological samples is required in pharmaceutical industry and research.[4] It is available in the various formulations such as injections, tablets, gel, suppositories and powdered form (Figure 1).[5-6]

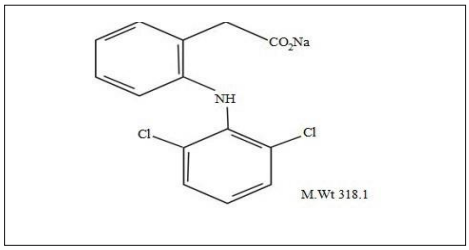

Figure 1: Diclofenac Sodium

Diclofenac Sodium is not recommended for children less than 18 months of age, and only when essential in pregnant or lactating women.[7] Solid dosage form like as Tablet is the most popular dosage form existing today because of its convenience of self-administration, compactness and easy manufacturing; sometimes immediate onset of action. Patient compliance, high-precision dosing, and manufacturing efficiency make tablets the solid dosage form of choice.[8] Diclofenac Sodium that is effective in the management of mild-to moderate postoperative pain. Their opioid sparing effect and availability in parenteral forms make them idea lf or day- only and short-stay admissions for elective surgery.[9-12] The rational for their use is that they produce inhibition of peripheral

hyperalgesia mediated by their anti- inflammatory properties.[13]

2. Materials and Methods

All chemicals and reagents were used for potency studies were of analytical grade. Standard Diclofenac Sodium sample (assay 99.54%) was given from Drug International Limited as a gift.

Collection of Samples: Four brands of marketed Diclofenac Sodium tablets were obtained from various drug stores. Samples were properly checked for their, Manufacturer name, Physical appearance, and Batch number, Date of manufacturing and Expiry date before purchasing.14 They were randomly coded, such as M1, M2, M3 and M4. The labeled active ingredient of Diclofenac Sodium was 50mg and packaged in strip or blister.

2.1 Equipment's used

A double beam Shimadzu UV-visible spectrometer (UV mini- 1700, Shimadzu Corporation, Kyoto, Japan with 1 cm quartz cells), HANNAHI2211 PH meter(Romania), Automated eight basket tablet dissolution tester UDP-80 USP Standard (Veego, India), Electronic balance AL204(Mettler Toledo, Japan), Hot air oven Labtech (Daihan, Korea) and Hardness Tester (Veego, India).

2.2 Preparation of standard solution of diclofenac sodium

10mg of Standard Diclofenac Sodium powder (99.54%pure) was dissolved in5ml of Milli-Q water in a 10ml volumetric flask then add volume upto mark with Milli-Q water. Then 1 ml of this solution was diluted to 50 ml by adding Milli-Q water. The concentration of this solution was 20 µg/ml.

2.3 Determination of λ*max*

The above solution was scanned in the SHIMADZU UV Spectrophotometer, model 1700 from 200 to 400 nm using Milli-Q water as blank and λ*max*was determined.

2.4 Preparation of calibration curve of diclofenac sodium

0.5 ml, 1 ml, 1.5 ml, 2.0 ml 2.5 ml, and 3.0 ml was taken from standard stock solution and diluted upto50ml by adding Milli-Qwater, the final concentration of these solution were 10 µg/ml, 20 µg/ml, 30 µg/ml, 40µg/ml, 50µg/ml and 60µg/ml respectively. Absorbance's of all solutions were measured at 275.8nm. The observations were recorded and graphically presented (Table 1, Figures 2 and 3).

2.5 Preparation of simulated buffer medium

To prepare Phosphate Buffer (pH6.8)11.45g of KH_2PO_4 and 28.8g of Na_2HPO_4 was dissolved in water and volume was adjusted by 1000 ml.

2.5.1 *Invitro* dissolution study

Invitro dissolution study vitro dissolution was performed by using US Pharmacopoeia dissolution type II apparatus at 37±0.5°C with a rotation speed 50rpm/min and 900ml of dissolution medium in per vessel used. The tablets were immersed into a phosphate buffer (pH=6.8) for 1 h. The sample solutions were analyzed for Diclofenac Sodium by UV absorbance at 275.8nm by using a UV spectrophotometer.[11]

Thus, for each sub-sample of four tablets tested simultaneously, every individual tablet result was identified with a particular vessel and position. At every 15-minute interval sample (5 ml) of the solution was withdrawn from the vessel and immediately replaced with equal volumes of dissolution medium. The withdrawn samples (5 ml) were then filtered and diluted, analyzed at 275. 8nm for Diclofenac Sodium by UV spectrophotometer. The amounts of drug present in the samples were calculated from calibration curve of standard Diclofenac Sodium.

Table 1: Data of the calibration curve of Diclofenac Sodium

Conc. (µg/ml)	**Abs. (λmax)**
0	0
10	0.319
20	0.64
30	0.973
40	1.313
50	1.601
60	1.945

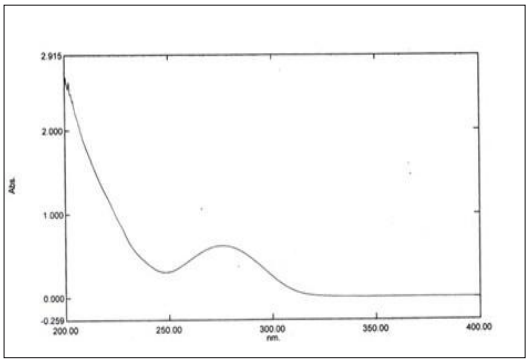

Figure 2: Determination of λmax

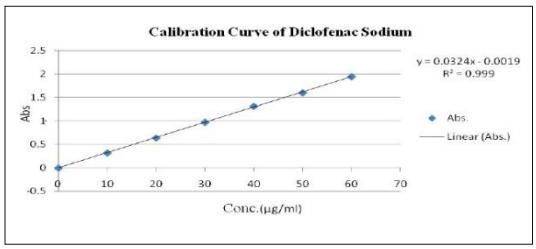

Figure 3: Calibration curve of Diclofenac Sodium

2.5.2 Hardness

Ten tablets from each batch were selected and hardness was measured using Veego hardness tester to find the average tablet hardness or crushing strength.[9] Hardness depends on pressure applied, dwell time and nature of formulation was shown in Table 2.[10]

3 Results

3.1 Determination of λmax: Figure 2.

Calibration Curve of Diclofenac Sodium: The solution of Diclofenac Sodium in the concentration of 10-60µg/ml was prepared. The observations were presented in the following table and figure.

3.2 *Invitro* dissolution test

Commercially available four brands of diclofenac sodium tablets were studied for their *invitro* dissolution behavior in using phosphate buffer (pH 6.8) dissolution medium. Release rate of the samples were determined for 1 h. In dissolution media, all the brands were fulfil the USP *in vitro* dissolution specification i.e., 80% drug release within 40 min in simulated phosphate buffer medium. Results of sample M1 to M4 were presented in below.

4. Discussion

From the above experiment it is found that the hardness of two samples M1 and M3 is 13 and 11.62 due to their increased hardness their release time became slower than the other two samples. The potency and dissolution of four marketed samples is within the BP and USP specifications. The potency determined were 99.30%, 103.38%, 98.22% and102.16% respectively. Hardness and invitro dissolution of the above four brands of Diclofenac Sodium tablets were also studied and reported in the paper. From all of the studies it seems that the samples were collected complies with the BP and USP requirements. The rate of drug release controlled by increase or decrease in the drug solubility and concentration of drug in matrix system and also dissolution rate depends on the surrounding medium. To understand the release kinetics of tablet matrix in dissolution corresponding data were canvassed by various dissolution kinetics models such as Zero Order, First Order, Higuchi, and Hixon-Crowell etc. According to percent release vs. time (Figure 4), the log of release percent release vs. time(Figure5), percent release vs. square root time(Figure6) and

cube root percent of release vs. time respectively (Figure 7). After 1 h dissolution release of DO1, M2, M3, and M4 are 94.16%, 93.97%, 96.94% and 98.5% respectively (Tables 3-5).

Table 2: Hardness test of Diclofenac Sodium: Commercially available four brands (10 tablets for each brand according to BP) of diclofenac sodium tablets were taken to check the hardness parameter are shown below.

Hardness(kg)	**Serial Number**										**Average**
	a	**b**	**c**	**d**	**e**	**f**	**g**	**h**	**i**	**j**	
Sample M1	14	13.5	14	13	12.5	11.5	13	13	12.8	13.2	13
Sample M2	7.0	7.2	7.2	7.0	7.0	7.4	7.8	7.6	8	7.4	6.66
Sample M3	14	13.5	14	13	12.5	11.5	13	13	12.8	13.2	11.62
SampleM4	8.8	7.8	8.0	6.8	7.0	7.8	7.4	7.2	7.8	7.8	7.64

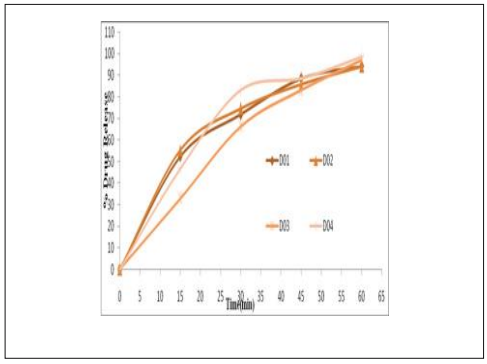

Figure 4: Zero order plots to ascertain release kinetics of Diclofenac Sodium samples.

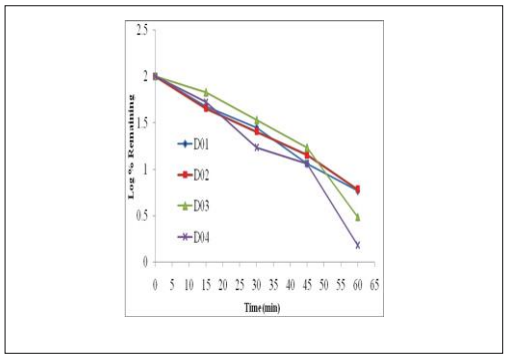

Figure 5: First order plots to ascertain release kinetics of Diclofenac Sodium samples

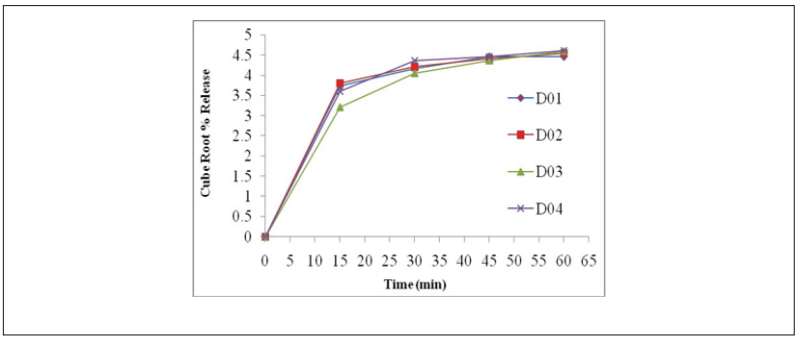

Figure 6: Higuchi plots to ascertain release kinetics of Diclofenac Sodium samples

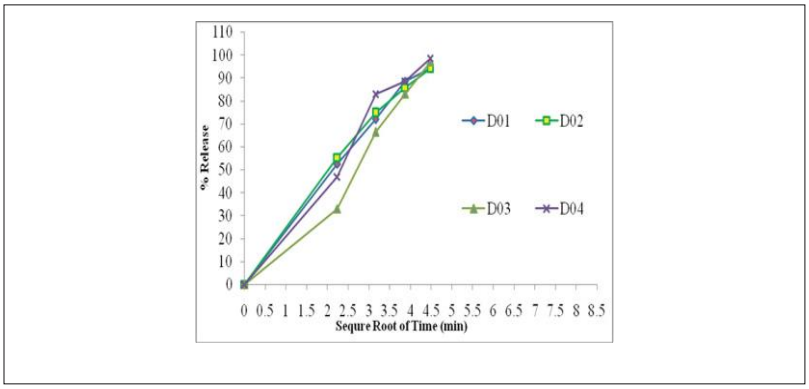

Figure 7: Hixon-Crowell plots to ascertain release kinetics of Diclofenac Sodium samples

Table 3: Data for determination of potency of Diclofenac Sodium from solid dosage form

Sample Code	Sample No.	Absorbance			Average Absorbance	Conc. From standard curve (µg/ml)	Potency calculate (mg)	% potency determined	Average % potency
M1	1a1b	0.970 1.611	0.954 1.572	0.969 1.637	0.964 1.606	29.81 49.62	49.68 49.62	99.36 99.25	99.30
M2	2a2b	0.949 1.668	1.018 1.691	1.025 1.691	0.997 1.683	30.83 52.0	51.38 52.0	102.76 104.0	103.38
M3	3a3b	0.948 1.594	0.972 1.554	0.956 1.589	0.959 1.579	29.65 48.79	49.42 48.80	98.84 97.6	98.22
M4	4a4b	0.991 1.661	0.979 1.668	0.978 1.672	0.983 1.667	30.39 51.50	50.66 51.50	101.32 103.0	102.16

Table 4: *In vitro* dissolution of four marketed diclofenac sodium coded as M1,M2, M3 and M4

Time(min)	% of drug release			
	M1	M2	M3	M4
0	0	0	0	0
15	52.5	55.28	33.05	46.94
30	71.94	74.72	66.39	83.05
45	88.61	85.83	83.06	88.61
60	94.16	93.97	96.94	98.5

Table 5: Hardness, %potency and %release (after1h) of Diclofenac Sodium.

S. No.	Hardness (kg)	Potency (%)	%Release (after 1h)
Sample M1	13.0	99.30%	94.16
Sample M2	6.66	103.38%	102.5
Sample M3	11.62	98.22%	96.17
Sample M4	7.64	102.16%	98.5

5. Conclusion

The results of our preliminary studies indicated that the *in vitro* dissolution Study and assay of Diclofenac Sodium from marketed solid Dosage form meet official specifications due to the maintenance of product quality.

6. Conflict of interest

The authors have no conflict of interest.

7. Acknowledgement

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8. References

1. Tonussi CR, FerreiraSH. Mechanism of diclofenac analgesia: direct blockade of inflammatory sensitization. Eur J Pharmacol. 1994; l251:173-179.

2. RoelofseJA, Vander BijlP, Joubert JJ. An open comparative study of the analgesic effects of ten oxicamand diclofenac sodium after third molar surgery. Anesth Pain Control Dent. 1993; 2: 217-222.

3. Giri TK, Parveen N, Thakur D, Tripathi DK. In vitro Evaluation of Commercially Available Enteric Coated Tablet Containing Diclofenac Sodium. IJRPBS. 2012; 3: 875-881.

4. UI-Hassan SS, YunusSH, LatifA. Study and Improvement of Methods for Determining Diclofenac Sodium in Pharmaceutical Preparations. Pak J Pharm. 2010; 23: 7-10.

5. Chandra R, Singh S, Sharma K, Alam N, Kumar S. Quantity-based quality estimation of diclofenac sodium by reversed-phase high-performance liquid chromatography separation method from formulated tablets. Int J Chem Pharm (IJCP). 2013;4:1.

6. Ahmed NR. High-performance liquid chromatographic method for determining diclofenac sodium in pharmaceutical preparations and environmental samples. Irq Nat J Chem. 2011; 44: 467-473.

7. Todd PA, Sorkin EM. Diclofenac sodium. A reappraisal of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy. Drugs. 1988; 35: 244-285.

8. Nyol S, Gupta MM. Immediate Drug Release Dosage Form: AReview. JDDT. 2013; 3: 155-161.

9. Perttunen K, Kalso E, Heinonen J, Salo J. IV diclofenac in post thoracotomy pain. Br J Anaesth. 1992; 68: 474-480.

10. Nayak AK. Thermodynamic study of the diclofenac sodium solubility in various oils. Chemistry. 2010;19: 121-128.

11. Timmakondu S, Prabu SL, Satyam T. In-vitro studies of diclofenacsodium controlled-release dosage from biopolymeric hydrophilic matrices.ArsPharm. 2011; 52: 20-24.

12. Mather LE. Do the pharmacodynamics of the nonsteroidal anti-inflammatory drugs suggest a role in the management of postoperative pain. Drugs. 1992; 44: 1-13.

13. Morrow BC, Bunting H, Milligan KR. A comparison of diclofenac and ketorolac for postoperative analgesia following day case arthroscopy of the knee joint. Anaesthesia. 1993; 48: 585-587.

14. Gelgor L, Cartmell S, Mitchell D. Intra cerebro ventricular microinjectionsofnon-steroidalanti-inflammatorydrugsabolishreperfusionhyperalgesiaintherat's tail. Pain. 1992; 50: 323-329.