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Dissolution Profile Comparison of Different Branded Formulations of Diclofenac Sodium Tablet

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ABSTRACT

Sustained release drug delivery system is a Drug Delivery System that achieves the release of a drug over an extended period independent of time. Here we have done the dissolution profile comparison of the diclofenac sodium sustained release tablet. Dissolution is the process by which a solid drug substance becomes dissolved in a solvent over time. Here we have compared the dissolution profile of different branded tablets of diclofenac sodium sustained release formulation of the national market. Comparison is completely based on the different dissolution model and the similarity & dissimilarity factors. Each of the tablets having the same amount of drug. The dissolution medium we have used was the phosphate buffer pH 6.8 and the dissolution apparatus type 2 paddle-type has been used. After the comparison of the dissolution profile, we can conclude that the different branded tablets follow different dissolution model with a high similarity factor.

INTRODUCTION:

Oral solid dosage forms are one of the most widely used formulations for prolonged-release products and they are the most preferable administration route for most of the drugs. There are so many advantages of sustained-release drug delivery system over the conventional doses forms like reduced dosing frequency, reduction in dose, improve patient compliance, reduced toxicity due to overdose or accumulation of the drug, reduces the fluctuation of peak valley concentration, night-time dosing can be avoided, constant level of drug concentration in blood plasma can be maintained, but there are several drawbacks of the systems as well[1,2].

Dissolution is the process by which a solid drug substance becomes dissolved in the solvent over time. Dissolution is a dynamic property. In a biological system, drug dissolution in an aqueous medium is an important prior condition for predicting systemic drug absorption. The rate at which drugs with poor aqueous solubility dissolve from an intact or disintegrated solid dosage form in the gastrointestinal tract often controls the rate of systemic absorption of the drug. Thus, the dissolution test may be used to predict bioavailability and may be used to discriminate formulation factors that affect drug bioavailability[3-5].

Diclofenac sodium is a non-steroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties. It is widely used in the long-term treatment of different degenerative joint diseases like rheumatoid arthritis, osteoarthritis, ankylosing spondylitis but it can produce a very high chance of gastrointestinal side effects due to its physicochemical reaction on the gastric mucus and the inflammatory action on the small bowel and the colon[4]. Because of these adverse effects and short biological half-life, diclofenac sodium is a great candidate for prolonged-release preparation[6].

It acts by inhibiting COX activity and the formation of pro-inflammatory mediators such as prostaglandin and the mode of action of diclofenac sodium is the inhibition (COX-2) causing a reduction in the conversion of arachidonic acid into inflammatory prostaglandins[7,8].

Diclofenac is a white to slightly yellowish crystalline powder that has a hygroscopic nature[7]. Diclofenac sodium has a weak acidic property and its pKa is about 4. It has solubility depends on Ph. It is slightly soluble in water, the solubility in phosphate buffer is very little and it's practically insoluble in hydrochloric acid[9,10]. According to biopharmaceutics classification or BCS, it is classified as a class 2 drug which means the drug diclofenac sodium has high

permeability but the solubility in aqueous media is not good or it has a very low solubility[11-13].

For this kind of drug or class 2 kind of drug, the dissolution is the rate-limiting step to absorption. So the choice of medium for in vitro dissolution test is very important and plays a very important role in the dissolution of class 2 drugs[8,10,11].

So the mean aim of the work is to compare the dissolution characteristics or the dissolution behavior of the different branded diclofenac sodium tablet formulations which have the same amount of drug and the other excipients as well. This dissolution profile characterization can play an important role in the bioavailability of the drug and further characteristics[13-15].

MATERIALS AND METHODS:

MATERIALS:

- Formulations- Different marketed formulation of Diclofenac Sodium SR tablets 100mg
- Instruments- USP Dissolution test Apparatus (type II), UV-VIS Spectrophotometer
- Glass and plastic wares- Measuring Cylinder, Pipettes (10ml), Test Tubes, Wash Bottle, Beaker.
- Chemicals- Double distilled water, Sodium dihydrogen phosphate, Sodium hydroxide.

METHODS:

- Fill up the warm tank of dissolution apparatus with distilled water up to the mark.
- Switch ON the mains.
- Switch ON the heater.
- When the temperature is 37°C, measure 900ml dissolution medium or buffer solution and pours in the dissolution bath.
- Attach the paddle to the shaft and immerse them into the dissolution bath.
- Add one tablet in each dissolution bath. Set the r.p.m to 50, and start the operation.

- Take 10ml dissolution medium out of the dissolution bath with a pipette and replace the volume with a fresh buffer with another pipette at 5mins, 15mins, 30mins, 45mins, 1hr, 1.5hr, 2hr, 3hr, 4hr, 5hr, 6hr, 7hr, 8hr time point.

- Filter the aliquot if required and keep in properly labeled test tube.

- Determine the optical density (OD) at 340 nm with a UV-spectrophotometer and calculate the content of Diclofenac Sodium as the specific absorbance at 304 nm.

- Calculate the Cumulative % drug released at different time points and plot the data to fit into different drug release kinetic models.

HOW TO DETERMINE WHICH ONE IS BEST FITTED MODEL?

After plotting the data according to a different model, we need to find out which one is the best-fitted model i.e. which model describes the drug release kinetics best. This can be done by comparing the value of the regression coefficient (R). The value closest to 1.00 is the best-fitted model.

RESULTS AND DISCUSSION:

Table No. 1: Drug release kinetics of Brand A

Time (mint)	ABSORBANCE	CONC	DRUG RELEASE	Cumulative amount.	Cumulative % R	Cumulative log % R	% drug Remain	Log % drug remaining	Square root of time	Log Time	Cube root of %drug remaining
5	0.023	1.06	958.33	212.09	0.21	(0.67)	99.79	2.00	2.24	0.70	**4.64**
15	0.040	1.85	1,666.67	1,685.19	1.69	0.23	98.31	1.99	3.87	1.18	**4.62**
30	0.060	2.78	2,500.00	2,529.17	2.53	0.40	97.47	1.99	5.48	1.48	**4.60**
45	0.074	3.43	3,083.33	3,140.28	3.14	0.50	96.86	1.99	6.71	1.65	**4.59**
60	0.130	6.03	5,429.17	5,520.37	5.52	0.74	94.48	1.98	7.75	1.78	**4.55**
120	0.161	7.45	6,708.33	6,859.86	6.86	0.84	93.14	1.97	10.95	2.08	**4.53**
180	0.247	11.44	10,291.67	10,517.73	10.52	1.02	89.48	1.95	13.42	2.26	**4.47**
240	0.255	11.81	10,625.00	10,965.42	10.97	1.04	89.03	1.95	15.49	2.38	**4.47**
300	0.344	15.93	14,333.33	14,791.81	14.79	1.17	85.21	1.93	17.32	2.48	**4.40**
360	0.347	16.06	14,458.33	15,076.06	15.08	1.18	84.92	1.93	18.97	2.56	**4.40**
420	0.391	18.10	16,291.67	17,070.05	17.07	1.23	82.93	1.92	20.49	2.62	**4.36**
480	0.460	21.30	19,166.67	20,126.06	20.13	1.30	79.87	1.90	21.91	2.68	**4.31**

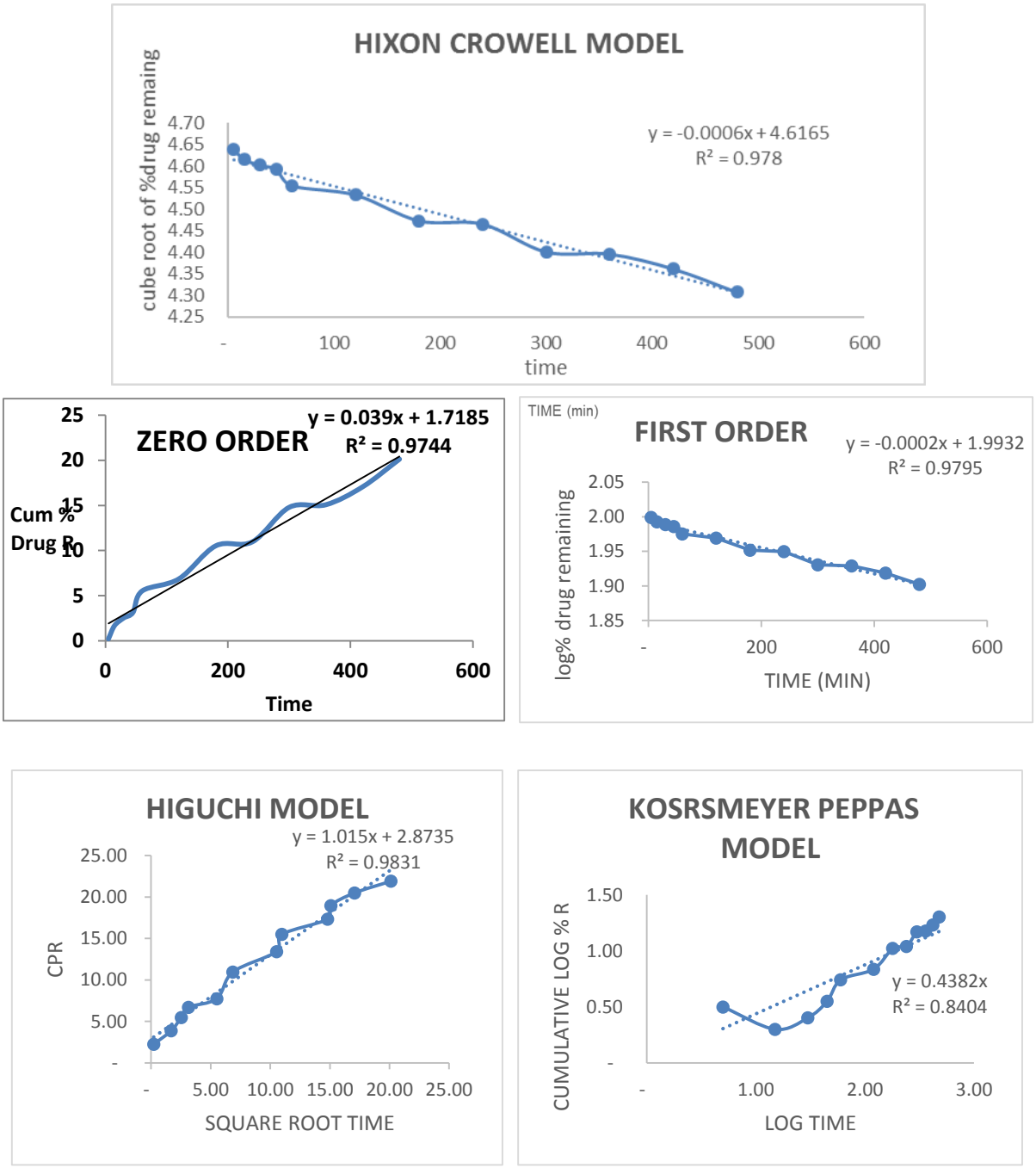


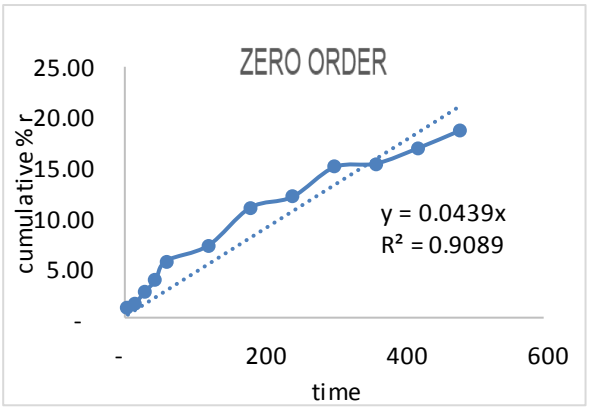
Figure No. 1: Drug release kinetics of Brand A

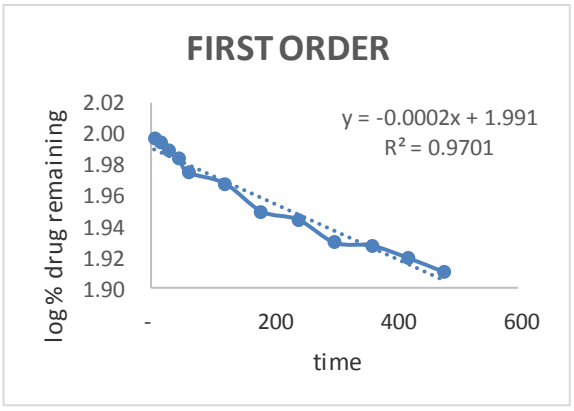
Table No. 2: Models and R-value

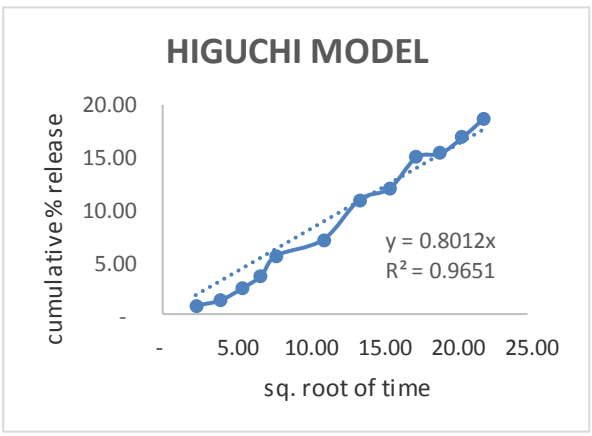
Sr. No.	Model Name	Value of R
1	ZERO ORDER MODEL	0.974
2	FIRST ORDER MODEL	0.979
3	HIGUCHI MODEL	0.983
4	HIXON CROWELL MODEL	0.840
5	KORSMEYER PEPPAS MODEL	0.978

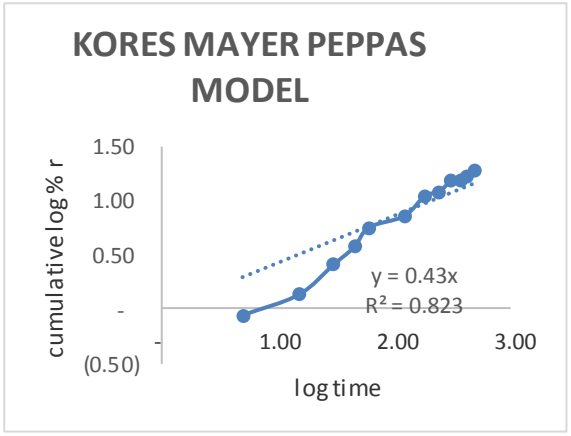
Table No. 3: Drug release kinetics of Brand B

Time (mint)	ABSORBANCE	CONC (µg/ml)	DRUG RELEASE	cum amt.	cumulative %R	Cumulative log %R	% drug Remain	log% drug remaining	square root of time	log Time	cube root of %drug remaining
5	0.021	0.97	875.00	875.00	0.88	(0.06)	99.13	2.00	2.24	0.70	4.63
15	0.032	1.48	1,333.33	1,348.15	1.35	0.13	98.65	1.99	3.87	1.18	4.62
30	0.061	2.82	2,541.67	2,566.20	2.57	0.41	97.43	1.99	5.48	1.48	4.60
45	0.088	4.07	3,666.67	3,719.44	3.72	0.57	96.28	1.98	6.71	1.65	4.58
60	0.133	6.15	5,537.50	5,631.02	5.63	0.75	94.37	1.97	7.75	1.78	4.55
120	0.168	7.78	7,000.00	7,155.05	7.16	0.85	92.84	1.97	10.95	2.08	4.53
180	0.257	11.90	10,708.33	10,941.16	10.94	1.04	89.06	1.95	13.42	2.26	4.47
240	0.280	12.96	11,666.67	12,018.47	12.02	1.08	87.98	1.94	15.49	2.38	4.45
300	0.348	16.11	14,500.00	14,981.44	14.98	1.18	85.02	1.93	17.32	2.48	4.40
360	0.353	16.34	14,708.33	15,350.88	15.35	1.19	84.65	1.93	18.97	2.56	4.39
420	0.386	17.87	16,083.33	16,889.31	16.89	1.23	83.11	1.92	20.49	2.62	4.36
480	0.424	19.63	17,666.67	18,651.34	18.65	1.27	81.35	1.91	21.91	2.68	4.33









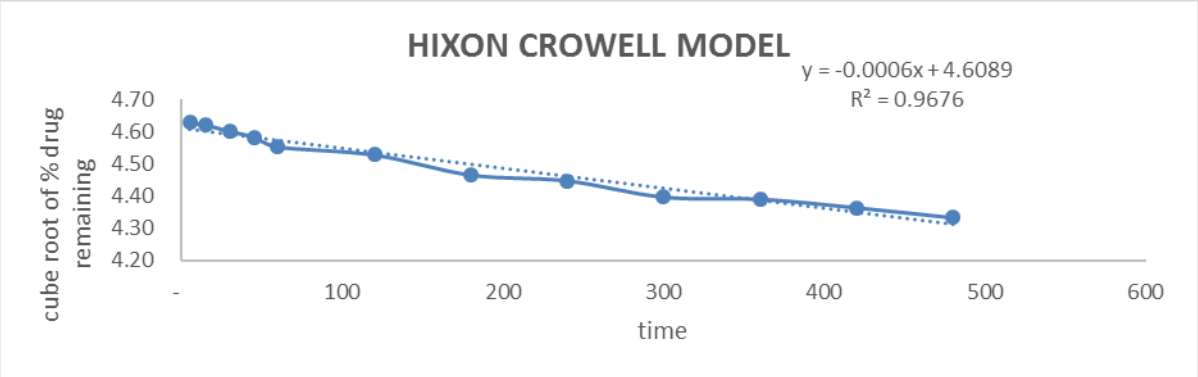


Figure No. 2: Drug release kinetics of Brand B

Table No. 4: Models and R-value

Sr. No.	Model Name	Value of R
1	ZERO ORDER MODEL	0.908
2	FIRST ORDER MODEL	0.970
3	HIGUCHI MODEL	0.965
4	HIXON CROWELL MODEL	0.823
5	KORSMEYER PEPPAS MODEL	0.967

Table No. 5: Cumulative % Drug release of Brand A and Brand B

Time (mins)	Brand A	Brand B
5	0.21	0.88
15	1.69	1.35
30	2.53	2.57
45	3.14	3.72
60	5.52	5.63
120	6.86	7.16
180	10.52	10.94
240	10.97	12.02
300	14.79	14.98
360	15.08	15.35
420	17.07	16.89
480	20.13	18.35

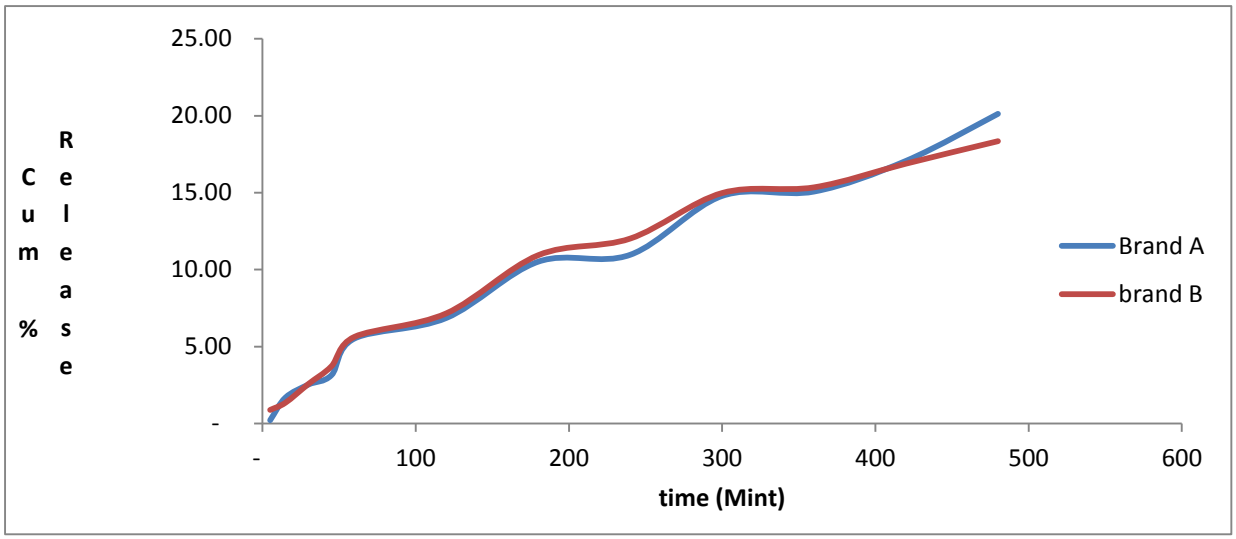


Figure No. 3: Cumulative % Drug release of Brand A and Brand B

Table No. 6: Similarity and Difference Factor

TIME (min)	Cum % r (REFERENCE){R}	Cum % r (TEST){T}	{R-T}	MOD{R-T}	Sq{R-T}
5	0.21	0.88	-0.6629	0.66291	0.43945
15	1.69	1.35	0.3370	0.337037	0.113594
30	2.53	2.57	-0.0370	0.037037	0.001372
45	3.14	3.72	-0.5792	0.579167	0.335434
60	5.52	5.63	-0.1106	0.110648	0.012243
120	6.86	7.16	-0.2952	0.295185	0.087134
180	10.52	10.94	-0.4234	0.423426	0.17929
240	10.97	12.02	-1.0531	1.053056	1.108926
300	14.79	14.98	-0.1896	0.18963	0.035959
360	15.08	15.35	-0.2748	0.274815	0.075523
420	17.07	16.89	0.1807	0.180741	0.032667
480	20.13	18.65	1.4747	1.474722	2.174806
SUM	108.49			5.618373	4.596398

$$f_1 = \frac{\sum[R_t - T_t]}{\sum R_t} \times 100$$

= (5.6183/108.49)×100

= 5.18

$$f_2 = 50 \cdot \log\left\{\left[1+\frac{1}{n}\sum_{t=1}^{n} w_t (R_t - T_t)^2\right]^{-0.5} \times 100\right\}$$

= 50×log {[1+ (1/12) × (4.59)] ^-0.5×100}

= 96.47919

Sum of mod {r-t} =5.618373

Sum of cum % of release of reference =108.49

So, difference factor = sum of mod {r-t}*100/sum of cum% of release of reference= 5.18 %

Sum of square of {r-t} =4.596398

1+ [1/12* sum of sq. {r-t}] =1+0.383033 = 1.383033

Square root of (1.383033) = 1.176024

1/1.176024 = 0.850323

100*0.850323 = 85.0323

50*(LOG (G20)) = 96.47919

So the similarity factor is = 96.47919 %

Table No. 7: Models and R-value of Brand A and B

Sr. No.	MODEL NAME	BRAND A (R)	BRAND B (R)
1	ZERO ORDER MODEL	0.974	0.908
2	FIRST ORDER MODEL	0.979	0.970
3	HIGUCHI MODEL	0.983	0.965
4	HIXON CROWELL MODEL	0.840	0.823
5	KORSMEYER PEPPAS MODEL	0.978	0.967

❖ **The Best Fitted Kinetic Release Model:**

- BRAND A: HIGUCHI MODEL
- BRAND B: FIRST ORDER MODEL

CONCLUSION:

The *in-vitro* dissolution release of the marketed product of Sustained release tablet of Diclofenac sodium was determined and was fitted in the best fitted kinetic release model. And the difference factor and similarity factor was also studied.

- Brand A tablet was best fitted to Higuchi Model which describes that (i) initial drug concentration in the matrix is much higher than drug solubility; (ii) drug diffusion takes place only in one dimension; (iii) drug particle is much smaller than system thickness: (iv) matrix swelling and dissolution are negligible; (v) drug diffusivity is constant, and (vi) perfect sink condition is always attained in the release environment.

- Brand B tablet was best fitted to the First Order Model which describes that (i) the rate of the reaction is proportional to the reactant's concentration.

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