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Research Article

A Comparative analysis: *In-vitro* dissolution study of different commercially available brands of diclofenac sodium

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Abstract

The study was aimed to compare in-vitro release behavior of four commercially available brands of diclofenac sodium sustained release tablets. Most commonly used brands of tablets were taken randomly that contained same quantity of active ingredients but differ in type or amount of excipients used. USP references standard Diclofenac Sodium was used to obtain standard curve. In-vitro dissolution was performed by USP Paddle apparatus employing two different dissolution medium one acidic (pH 1.2) and other buffer medium (pH 6.8). Weight variation of these formulations was found to be 1.4%, 2.1%, 2.6% and 0.9%. In-vitro dissolution rate of these commercially available brands of diclofenac sodium were 97.867%, 90.979%, 95.639% and 99.494% respectively. The result showed variability in release profile. Sustained quality control and constant market monitoring on these products and its formulation factors can lead to improvement in quality of medicine.

Keywords: Release rate, Sustained release tablets, diclofenac sodium

Introduction

Pain and inflammation is a global issue. Severe medical illness, emergency, trauma, natural calamities, poor dietary conditions and overburdened life are some of the reasons that needs management (Dolin *et.al.*). The Support study (1995) concluded that almost half of patients with diseases had moderate to severe pain (during their end days of life) (Joranson *et.al.*, 2000). Its management is done at different level depending upon the condition of patients. Among various analgesics used in pain management non-steroidal anti-inflammatory drug substance NSAIDS are most common (Karmoker *et.al.*, 2016).

Diclofenac is frequently prescribed as (NSAID) (Siddik *et.al.*, 2001), commonly indicated in reducing pain, inflammation (Huang *et.al.*, 2008) and in various other conditions (rheumatoid arthritis, acute injury, osteoarthritis, gout attacks, spondy arthritis, and in kidney stone pain). Menstrual pain acute migraines, post traumatic pain, female breast cancer and body metastatic pain can be well managed by diclofenac (Tunçay *et.al.*, 2000). Gastrointestinal disturbances are the major adverse effects of diclofenac therapy after oral administration due to reason. This drug is usually formulated as coated tablets. Tablets that have enteric coating along with sustained release effect give a new perspective to gastroirritant active pharmaceutical ingredients. These advanced formulations provide an initial release of dosage form to initiate sufficient therapeutic effect and then a gradual release of maintenance dose over a prolonged period of time. Hence these type of formulation exhibits quick onset of action and continued for extended period (Dutta *et.al.*, 2011).

The *in-vitro* dissolution process always played a pivotal role in releasing drug from tablet matrix and in making inference whether it is obtainable for subsequent gastrointestinal absorption (Bravo *et.al.*, 2002). The nature of formulation, process of manufacturing, and drug physiochemical properties contributes to *In-vitro* dissolution process. To check the quality of the product and differentiation among formulations

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(same therapeutic agent but different pharmaceutical excipients) (Maggio *et.al.*, 2008), *in-vitro* dissolution studies serve as an effective tool, as it is an indicator for evaluation of formulation (Löbenberg *et.al.*, 2000).

Different brands of diclofenac sodium are available in Pakistan under different names. Our comparative study involved randomly selected three national as well as one international brand of diclofenac sodium sustained release matrix tablets.

Material and Methods

Chemicals: USP references standard of Diclofenac Sodium (Merk, Germany).

Reagents: Hydrochloric acid (Merk, Germany); Sodium Hydroxide (Merk, Germany); Ortho-phosphoric acid (Merk, Germany):

Equipments: Simadzu UV spectrophotometer; Digital pH meter; Electrolab Tablet Dissolution Test machine (XXII); Sartorius electronic balance.

Dosage forms

Three local and one multinational brand of (manufactured date less than four months from purchasing) diclofenac sodium SR purchased from different stores. These test products were examined for manufacturing license, batch history, manufacture date and expiry prior to buy.

They were labelled (DS-1, DS-2, DS-3) for local brands and (DS-X) multinational brand. The blister packs of all four brands were stored at temperature of 25±2°C for one month before the experiment to check any tablet defect in formulations. Statistics of the brand under study are given in Table 1 and practical data for drug release experiment is given in Table 2:

Table 1: Statistics of brand under study

Statistics of Brands under study					
Code	**Brand**	**Manufacturer**	**Batch.No**	**Mfg.Date**	**Exp.Date**
DS- 1	Dicloran	SAMI	04k	1-2011	12-2013
DS-2	Sofac	Saffron	00618	1-2009	11-2014
DS- 3	Diclocon	Alcon	0002	1-2010	4-2012
DS-X	Voltral	Novartis	J0218	1-2011	12-2015

Table 2: Practicle data for drug release experiment

Parameters for Drug release experiment	
• No.of replicates	6 Tablets per experiment
• Dissolution Medium	Phosphate buffer of PH 1.2 & 6.8
• Volume of Dissolution	900ml
• Temperature	37 C
• Rotation speed	50rpm
• Sampling Time	15minutes
• Determination of Release of Diclofenac Sodium	Paddle appratus UV-spectrophotometer at wavelength of max.at 276nm

Weight Variation

All the brands were analysed, according to USP specifications (for their uniformity of weight). Twenty tablets (of each brands) were selected randomly and were weighed on Sartorius electronic balances. The average weight of those twenty tablets was calculated, weight deviations were estimated by equation 1 (Attama *et.al.*, 2003) to comply with the USP standrads.

Weight variation = $(I_w - A_w)/A_w \times 100\%$

equation (1)

I_w = Individual weight of the tablet

A_w = Average weight of the tablet

Dissolution study

The study was performed in Paddle apparatus II with six section assembly (according to XXII and NF XVII, 1995) (Yeole *et.al.*, 2006). Simulated gastric medium at pH 1.2 and simulated intestinal medium at pH 6.8 was placed in the vessels (900 ml) at temperature of 37±0.5°C with rotation speed 50 rpm. Preheated medium at 37°C was used, rotation started and waited for 15 min until equilibrium has attained. To avoid any error in

results vessel, corresponding tablets and vessel position have assigned the same number. The result was identified for each individual tablet with a particular vessel and position. The duration of dissolution study was 3 hours where in first 2 hours the tablets were exposed to simulated gastric media (0.1N HCl pH 1.2) and in last 10 hour the tablet matrices were exposed to simulated intestinal media (Buffer pH 6.8). Table 2 shows the technical data for drug release experiment.

Preparation of simulated gastric medium

1000 ml solution was prepared by adding 11.4 ml of 0.1 N Hydrochloric acid (32% w/v, pH 1.2) and sufficient water to make up final volume.

Preparation of simulated intestinal medium

1000 ml buffer solution (pH 6.8) was prepared, it is composited from 20 ml Sodium Hydroxide (25% w/v) in quantity sufficient water. The pH was adjusted using 0.1 N Hydrochloric acid to 6.8 by the USP XXIII procedure with minor modification (adding 1.2 ml *O* -phosphoric acid).

Preparation of standard curve

Stock solution of diclofenac sodium reference substance was prepared, serial dilutions were made and calibration curves were obtained by measuring the absorption of each dilution at the maximum absorption wavelength of 277 nm (Table 3, Figure 1). Limit of detection and limit of quantification was performed six times and their values were calculated (table 4) from calibration curve using formula 3.3s/S (LOD) and LOQ (10s/S), S is slope of calibration curve and s is standard deviation.

Table 3: Standard curve for diclofenac sodium

Diclofenac Sodium Standard Curve	
Concentration (µg/ml)	**Absorbance (A)**
10	0.134
20	0.235
30	0.328
40	0.429
50	0.533
60	0.63

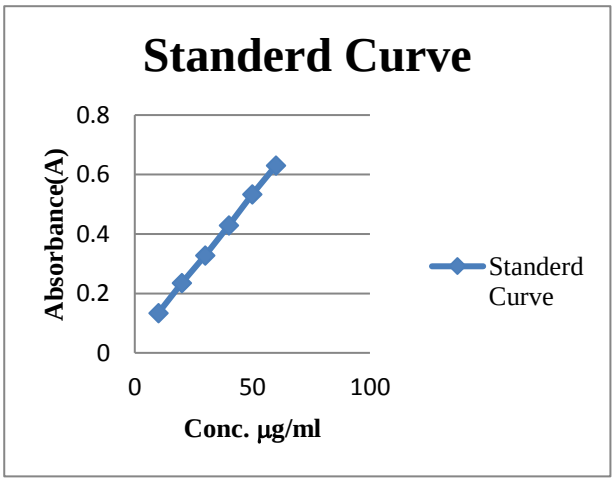

Figure 1: Standard curve of diclofenac sodium reference.

Table 4: Validation parameters

Parameters	Values
Working λ.max	277nm
Beer's lambert limt	0-60 µg
Slope	0.009
LOD	0.951
LOQ	3.17
R^2	0.999

Results and discussion

Weight variation

Weight variation of various brands of diclofenac sodium DS-1, DS-2, DS-3 and DS-X are shown in table. The average percentage deviation of all these different brands of diclofenac sodium comes out to be 1.49%, 1.13%, 1.32% and 0.66% respectively (Table 5). Similar results have been shown in one of the previous studies on diclofenac sodium prolonged released tablets (Bertocchi *et.al.*, 2005).

Table 5: Data Table of weight variation Test

Sr. No	DS-1		DS-2		DS-3		DS-X	
	Weight	% Deviation	Weight	% Deviation	Weight	% Deviation	Weight	% Deviation
1	0.283 g	0.70	0.230 g	0	0.254 g	0.7	0.220 g	0
2	0.280 g	0.3	0.232 g	0.8	0.254 g	0.7	0.222 g	0.9
3	0.271 g	3.5	0.228 g	0.8	0.251 g	1.1	0.218 g	0.9

4	0.276 g	1.7	0.229 g	0.4	0.254 g	0.7	0.220 g	0
5	0.286 g	1.7	0.227 g	1.3	0.252 g	0.7	0.224 g	1.8
6	0.284 g	1.0	0.231 g	0.4	0.252 g	0.7	0.217 g	1.3
7	0.277 g	1.4	0.238 g	3.4	0.263 g	3.2	0.221 g	0.4
8	0.290 g	3.2	0.225 g	2.1	0.261 g	2.8	0.217 g	0.4
10	0.285 g	1.4	0.235 g	2.1	0.247 g	2.6	0.222 g	0.9
Average weight	**0.281 g ±1.49**		**0.230 g ±1.13**		**0.253 g ±1.32**		**0.220 g ±0.66**	

Dissolution

Four commercially available brands of diclofenac sodium were tested using USP II dissolution apparatus, in acidic as well as in basic medium. In acidic stage, 900 ml 0.1N hydrochloric acid was poured in the vessel and accurately weighed six tablets from each brand then put in the baskets. The process time was of 2 hours. 10 ml of the sample was drawn at regular time interval and drug released was analyzed using UV spectrophotometer at 277 nm. The concentration of the different brands of diclofenac sodium at acid stage is given below in table 6.

Table 6: Drug release Percentage of DS-1, DS-2, DS-3 and DS-x at pH 1.2

Time (Minutes)	DS-1	DS-2	DS-3	DS-x
	% age	% age	% age	% age
0	0	0	0	0
15	0.9	1.04	1.64	0.58
30	2.3	1.86	3.42	1.8
45	3.8	3.3	4.66	3.4
1 h	5.4	4.64	6.02	4.2
1 h 25 min	6.2	5.8	7.5	5.2
1.h 30 min	7.6	7.0	8.8	6
1h 45 min	8.84	8.4	9.9	7.5
2 h	9.7	9.5	11.2	8

After carrying the procedure for 2 hours in the acid medium, 20 ml sodium hydroxide (25%) was poured to the previous medium. The pH was set to 6.8 ±0.05 by adding *O* - phosphoric acid (1.2ml). The process was carried out for 10 hours and sample was again withdrawn at regular time interval. The dissolution medium was then replaced to maintain the volume of medium. The withdrawn samples (10ml filtered, diluted and analysed at 277nm for diclofenac sodium by spectrophotometer). Standard or calibration curves formed from the Standard solution of USP reference standard test drugs were then used to analyse the quantity of drug in the samples.

Table 7: Percentage drug release of DS-1, DS-2, DS-3 and DS-X at pH 6.8

Time (hrs.)	DS-1	DS-2	DS-3	DS-X
	% age	% age	% age	% age
3	18.759	18.706	19.889	16.925
4	26.612	23.269	26.929	19.354
5	31.123	41.736	36.2210	26.032
6	41.736	45.981	45.654	32.812
7	45.217	56.593	49.174	42.627
8	56.254	64.553	52.694	57.501
9	66.951	70.815	62.549	64.888
10	77.458	77.501	72.405	79.763
11	95.754	86.309	82.260	95.242
12	97.867	90.979	95.636	99.494

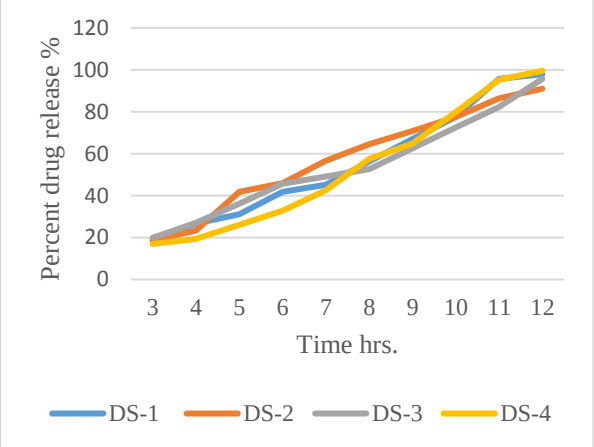

Figure 2: Percent drug release of DS-1, DS-2, DS-3 and DS-X at pH 6.8

Table 7 and figure 2 represents the release rate of different brands of diclofenac sodium sustained release tablets, DS-x showed maximum drug release of 99.494%, DS-1 showed 97.867%, 95.636% of DS-3 and DS-2 release percentage was found to be less as

compare to other formulations (90.979%). Another study has shown in which all of the drug released between 80 and 100% within 8h and showed quicker releases at pH 6.8 due to less pka pf diclofenac sodium (Bertocchi *et.al.*, 2005).

Conclusion

It was concluded that all commercially available brands of diclofenac sodium sustained release tablets meet official criteria but showed difference in their release profile to some extent. Few exhibited less drug release compared to others, the reason can be the manufacturing process, use of different excipients and other formulation factors that affected its drug release. There is need of constant quality control of all pharmaceutical products which will help in improvement of quality of medicine and quality of life.

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