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RESEARCH ARTICLE

STUDIED ON THE EFFECT OF pH OVER DISSOLUTION PROFILE OF DICLOFENAC SODIUM SUSTAINED RELEASE TABLETS

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ABSTRACT

The present study was performed to illustrate the effect of pH on dissolution profile of diclofenac sodium sustained release tablets. Diclofenac sodium has analgesic, antipyretic and anti- inflammatory activities. It is a potent relatively non-selective cyclooxygenase inhibitor. It is absorbed rapidly and completely after oral administration; peak Concentrations in plasma reached within 2-3 hours. The drug extensively binds to plasma proteins (99%) and its half- life in plasma is 1-2 hours. Diclofenac sodium extended release tablets are prescribed for long-term symptomatic treatment of Rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Dissolution studies in different pH mediums were performed to mimic the in-vivo condition by doing in-vitro tests. The pH/buffer selection bases on the exposure of drug from stomach to intestine/colon and ensures the impact of pH changes on dissolution and release of drug substance for absorption. The study ensures the impact of pH changes on dissolution and release of drug substance for absorption.
Keywords: Diclofenac sodium, Dissolution studies, pH

INRODUCTION

The Molecular formula of Diclofenac sodium is $C_{14}H_{10}O_2C_{L2}N.Na$ and chemical name, 2-[(2, 6-dichlorophenyl)-amino] phenyl acetate. It is freely soluble in methanol, soluble in ethanol (95%), sparingly soluble in water and glacial acetic acid, practically insoluble in ether, chloroform and toluene.

Diclofenac has analgesic, antipyretic and anti-inflammatory activities. It is a potent relatively non-selective cyclooxygenase inhibitor and its potency is greater than that of indomethacin, naproxen, or several other agents. In addition, diclofenac appears to reduce intracellular concentration of free arachidonate in leucocytes, perhaps by altering the release or uptake of the fatty acid. Diclofenac is rapidly and completely absorbed after oral administration; peak Concentrations in plasma are reached within 2-3 hours. It is given in the dosage 75-150mg daily in divided doses [1-5].

Sustained release drug delivery system is designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. Multimedia dissolution is to mimic the in-vivo condition by doing in-vitro test and pH/buffer selection is based on the exposure of drug from stomach to intestine/colon and to ensure the impact of pH changes on dissolution and release of drug substance for absorption [7-9].

MATERIALS UNDER METHODS

Diclofenac sodium sustained release tablets were purchased from the market. The drug content in each tablet was 100mg**.** Calcium chloride, sodium hydroxide, potassium dihydrogen phosphate, oxalic acid,

Sodium chloride and other reagents used were of analytical grade. Eqiupments used were UV/visible spectrophotometer - SHIMADZU-1700, Tablet dissolution test apparatus USP III paddle and Friability test apparatus (Rosche Friabilator).

Physical Characterization:

The tablets were subjected to their physical characterization, Hardness, friability and weight variation.

Assay: The assay was performed by triturating the tablets to form a fine powder and transferred to a 100 ml volumetric flask and dissolved in phosphate buffer pH 7.2 and made up to the volume to get stock solution. 1ml of this stock solution was taken in a 100ml volumetric flask and diluted with phosphate buffer pH 7.2 and made up to the volume. The absorbance of this solution was measured at 276nm using uv spectrophotometer. The drug content was estimated from the absorbance obtained.

DISSOLUTION STUDIES

In order to study the effect of the dissolution medium pH on the drug release pattern, drug release was studied in phosphate buffer of pH 2.4, 6.8 and 7.4. The dissolution mediums of different pH were prepared in following manner

Simulated Gastric fluid – 2g of NaCl and 3.2 g of pepsin were dissolved in water. Then added 80 ml. of 1 M HCl and diluted to 1000 ml. with water.

Phosphate buffer pH 6.8 –28.80 g of Na_2HPO_4 and 11.45 g. of KH_2PO_4 were dissolved in sufficient water to produce 1000 ml.

Phosphate buffer ph 7.4 – **Solution I** – 119.31 g of Na_2HPO_4 was dissolved in sufficient water to produce 1000 ml. **Solution II** – 45.36 g of KH_2PO_4 was dissolved in sufficient water to produce 1000 ml. Then 85 ml. of solution I and 15 ml. of solution II were mixed and adjusted the pH.

RESULTS AND DISCUSSION

Physical properties of the tablets were found within the probable limits as shown in Table (1). The drug content was estimated from the absorbance obtained. Three tablets of were taken into three different pH of phosphate buffer (pH2.4, pH 6.8 and pH 7.4).The USP dissolution apparatus was set at rotation 50 rpm and temperature of the assembly was set at 37^0 C. The tablets were placed in above prepared three different media of different pH. Absorbance was determined at 276 nm by collecting sample at different time intervals up to 12hrs. The percentage drug release was calculated at different time intervals at different pH and shown in Table (2). The graph was plotted between percent drug release and time for different dissolution media and shown in Fig (1).

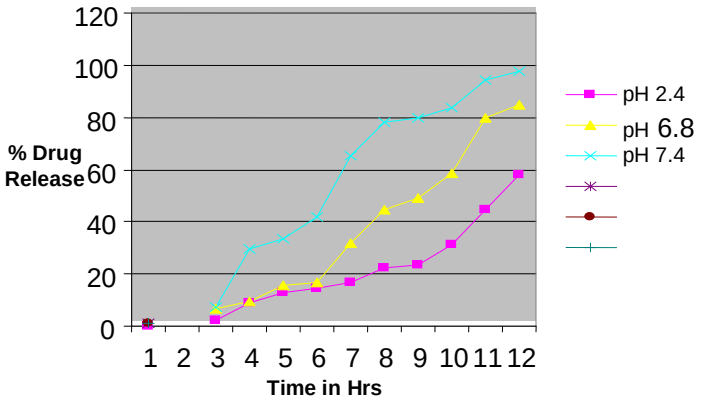

Figure 1: Percent drug release V/s Time

Table 1: Physical characteristics of the tablets

Tablet	Hardness (kg./cm.^{2})	Average % weight variation	% Friability	% Drug content
Marketed Sustained Release	7 to 7.5	0.702	0.22	101.86

Table 2: Result of dissolution studies with different pH

Sr. No.	Time hrs.	Absorbance (nm.)			% Drug release		
		pH 2.4	pH 6.8	pH 7.4	pH 2.4	pH 6.8	pH 7.4
1.	.5	0.069	0.074	0.228	8.896	9.66	29.39
2.	1	0.100	0.123	0.259	12.89	15.85	33.38
3.	1.5	0.113	0.131	0.324	14.56	16.88	41.83
4.	3.00	0.130	0.246	0.505	16.75	31.71	65.08
5.	5.5	0.172	0.346	0.608	22.16	44.60	78.38
6.	6.00	0.181	0.380	0.619	23.33	48.96	79.80
7.	8.5	0.270	0.452	0.650	31.31	58.35	83.80
8.	10.5	0.345	0.619	0.733	44.54	79.80	94.48
9.	12.00	0.449	0.658	0.756	57.96	84.90	97.55

CONCLUSION

The release profile of diclofenac sodium from the tablets increased continuously with time, and the amount of drug release increased as the media pH increased. The cumulative amount of drug release is higher at pH 7.4 than that of pH 6.8 by 15 %. This increase in drug release at higher pH can be attributed to pH dependent solubility of of diclofenac sodium. As the pH increases, the solubility of diclofenac sodium increases which might increase drug release.

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