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In Vitro Dissolution of Aceclofenac Loaded Hydrophilic Polymer Based Matrix Tablets and its Release Mechanism

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Abstract

Hydrophilic polymers are widely used to prepare sustained release matrix tablets. These polymers showed their sustained action by forming a barrier of thick gel layer around the matrix. Here swelling of the polymer and erosion of matrix plays a major role to control the release of the drug. In this present study the swelling and erosion properties of some hydrophilic polymers were correlated to their sustaining and rate controlling behavior. Matrix tablets containing hydroxypropyl methylcellulose (HPMC K100cps), carboxymethyl cellulose (CMC 50,000 cps) and methocel K15M CR polymers were prepared. The powder mixture was evaluated for their flow properties and the prepared tablets for their physical parameters. Swelling and erosion index of the tablets were carried out in pH 6.8 phosphate buffer and dissolution in 0.1N HCl (2 hours) followed by pH 6.8 phosphate buffer (8 hours) using USP apparatus II (paddle method) at 50 r.p.m. HPMC K100 cps was found to be not as rate retarding as the other two. From the all results it was observed that F-6 (containing 43.243% methocel K15M CR) showed highest swelling and erosion index (740.589% and 12.017% respectively), slowest release rate (24.491% at 8 hours) and highest MDT value (55.401 hours). Finally it can be concluded that increasing the polymer concentration or polymer's viscosity grade, swelling and erosion index increases, release rate decreases and MDT value increases.

Key words: Aceclofenac, Matrix tablets, HPMC, CMC, Physical parameters, Release kinetics.

Introduction

Many strategies are available for the design and development of modified-release drug delivery formulations. The primary purpose of these drug delivery devices is to improve the state of disease management by modifying the pharmacokinetic profiles of therapeutic agents normally administered as conventional tablets or capsules. Conventional oral dosage forms often produce fluctuations of drug plasma level that either exceed safe therapeutic level or quickly fall below the minimum effective level; this effect is usually totally dependent on the particular agent's biologic half-life, frequency of administration, and release rate. It is recognized that many patients can benefit from drugs intended for chronic administration by maintaining plasma levels within a safe and effective range (Theeuwes, 1983). Hydrophilic polymer matrix systems are widely used in oral controlled drug delivery because they make it easier to achieve a desirable drug release profile, they are cost effective, and they have broad US Food and Drug Administration acceptance (Alderman, 1984).The hydrophilic polymer matrix system consists of hydrophilic polymer, drug, and other excipients distributed throughout the matrix. This dynamic system is dependent on polymer wetting, hydration and dissolution for controlled release of drug. At the same time, other soluble excipients or drug substances will also wet, dissolve and diffuse out of the matrix, whereas insoluble excipients or drug substances will be held in place until the surrounding polymer, excipients, or drug complex erodes or dissolves away (Dow chemical Company 2006). Hydrophilic matrices containing swellable polymers are referred to as hydrogel matrices, swellable controlled release systems or hydrophilic matrix tablets. A number of polymers have been investigated to develop in situ gel-forming systems, due to the ability of these hydrogels to release an entrapped drug in aqueous medium and to regulate the release of such drug by control of swelling and cross-linking (Krowczynsky, 1987). Nonsteroidal anti-inflammatory drugs (NSAIDs) are considered to be the first-line drugs in the symptomatic treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Aceclofenac is one of the emerging NSAID molecules for arthritis treatment. It is a newer derivative of diclofenac and has less gastrointestinal complications (Parfitt, 1999). The short biological half-life (about 4 h) and dosing frequen-

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cy more than one per day make aceclofenac an ideal candidate for sustained release (Parfitt, 1999). Hydroxypropyl methylcellulose (HPMC), which is commonly used in hydrophilic matrix drug delivery systems, is a mixed alkyl hydroxyalkyl cellulose ether containing methoxyl and hydroxypropyl groups. The hydration rate of HPMC depends on the nature of these substituents, such as the molecular structure and the degree of substitution. Specifically, the hydration rate of HPMC increases with an increase in the hydroxypropyl content. The solubility of HPMC is pH independent (Alderman, 1984). HPMC has been found to be a very versatile material for the formulation of soluble matrix tablets. It is a widely accepted pharmaceutical excipient and is included in all major compendia. Because HPMC is available in a wide range of molecular weights, effective control of gel viscosity is easily provided (Dow chemical company 2006).

The purpose of the present study was to develop a sustained release dosage form of aceclofenac prepared by using some hydrophilic polymer, such as methocel K15M CR, hydroxyl propylmethyl cellulose (HPMC K100 cps) and carboxy methyl cellulose (CMC 50,000 cps). The release mechanism of drug from the hydrophilic matrix is commonly governed by the swelling of the polymer in contact with water and diffusion of drug from depot which is surrounded by viscous gel barrier in a controlled way. The present study was mainly focused on the actual release pattern of the drug from the matrix, to find out whether it relates with the theoretical concept.

Materials and Methods

Aceclofenac, CMC 50,000 cps and HPMC K100 cps were purchased from TecnoPharma (Bangladesh), methocel K15M CR was a gift sample from Incepta Pharmaceuticals Ltd. (Bangladesh), kollidone K30 (Albright and Wilson Ltd.), Pre gelatinized starch (Starch 1500), magnesium stearate and talc were from Chaina. Among the instruments, electronic balance (Shimadzu, Japan), hydraulic press (Perkin-Elmer, USA), dissolution apparatus (Veego, India), uv-visible spectrophotometer (Shimadzu, Japan), pH meter (Eutech instrument, Singapore), hardness tester (Veego, India), friabilator (Veego, India), digital vernier caliper (SDK, China), sonicator (Hwasin Technology, Korea) and densitometer (Veego, India) were used.

Preparation of matrix tablets

According to the formulation given in Table I, accurately weighted ingredients (except magnesium stearate and talc) were taken in a mortar and blended well with pestle for about 5 minutes. Then magnesium stearate and talc were added and mixed with the previous mixture. Particular attention has been given to ensure through mixing and phase homogenization. The appropriate amounts of the mixture were accurately weighted in an electronic balance for the preparation of each tablet. Now, this mixture was taken in a Perkin-Elmer hydraulic press equipped with 13 mm diameter flat faced punch and die set (punch and die were previously lubricated with a 1% dispersion of magnesium stearate in ethanol) and using 5 tonnes pressure it was compacted and it was left in this compact state for about 5 minutes. Finally the upper punch was withdrawn and tablet was ejected. Thus each tablet of 13 mm diameter was prepared.

Table I. Formulation of different hydrophilic polymer based matrix tablets.

Formula	Drug (Aceclofenac)	HPMC K 100 cps	CMC 50,000 cps	Methocel K15M CR	Kollidon K30	Starch 1500	Mg-Stearate	Talc	TOTAL
1	100	80	-	-	20	160	5	5	370
2	100	160	-	-	20	80	5	5	370
3	100	-	80	-	20	160	5	5	370
4	100	-	160	-	20	80	5	5	370
5	100	-	-	80	20	160	5	5	370
6	100	-	-	160	20	80	5	5	370
7	100	-	80	80	20	80	5	5	370
8	100	-	50	110	20	80	5	5	370
9	100	-	110	50	20	80	5	5	370

Evaluation of flow property of the powder mix and physical parameters of the prepared tablets

The powder mixture (without adding magnesium stearate and talc) was tested for their flow property. Bulk density, tapped density, Carr's compressibility index (Wells *et al.*, 1998), Hausner ratio ((Wells *et al.*, 1998) and angle of repose (Raghuram *et al.*, 2003) were determined. Tablets were evaluated for their diameter, thickness, weight, hardness, axial tensile strength (Fell *et al*., 1968), radial tensile strength (Fell *et al.*, 1968)) and friability (Ruiz *et al.*, 2006).

***In vitro* dissolution study**

In vitro drug release studies from the prepared matrix tablets were conducted for a period of 10 hours using an USP dissolution apparatus II (perfect sink conditions) set at 50 r.p.m. and a temperature of 37 ± 0.5° C. The tablets were placed in 750 ml of a 0.1N HCl solution at pH 1.5 for 2 hours. After 2 hours, the acid stage was changed into buffer stage followed by addition of 250 ml 0.2 M tribasic sodium phosphate into 750 ml of 0.1N HCl to raise the pH up to 6.8. The study continued for a further 8 hours. At specified intervals (2 hours) 10 ml samples were withdrawn from the dissolution medium and replaced with fresh medium to keep the volume constant. After appropriate dilution, the samples were filtered through a Whatmaan filter paper (0.45 µm) and diluted to a suitable concentration with required media. The sample solution was analyzed at 276 nm for the presence of aceclofenac, using UV Spectrophotometer. The amount of drug released was calculated using the calibration curves constructed in the two dissolution media.

Release kinetics

The suitability of several equations that are reported in the literature to identify the mechanisms for the release of NAP from SR portion was tested with respect to the release data. The data were evaluated according to the following equations:

Zero-order model (Donbrow et al., 1980):

$M_t = M_0 + K_0 t$ …… (1)

Higuchi model (Higuchi, 1961; Higuchi, 1963):

$M_t = M_0 + K_H t^{0.5}$ …….. (2)

Korsmeyer-Peppas model (Korsmeyer *et al.*, 1983; Peppas, 1985):

$M_t = M_0 + K\, t^n$ ……... (3)

Where Mt is the amount of drug dissolved in time t, M_0 is the initial amount of drug, K_0 is the zero-order release constant, K_H is the Higuchi rate constant, K is a release constant and n is the release exponent that characterizes the mechanism of drug release.

The magnitude of the exponent n indicates that the release mechanism is Fickian diffusion, case II transport or anomalous transport. In the present study (cylindrical shape) the limits considered were n = 0.45 (indicates a classical Fickian diffusion-controlled drug release) and n = 0.89 (indicates a case II relaxational release transport: polymer relaxation controls drug delivery). Values of n between 0.45 and 0.89 can be regarded as indicators of both phenomena (transport corresponding to coupled drug diffusion in the hydrated matrix and polymer relaxation), commonly called anomalous non-Fickian transport. Values of n greater than 0.89 indicates super case II transport, in which a pronounced acceleration in solute release by a film occurs toward the latter stages of release experiments, resulting in a more rapid relaxation-controlled transport (Jacques *et al.*, 1974).

Due to the differences in drug release kinetics, the constant k, though one of the measures of release rate, should not be used for comparison. Therefore, to characterize the drug release rates in different experimental conditions, mean dissolution time (MDT) was calculated from dissolution according to Mockel and Lippold (Mockel *et al.*, 1993) using the following equation:

$MDT = n \times (K^{-1/n})/ (n+1)$……. (4)

Where n is the release exponent and K is the kinetic constant calculated from Equation 3.

The similarity factor was used to compare the difference of dissolution profiles of the test matrix tablets is given below:

$$f_2 = 50\log\left\{\left[1 + \frac{1}{n}\sum_{t=1}^{n}(R_t - T_t)^2\right]^{-0.5} \times 100\right\} \quad (5)$$

where R_t and T_t are the percentage of drug dissolved at each time point for the test and reference products, respectively and n is the number of dissolution samples taken The US Food and Drug Administration and the European Agency for the Evaluation of Medicinal Products have suggested that 2 dissolution profiles can be considered similar if f_2 is between 50 and 100 (CDER, 2006; EMEA, 2006).

Determination of Swelling: Eroding Behavior

The swelling-eroding behavior of matrix tablets was determined by the method reported by Al-Taani *et al.,* 2003. Matrix tablet was introduced into the dissolution apparatus under the standard set of conditions as specified for determination of *in vitro* drug release. The tablets were removed using a small basket and swollen weight of each tablet was determined. To determine matrix erosion, swollen tablets were placed in a vacuum oven at 40^{o} C and after 48 hours tablets were removed and weighed. Swelling (%) and erosion (%) was calculated according to the following formula, where S is the weight of the matrix after swelling; R is the weight of the eroded matrix; and T is the initial weight of the matrix

% Swelling = S/Rx100 …… (7)

% Erosion = (T - R)/T x100 ……..….. (8)

Statistical analysis

The dissolution data were treated using one way repeated measure ANOVA (SPSS software, version 16.0).

Results and Discussion

The granules of different formulations were evaluated for angle of repose, tapped density (TD), poured density (PD), Carr's index and Hausner ratio (HR) (Table II). The results of angle of repose and Carr's index ranged from 30.890 to 34.890 and 19.231 to 26.485 respectively. A good correlation observed between Carr's compressibility index and angle of repose in case of nine formulations (Fig. 1). Hausner ratios were within the range of 1.238 to 1.360. If the value of angle of repose present in the range of 30-34, it indicates the flow property of the powder mix is passable (the flow can be improved by adding glident) (Wells *et al.,* 1998). If the value of Carr's compressibility index is within the range of 18-21, it indicates the flow might be fair to passable and if it is within 23 to 25, it indicates poor flow (Wells *et al.,* 1998). From the Carr's compressibility index given in table II, it is observed that F-3 and F-5 showed fair to passable flow and the rest of the formulations gave poor flow, which can be improved by using glident. If the Hausner ratio is less than 1.25, it indicates good flow and if it is within 1.25 to 1.50, it gives poor flow which also can be improved using glident. Due to the above reason, magnesium stearate and talc were used in all formulation to improve their flow property.

The tablets were prepared according to the formulation given in table I by direct compression method. The prepared tablets were evaluated for their diameter, thickness, uniformity of weight, friability, axial tensile strength and radial tensile strength (Table III). The average weight, average diameter and average thickness ranged from 369.520 mg to 371.500 mg, 13.090 mm to 13.150 mm and 2.220 mm to 2.660 mm respectively. The friability value lied within 0.140% to 0.880%. From the values of axial and radial tensile strength, it can be stated that F-3 and F-6 showed highest radial (0.100 and 0.183 kg/mm^2 respectively) as well as axial tensile strength (0.038 and 0.074 kg/mm^2). The correlation between axial and radial tensile strength was shown in Fig. 2.

Swelling studies were carried out in order to investigate whether the extent of swelling varied for the different formulations. When a matrix comes into contact with an aqueous solution, wetting occurs at the surface and then progressing into the matrix through microscopic pores. The nature of the polymer plays an important role in this swelling process of the matrix tablets. The presence of water in the polymer

Table II. Flow properties of powder mix (without adding glident) of different formulations

Formula	Bulk density (gm/cm^3)	Tapped desity (gm/cm^3)	Compressibility index (in percent)	Hausner ratio	Angle of repose (Degree)
F-1	0.500	0.670	25.373	1.340	34.890
F-2	0.444	0.591	24.758	1.329	33.560
F-3	0.590	0.735	19.672	1.245	30.890
F-4	0.552	0.750	26.485	1.360	34.250
F-5	0.538	0.667	19.231	1.238	30.890
F-6	0.500	0.656	23.810	1.313	31.420
F-7	0.519	0.683	24.074	1.317	33.890
F-8	0.520	0.698	25.488	1.342	34.120
F-9	0.533	0.690	22.671	1.293	32.560

θ

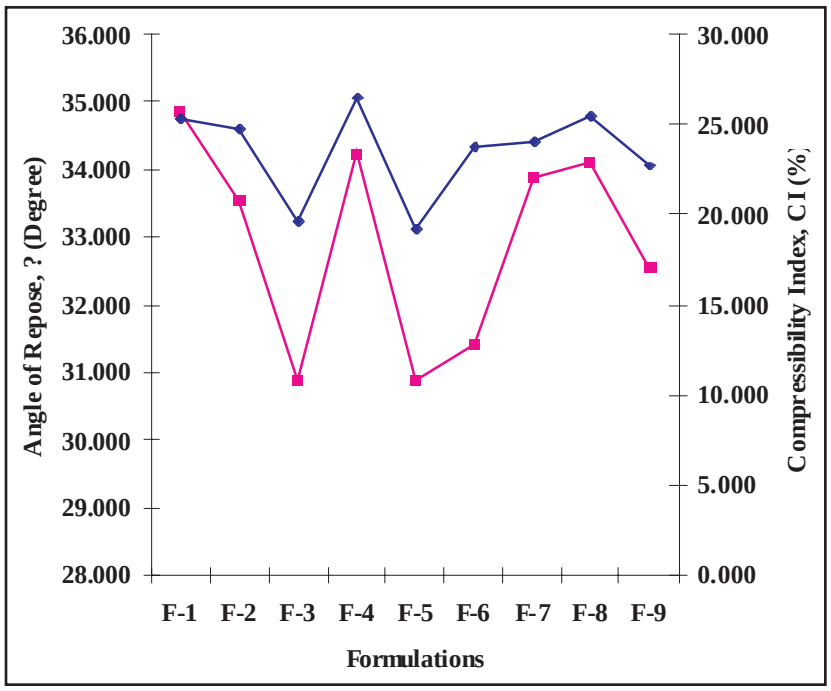

Fig. 1. Relationship between Carr's Compressibility Index, CI (%) and Angle of Repose, θ (degrees) of different formulations of hydrophilic polymer based matrix tablets

Table III. Physical parameters of different formulations of hydrophilic polymer based matrix tablets*

Formula	Avg. wt. (mg)	Avg. diameter (mm)	Avg. thickness (mm)	Friability (in percent)	Axial tensile strength (kg/mm^2)	Radial tensile Strength (kg/mm^2)
F-1	371.500	13.090	2.460	0.850	0.010	0.028
F-2	370.250	13.140	2.420	0.880	0.018	0.048
F-3	371.060	13.140	2.520	0.140	0.038	0.100
F-4	369.880	13.150	2.220	0.260	0.015	0.044
F-5	369.520	13.100	2.480	0.250	0.015	0.039
F-6	370.450	13.100	2.660	0.150	0.074	0.183
F-7	370.520	13.110	2.440	0.250	0.001	0.004
F-8	369.890	13.110	2.440	0.260	0.024	0.064
F-9	370.450	13.120	2.360	0.250	0.013	0.037

* Mean value of three tablets

causes a certain amount of stress, resulting in hydration of the polymer, which starts to swell yielding a gelatinous viscous layer (Korsmeyer *et al.*, 1983). Matrix erosion and dissolution systems can provide means of overcoming the well-known advantage of a purely diffusion control system. Synchronization between erosion and diffusion fronts has been identified to produce zero order drug release (Durig *et al.*, 1999). In order to understand the influence of the hydrophilic polymer system on drug release, swelling and erosion study on matrices containing the polymers only was evaluated. Since both swelling and erosion occurred simultaneously in the matrix, zero order release can be obtained in such types of matrices (Padmalatha *et al.*, 1989). This behavior is responsible for maintaining zero order release in which the increase in diffusion path length due to swelling is balanced with the decrease in the diffusion path length due to matrix erosion. Overall a constant diffusion path length is maintained. From the swelling and erosion study, it was observed that swelling and erosion took place simultaneously.

2 2

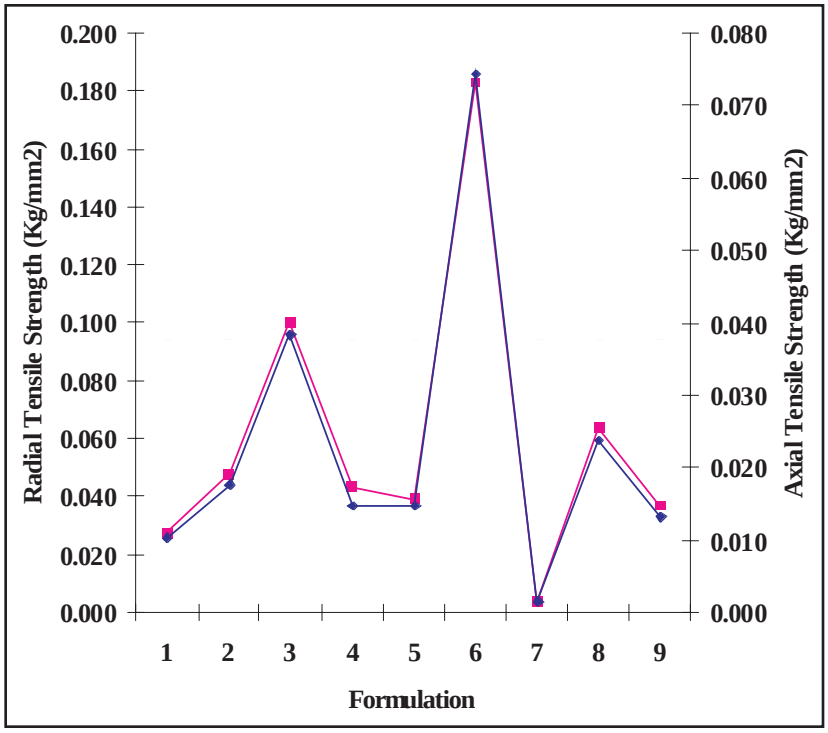

Fig. 2. Relationship between axial tensile strength (Kg/mm²) and radial tensile strength (Kg/mm²) of different formulations of hydrophilic polymer based matrix tablets

Upon placement in an aqueous medium, several processes occur simultaneously and influence drug release, namely, solvent uptake, swelling of the matrix, dissolution of the drug, and hydration and dissolution of the polymer chain due to chain disentanglement (Reynolds *et al*., 1999). Tablets of nine formulations were tested for swelling and erosion study. F-1 and F-2 showed no swelling of the matrix rather rapid disintegration. That's why figure 3 was constructed to represent the swelling and erosion index of F-3 to F-9. All of the seven formulations were found to be swelled up to 7 hours.

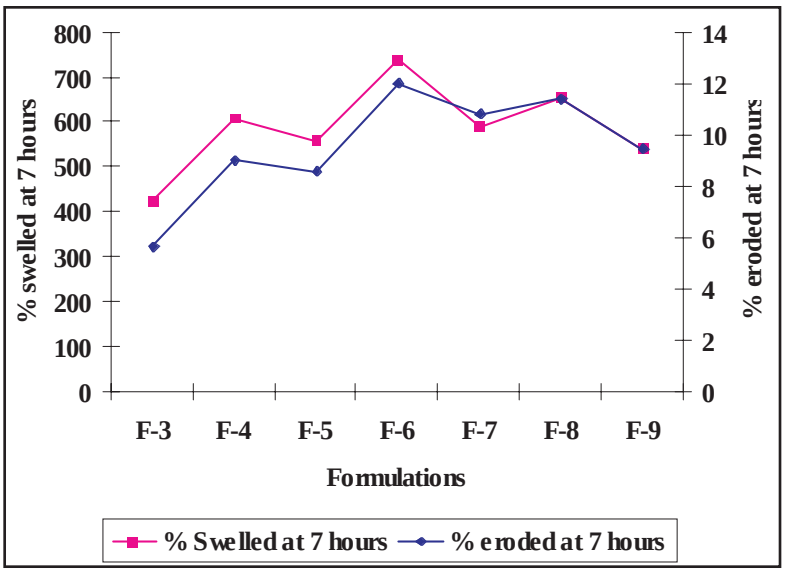

Fig. 3. Comparison of swelling and erosion index (at 7 hours) of different formulations of hydrophilic polymer based matrix tablets

Between F-3 (contained 21.622% CMC 50,000 cps) and F-4 (contained 43.243% CMC 50,000 cps), F-4 showed more swelling and erosion index than F-3. The same result was observed for F-5 (contained 21.622% methocel K15M CR) and F-6 (contained 43.243% methocel K15M CR). From the observation it is clear that with increasing hydrophilic polymer concentration, swelling index were increased. Swelling and erosion index of F-5 and F-6 were more than that of F-3 and F-4. Methocel K 15M CR is a hydrophilic polymer with higher viscosity and control release grade. So, the swelling and eroding property of this polymer was found to be more than CMC 50,000 cps. Among all of the formulations F-6 showed highest swelling index (740.55%) as well as erosion index (12.017%) at 7 hours. In case of combined polymer containing formulations, F-8 showed more swelling index (652.439%) and erosion index (11.351%) than F-7 and F-9 (Fig. 3).

From the dissolution study it was observed that the release rate of aceclofenac in first two hours in acid media was so negligible (less than 1%), that's why the result was not shown in the release curve (Figure 4). At this pH, aceclofenac exists in its acidic form which is well known to be practically insoluble in the stomach (Sheu *et al.*, 1992). When the dissolution was changed to pH 6.8 phosphate buffer media, the drug release rate was slightly increased, possibly because the aceclofenac was partially converted to aceclofenac salt which is soluble (Yesmin *et al.*, 2008). In pH 6.8 phosphate buffer media, F-1 (contained 21.622% HPMC K100 cps) and F-2 (contained 43.243% HPMC L100 cps) released about more than 65% drug at 1 hour. So, it can be said that HPMC K100 cps had not so much sustained action at those concentrations. F-3 and F-4 contained 21.622% and 43.243% CMC 50,000 cps respectively and released about 68.705% and 45.901% drug at the end of 8 hours. CMC 50,000 cps had the capability to retard the release of aceclofenac upto 8 hours. Again, F-5 and F-6 (having 21.622% and 43.243% methocel K15M CR) showed the release of 30.350% and 34.491% drug at 8 hours. Among the three types of hydrophilic polymers, methocel K15M CR was found to be more rate retarding than the other two. By increasing the concentration of polymers, release rate of drug were found to be decreased. F-7 to F-9 were prepared using combined hydrophilic polymers. F-7 (contained 21.622% CMC 50,000 cps and same percent of methocel K15M CR) released 33.791%, F-8 (contained 13.514% CMC 50,000 cps and 29.729% methocel K 15M CR) released 29.070% and F-9 (contained 29.729% CMC 50,000 cps and 13.514% methocel K 15M CR) released 40.021% aceclofenac at 8 hours. Among the combined polymer containing formulations, F-8 was found to be more rate retarding than F-7 and F-9 as it contained higher concentration of methocel K15M CR, which was found to be more sustaining one.

The dissolution data were used to calculate repeated measures ANOVA and post hoc test using SPSS software (version

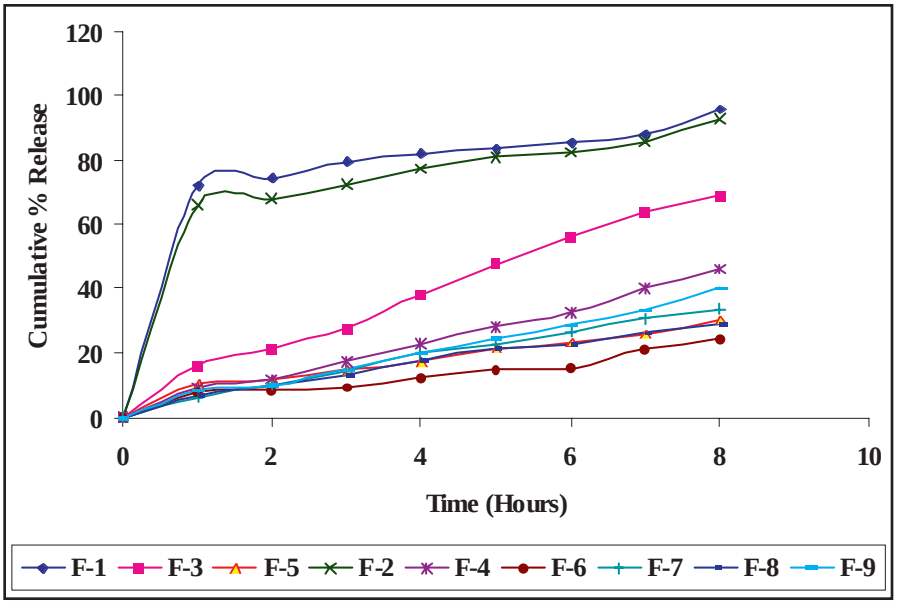

Fig. 4. Zero order release kinetics of different formulations of hydrophilic polymer based matrix tablets

16.0). The within subject effect showed calculated F = $2.509X10^6$ for all methods p value = 0.000. So, time is highly significant at any reasonable level of significance. Thus it can be concluded that the percent release on time differed significantly. The multiple comparisons (Bonferroni and Dunnett) were also carried out. Dunett t tests treat one group as a control and compare all other groups against it. The paired comparison of the six groups with the control group give p value = 0.001, whereas the comparison among F-5, F-7 and F-8 gives p value = 1.0, meaning the release profile of F-5, F-7 and F-8 measured at different time points are very much similar to that of the control group. Finally it can be stated that there was significant difference between the release patterns of aceclofenac from F-1 to F-6 and F-9 ($p< 0.05$). While determining similarity factor, f_2, the dissolution data of F-6 was considered as reference standard and that of F-4 to F-5 and F-7 to F-9 formulations were found to be more similar to F-6 as their value were within 50-100 (Table IV). This is according to the result obtained from ANOVA.

Table IV. Kinetic data obtained from various plot and f_2 values.

Formulation	Zero order		Higuchi		Korsmeyer			MDT	
	K_o	R^2	K_H	R^2	R^2	K_k	n		f_2
F-1	15.156	-0.221	38.205	0.663	0.894	0.699	0.122	2.064	30.306
F-2	14.551	-0.040	36.487	0.749	0.919	0.629	0.159	2.525	31.218
F-3	9.154	0.980	21.625	0.920	0.970	0.141	0.745	5.897	42.056
F-4	5.691	0.990	13.350	0.885	0.962	0.080	0.792	10.725	60.509
F-5	4.017	0.890	9.639	0.969	0.944	0.091	0.525	33.057	75.617
F-6	3.002	0.910	7.133	0.895	0.851	0.064	0.542	55.401	REF
F-7	4.458	0.988	10.513	0.918	0.996	0.059	0.839	13.238	68.706
F-8	3.917	0.961	9.311	0.949	0.985	0.065	0.708	19.560	77.066
F-9	4.917	0.990	11.540	0.888	0.960	0.068	0.799	12.746	65.704

The data were treated with zero order, Higuchi and Korsmeyer model to interpret the release mechanisms from different formulations of tablets. The results were shown in Table IV. From Table IV, it was shown that release kinetics of most of the formulation were fitted to zero order (F-3, F-4, F-6 and F-9) and Korsmeyer model (F-1, F-2, F-7 and F-8) with regression coefficient of 0.910 to 990 (for zero order) and 0.894 to 0.996 (for Korsmeyer) respectively. So, it can be predicted that the release of aceclofenac from F-3, F-4, F-6 and F-9 is independent of the concentration of drug in depot. F-1 and F-2 showed quick release of aceclofenac within 1 hour (which can be justified by observing their rate constant value). F-7 and F-8 had the release exponent (n) value of 0.839 and 0.708 respectively. These values were-within 0.45 to 0.89, indicating the release mechanism from F-7 and F-8 were anomalous or non-Fickian or coupling of diffusion and erosion controlled. Only F-5 showed highest fitting with Higuchi model (R^2 = 0.969), indicating the release mechanism of aceclofenac from F-5 is mainly diffusion through porous matrix (Higuchi, 1963). Diffusion is related to transport of drug from the dosage matrix. As gradient varies, the drug is released, and the distance for diffusion increases. This could explain why the drug diffuses at a comparatively slower rate as the distance for diffusion increases, which is referred as square-root kinetics or Higuchi's kinetics (Korsmeyer *et al.*, 1983).

MDT is used to characterize the drug release rate from the dosage form and the retarding efficacy of the polymer. A higher MDT indicates a higher drug-retarding ability of the polymer and vice versa. The MDT value was found to be a function of polymer loading and viscosity grade of polymer. Table IV showed that MDT value was highest for F-6 (55.401 hours), then for F-5 (33.057 hours) and for F-8 (19.560 hours). Increasing the polymer concentration, the MDT's were found to be increased for these nine formulations. These observations are similar to the reported (Reza *et al.*, 2003).

Conclusion

The matrix tablets were prepared successfully using hydrophilic polymers. It can be concluded that with some rare exception, swelling and erosion index were increased with the increasing hydrophilicity as well as the viscosity grade of the polymer. Thus the hydrophilic polymer based

matrix tablets might release drug more slowly. A very viscous gel layer was formed around the matrix tablet and prevented the release of drug from depot. For that reason, their release rate constants were decreased and their MDT values were found to be increased.

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