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**Original Article**

# Formulation and *in vitro* evaluation of sustained release tablets of aceclofenac

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## ABSTRACT

The present work is based in designing sustained release Aceclofenac tablets that could be given once daily for the symptomatic treatment of pain and inflammation. Hydrophilic matrix Aceclofenac tablets by direct compression were formulated with HPMC K4M and HPMC K100M in the concentration of 6%, 9% and 11%. A total of such six formulations were analyzed in terms of pre-compresion and post compression parameters. They were then compared with marketed products in terms of dissolution. The results revealed that drug release decreases with increase in viscosity of polymer and on increasing polymer concentration, the dissolution retards. The dissolution of formulated tablets showed good similarity and difference factor with marketed products. The formulation with highest similarity factor and lowest difference factor was chosen as an optimized formulation and the correlation of dissolution of marketed product with optimized formulation was carried which showed good correlation with $R^2$=0.961. The drug release was fitted in different mathematical models to study model dependent analysis which showed that most formulations followed Higuchi model, some followed peppas and some zero order. Therefore, sustained release Aceclofenac tablets prepared using HPMC K100M could be the best rather than HPMC K4M for its sustaining actions.

Key words: Aceclofenac, sustained release, HPMC, dissolution, NSAID

## INTRODUCTION

The four most important goals in drug delivery systems are safety, stability, efficacy and convenience. With many drugs, the basic goal of therapy is to achieve a steady-state blood or tissue level that is therapeutically effective and nontoxic for an extended period of time. The design of proper dosage regimens is an important element in accomplishing this goal. A basic objective in dosage form design is to optimize the delivery of medication so as to achieve a measure of control of the therapeutic effect in the face of uncertain fluctuations in the in vivo environment in which drug release takes place. This is usually accomplished by maximizing drug availability, i.e., by attempting to attain a maximum rate and extend of drug absorption. However, control of drug action through formulation also implies controlling bioavailability to reduce drug absorption rates [1].
The basis of controlled drug delivery system is to alter the pharmacokinetics and pharmacodynamics of pharmacologically active moieties by using novel drug delivery system or by modifying the molecular structure and/ or physiological parameters inherent in a selected route of administration [2].

The U.S. Food and Drug Administration (FDA) defines an "sustained release dosage form is one that allows a reduction in dosing frequency from that necessitated by a conventional dosage form, such as a solution or an immediate release dosage form". Sustained release tablets and capsules are commonly taken only once or twice daily, compared with conventional forms that may have to take three or four times daily to achieve the same therapeutic effect. The sustained release product typically shows a smaller absorption rate constant compared to an immediate release product, because of slower absorption of the sustained release product. These dosage forms are designed to deliver the drug at a controlled and predetermined rate, thus maintaining a therapeutically effective concentration of the drug in the systemic circulation for a long period of time and therefore reducing the frequency of dosing and improving patient compliance. The basic goal of therapy is to

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achieve steady state blood level that is therapeutically effective and non-toxic for an extended period of time.

## MATERIALS AND METHODS

**Materials:** The drug molecule Aceclofenac was received as gift sample from Lomus Pharmaceuticals Pvt. Ltd., Gothatar, Bhaktapur, Nepal. Methocel K4M Premium CR was obtained from Deurali-Janta Pharmaceuticals Pvt. Ltd., Dhapasi, Kathmandu, as gift sample and Methocel K100M Premium CR was purchased from Vijayadeep Pharmaceuticals Ltd., Saibu, Lalitpur. Other materials like microcrystalline cellulose, crosprovidone, magnesium stearate, purified talc, were also obtained from Lomus Pharmaceuticals Pvt. Ltd. Sodium hydroxide, potassium dihydrogen phosphate, methanol were obtained from Research Laboratory of National Model college for Advanced Learning. Aceclofenac standard was obtained from National Medicine Laboratory (NML) as gift sample. Marketed products were obtained from the local drug store (coded as MSR01 and MSR02) and used as reference product for Data analysis.

### Instruments and devices

1. Analytical balance (0.0001g); OHAUS AV114 Adventurer Pro.
2. 10- Station tablet Compression Machine; Model no.SPE-010, Shiv Pharma Engineers.
3. UV/Visible spectrophotometer; Model no. UV-1800, Shimadzu.
4. Dissolution Test Apparatus; Model 1918 & 1916, Electronics India.
5. Bath Sonicater; PCI Analytics Pvt. Ltd.
6. pH Meter; Labline Technologies Pvt. Ltd.
7. Friability Tester
8. BorosilGlasswares
9. Digital Vernier calipers, Mitutoyo
10. Tablet Hardness Tester, C-DHT 200/ Thermonik

### Methods

**Tablet Manufacture:** Tablets are the most popular type of dosage form for oral drug delivery, due their ease of administration, relatively simple fabrication and low cost. As described previously, they can readily be adapted to produce sustained drug delivery. For sustained release applications, tablets may be manufactured using the same techniques as for immediate release formulations, which include wet granulation, dry granulation and direct compression.

**Direct compression:** Direct compression offers improved efficiency, simplicity, and minimization of potential handling errors during manufacture, and it eliminates the intermediary processes of wet granulation, in that powders are merely weighed, sieved, blended and subsequently compressed. The simplicity of this method of manufacture is offset by the limited number of excipients with the suitable flow and cohesive properties that may be tableted in this way, and by practical complications that arise due to variables such as ambient temperature and relative humidity. In recent years, a variety of free-flowing, highly compressible excipients have become available as a result of novel methods of preparation. Excipients such as spray-dried lactose and microcrystalline cellulose fall into this category. In addition, tablet presses using forced or induced feeders can ensure adequate and constant filling of die cavities with powders that do not exhibit optimum gravitational flow thus enhancing the tableting process.

**Formulation of Aceclofenac SR by direct compression methods:** Tablets of six different formulations of matrix tablets were formulated as shown in table 1. The tablets were prepared by direct compression using two viscosity grades of HPMC i.e. K4M, K100M as matrix former. Initially drug and other additives (polymer and diluents) except magnesium stearate and talc were passed through 80 mesh sieve and thoroughly mixed in a polybag for 10 minutes. Then magnesium stearate and talc was added and further mixed for 5 minutes. The resulting mixture was fed into the die of 10 station tablet machine to produce matrix tablet using flat and round punches of 10 mm diameter. Each tablet contains aceclofenac BP 200mg.

### Preparation of chemical reagents [3].

***0.2M potassium dihydrogen phosphate:*** 21.7 gm of potassium dihydrogen phosphate was dissolved in about 500ml of water in 1000ml volumetric flask and the volume was then adjusted to 1000ml with purified water.

***0.2M sodium hydroxide:*** 8gm of sodium hydroxide was dissolved in about 500ml of purified water in 1000ml volumetric flask and the volume was adjusted to 1000 ml with purified water.

***Phosphate buffer pH 7.2:*** 50ml of 0.2 M potassium dihydrogen phosphate solution and 34 ml of 0.2M sodium hydrogen solution were taken in 200 ml of volumetric flask and the volume was adjusted to 200ml with purified water.

### Preparation of standard calibration curve

**Determination of λmax:** Weighed amount of Aceclofenac was dissolved in phosphate buffer pH 7.2 to obtain a 1000mcg/mL solution. This solution was subjected to scanning between 200 – 400 nm and absorption maximum was determined. The effect of dilution on absorption maxima was

studied by diluting the above solution to 20mcg/mL and scanned from 200 – 400nm.

**Preparation of standard calibration curve in phosphate buffer pH7.2:** A stock solution of standard aceclofenac of 100µg/ml concentration was prepared in phosphate buffer pH7.2. The stock solution was then used to prepare the standard working solution of five different concentrations 10, 15, 20, 25, 30 µg/ml respectively. The absorbance of each sample solution was measured at 273nm using phosphate buffer pH7.2 as a blank and calibration curve with absorbance vs. concentration was plotted.

**Preparation of standard calibration curve in methanol:** A stock solution of standard aceclofenac of 100µg/ml concentration was prepared in methanol. The stock solution was then used to prepare the standard working solution of five different concentration 10, 15, 20, 25, 30 µg/ml respectively. The absorbance of each sample solution was measured at 275nm using methanol as a blank and calibration curve with absorbance vs. concentration was plotted.

**Physical characterization of tablet**

**Weight variation:** Twenty tablets were randomly selected and weighed individually to determine the weight variation. The result was expressed as average weight± standard deviation.

**Thickness:** 10 tablets were randomly selected and thickness was measured using digital vernier calipers. The result was expressed as average thickness ± standard deviation.

**Hardness:** Ten tablets were randomly selected and hardness was measured using monchanto hardness tester. The result was expressed as average hardness ± standard deviation.

**Friability:** Twenty tablets (>6.5g) from each batch were selected randomly and were weighed. The tablets were transferred to friability test apparatus which was operated at 25 rpm for 4 minutes or up to 100 revolutions. The difference in the weight is noted and expressed as percentage. Permitted friability limit is 1.0%.

**Assay:** 20 tablets from each batch were weighed and pulverized in a mortar. The samples of powder equivalent to average weight were taken and transferred to a 50ml volumetric flask. The powder was then dissolved in a methanol for 20 minutes. The solution was then filtered through Whatman no.1 filter paper and the filtrate was suitably diluted to produce final solution of 20µg/ml concentrations. The absorbance of the resulting solution was measured at 275nm. The process was repeated thrice and corresponding three reading were recorded.

***In- vitro* dissolution studies**

***In vitro* dissolution studies in 0.1 HCl:** The dissolution studies of formulated product was carried out in the tablet dissolution apparatus USP type II using 0.1 HCl thermostatically controlled at 37±0.5 °c. The dissolution studies were carried out at speed of 50 rpm for 2 hours. Samples were filtered and absorbance was measured using UV spectrophotometer at 272nm.

***In vitro* dissolution studies in 7.2 phosphate buffer:** The dissolution studies of formulated products and marketed products were carried out in the tablet dissolution apparatus USP type II using phosphate buffer pH 7.2 thermostatically controlled at 37±0.5 °c. The dissolution studies were carried out at speed of 50 rpm for 10 hours. 10ml of the sample was withdrawn at predetermined time interval followed by replacement with equal volume of the dissolution medium maintained at same condition. Samples were filtered and assayed using UV spectrophotometer at 273nm.

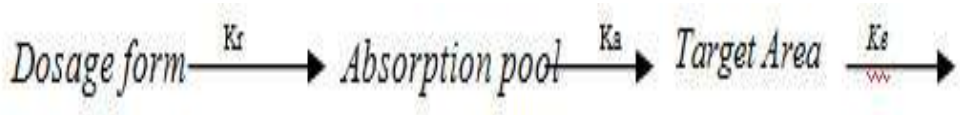
**Criterion for Controlled Drug Delivery Systems:**

To achieve the objectives of sustaining constant plasma drug level, the rate of drug delivery from the dosage form should be analogous to that achieved by continuous intravenous infusion. In intravenous infusion a drug is provided to the patient at a constant rate just equal to its elimination [4]. Therefore ideally, release from the dosage form should follow zero order kinetics, as shown by the equation

$K^0_r$=Rate In = Rate Out = $k_eC_dV_d$.. .. .. .. (4),

where $K^0_r$ is the zero-order rate constant for drug release (amount / time), $k_e$ is the first order rate constant for overall drug elimination (time $^{-1}$), $C_d$is the desired drug level in the body (amount /volume) and $V_d$is the volume space in which the drug is distributed.

In the case of conventional dosage form, the drug release from the dosage form is rapid and is immediately available for absorption. The rate of drug absorption is very slow as compared to the rate at which the drug is made available for absorption. This situation can be represented by the following simple kinetic scheme:



The absorption pool represents a solution of the drug at the site of absorption and the terms $K_r$, $K_a$ and $K_e$ are the first order rate constants for drug release, absorption, and overall elimination respectively. This implies that

$K_r >>> K_a$.. .. .. .. .. (5)

The rate of absorption of drug across a biological membrane is the rate-limiting step in delivering to its target area. But since the absorption of drug across biological membrane follows first order kinetics, this situation of rate of drug release being higher than the rate of drug absorption cannot fulfill the condition to achieve a constant plasma drug concentration. Initially the amount of drug at the site of absorption is high, and the rate of absorption is very high causing plasma concentration to rise sharply, whereas when the drug amount at the absorption site falls to a minimum, the rate of absorption is insufficient to replenish the depleted amount of drug in the plasma due to continuous excretion process causing plasma concentration to fall.

To achieve the condition of rate of elimination of drug being continuously compensated by the rate of drug input, the absorption phase should be insignificant and the rate-limiting factor for the drug delivery should be the release of the drug from the dosage form, i.e., the amount of drug released from the dosage form should be sufficiently enough to maintain the plasma concentration enough to elicit therapeutic effect and it should be immediately and completely absorbed into the blood stream. The critical criterion for achieving the sustained drug level in the plasma should therefore be

$K_r <<< K_a$ .. .. .. .. .. (6)

and the effort to develop a sustained release delivery system must be directed primarily at altering the release rate by affecting the value of $K_r$ to meet the criterion.

With this criterion drug release becomes the rate-limiting factor for drug absorption, and the zero-order release kinetics will result in zero-order drug absorption, and slow first order release kinetics will result in the first -order drug absorption kinetics. Accordingly four models have been proposed to define the pharmacokinetic parameters as they relate to sustained release dosage forms [5]. They are:

- Zero-order absorption followed by first-order elimination when the drug release is zero order kinetics,
- Slow first-order absorption followed by first-order elimination when the drug release follows slow first order kinetics,
- Rapid first-order absorption of part of the dose, then release and absorption of the remainder over an extended period of time by a zero-order kinetic process followed by first order elimination process, when there is an immediate release loading dose followed by a second maintenance dose released by zero-order kinetics over a prolonged period of time, and
- Rapid first-order absorption of part of the dose, then release and absorption of the remainder over an extended period of time by a slower first-order kinetic process followed by a first-order elimination process, when the loading dose is followed by slow first order release of drug over a long period of time.

Various mathematical models have been developed to study the release of the release of the drugs from dosage form.

**Zero-order Kinetics:** Drug dissolution from pharmaceutical dosage forms that do not integrate and release the drug slowly follows zero that area does not change and no equilibrium conditions are obtained i.e. the sink condition prevails throughout process, then it follows zero order kinetics. It can be represented as:

$Q_t = Q_o + K_o t$.... .. .. .. .. .. .. .. .. .. ..*(7)*

Where $Q_{t=}$ Amount of drug dissolved in time t

$Q_{o =}$ Initial amount of drug in the solution, which is often zero

$K_{o =}$ is the zero order release constant.

**First order kinetics:** This model was first proposed by Gibaldi & Feldman (1967) later by Wagner (1969). The pharmaceutical dosage forms containing water-soluble drugs in porous matrices follow first order release kinetics, and can be expressed by the equation:

$\text{Log } Q_t = \log Q_o + kt/ 2.303$.. .. .. .. .. .. .. ..*(8)*

This equation implies that a graphic of the decimal logarithm of the amount of drug versus time will be linear. The dosage forms that follow this dissolution profile release the drug in a way that is proportional to the amount remaining in the interior of the dosage form, in such a way that the amount of drug released by unit of time diminishes.

**Korsmeyer-Peppas model:** Power law equation is more comprehensive very simple and semi-empirical equation developed by Korsmeyer-Peppas which can be used to analyze data of drug release from polymers. The equation implies that the fractional release of drug is exponentially related to release time and can be expressed as:

$Mt / M^{\infty} = kt^{n}$.. .. .. .. .. .. .. .. .. .. ..*(9)*

Where, Mt & $M^{\infty}$ are the absolute cumulative amounts of drug released at time t and infinity respectively k is a constant incorporating structural and geometrical characteristics of the device, and n is the exponent, indicative of the mechanism of drug release.

In many experiments including the case of drug release from polymeric systems, the mechanism of diffusion deviates from the Fickian equation and follows a non-Fickian (anomalous) behavior and the value of the exponent **n** changes. Peppas used the **n** value in order to characterize different release mechanisms. For a cylindrical shape, the value of the exponent suggested for Fickian diffusion is 0.45, and for Case II transport 0.89. A circular flat tablet matrix is considered as a cylindrical disc. For a spherical shape, the n for fickian diffusion is 0.43, and for Case II transport it is 0.85.

For drug release from a circular tablet matrix following Fickian diffusion, the exponent takes the value of 0.45, and therefore, plots of the initial drug release data from experiments carried out under perfect sink conditions, versus (time) $^{0.45}$ should give a straight line if Fickian diffusion is the predominant mechanism of release.

The Peppas model makes the following assumptions:

i) The generic equation is applicable to small values of *t* or for short times, and the portion of release curve where $M_t/M_\infty < 0.6$ should only be used,

ii) drug release occurs in one dimension only,

iii) The system's length to thickness ratio should be at least 10.

This model is generally used to analyze the release of polymeric dosage forms, when the release mechanism is not well known or when more than one type of release phenomena could be involved.

The generic equation takes the modified forms where there is lag time in the beginning of the drug release, and when there is a burst effect respectively as

$M_{(t-l)} / M_\infty = a (t-l)^{n}$ . . .. . . .. .. (10)

Where, l is the lag time.

And, $M_t / M_\infty = atn+b$.. .. .. .. .. (11)

Where, *b* is the burst effect.

When there is absence of lag time and burst effect, l=0 and b=0, therefore the equations simply revert to the generic equation.

Using the Power Law to analyze the drug release mechanism:

The generic equation of the Power Law in the natural logarithmic form takes the following form,

$\ln M_t / M_\infty = \ln a + n \ln t$ .. .. .. .. .. (12)

This form is analogous to a straight -line equation;Y=mX+ C

With Y= $\ln M_t / M_\infty$;m=n, and C=ln a.

Therefore a plot of $\ln M_t / M_\infty$ versus ln t should give a straight-line. The slope is the value of the exponent which indicates the mechanism of drug release, and from the constant C we can calculate the value of ***a***, the constant associated with the geometry of the matrix. The *n* is also known as the diffusional exponent and the constant *a*, is known as the kinetic constant.

**Higuchi Model:** In 1961 Higuchi introduced the most famous and often used mathematical equation to describe the release rate of drugs from matrix system initially; it was valid only for planar systems. It was later modified and extended to consider different Geometries and matrix characteristics including porous structure. Higuchi developed an equation for the release of a drug from an ointment base and later applied it to diffusion of solid drugs dispersed in homogeneous and granular matrix dosage system. This can be expressed as:

$Q = Kt^{1/2}$.... .. .. .. .. .. .. .. .. .. (13)

Where k is the constant, so that a plot of amount of drug released vs the square root of time should be linear if the release of the drug from the matrix is diffusion controlled. The release rate of the drug from such device, however, is not zero.

**The Hixson-Crowell cube root:** The Hixson-Crowell cube root describes the release from systems where there is a change in surface area and diameter of particles or tablets. This can be expressed as:

$$\sqrt[3]{M_0} - \sqrt[3]{M_t} = kt \quad \ldots\ldots\ldots\ldots\ldots\ldots (14)$$

Where $M_0$ is the initial amount of drug in the pharmaceutical dosage form, $M_t$ *is* the remaining amount of drug at time t and k is a constant incorporating surface volume relation [6, 7].

## RESULTS AND DISCUSSIONS

**Calibration curve of Aceclofenac in phosphate buffer pH 7.2:** Calibration curve prepared for a concentration of 10, 15, 20, 25, 30µg/ml of Aceclofenac reference standard in 7.2 phosphate bufferon272 nm showed correlation coefficient ($R^2$) value of 0.9875 (Figure 1).

**Calibration curve for Aceclofenac in methanol:** Calibration curve for Aceclofenac RS in methanol was prepared to determine the assay of the marketed and formulated products (Figure 2 and Table 3). The correlation coefficient ($R^2$) value of the calibration curve of Aceclofenac standard in methanol was found to be 0.9969.

**Dissolution in 0.1 HCl:** The absorbance of 20 µg/ml Aceclofenac RS in 0.1 HCl at 272 nm was found to be 0.009 and formulated batch ASR01 was found to be 0.007 which was far less in comparison to the 7.2 Phosphate buffer. This was due to the very low solubility of Aceclofenac in 0.1 HCl.

**Physicochemical parameters of marketed and formulated products:** The weight of marketed products ranged between 350 to 366 for MSR01 and 367.9 to 375.1 for MSR02. The weights of all formulated products also were within the limit as shown in table 4. The thickness of marketed product was found between 4.22mm to 4.24mm for MSR01 and 4.34mm to 4.36mm and that of formulated products was found in the range of 3.51mm to 3.52mm for ASR01, 3.31mm to 3.42mm for ASR02, 3.19mm to 3.26mm for ASR03, 3.32mm to 3.38mm ASR04, 3.26mm to 3.35mm for ASR05, 3.16mm to 3.29mm for ASR06 as shown in table 4. The hardness of marketed products was found within the range of 14.8kg/cm$^2$to 15.4 kg/cm$^2$for MSR01 and 12kg/cm$^2$ to 12.4kg/cm$^2$ for MSR02 and that of formulated products was found in the range of 14kg/cm$^2$ to 14.7 kg/cm$^2$as shown in table 5. The assay values of two marketed products were 100.42% for MSR01 and 104.32% for MSR02 on an average. The assay values of formulated products were found in the range of 97.85% to 105.05% in average as shown in table 5.

### *In Vitro* Dissolution Study

**Effect of polymer level on dissolution profile:** The dissolution profile of ASR01, ASR02 and ASR03 with 11%(40mg), 9%(30mg) and 6%(20mg) of HPMC K4M respectively was studied which showed that increasing the concentration of HPMC K4M retards the drug release in a linear fashion as shown in Figure 4. The mechanism underlying this is that the drug release from hydrophilic matrix system is controlled by the hydrogel of HPMC, which forms a gelatinous barrier layer at the surface of the matrix, through which the included drug diffuses [4]. The primary factor for controlled drug release is the interaction between the water, drug and the polymer. The dissolution profile of ASR03, ASR04 and ASR05 with 11%(40mg), 9%(30mg) and 6% (20mg) of HPMC K100M respectively was studied which showed that increasing the concentration of HPMC K100M retards the drug release in a linear fashion as shown in Figure 5.

**Effect of level of polymer viscosity in dissolution profile:** The dissolution profile of two formulations ASR01 and ASR04 with 11% i.e. 40mg of polymer were studied. Initial burst release was high with polymer HPMC K4M, but with HPMC K100M burst release and dissolution profile was slightly different as given in figure 6. The reason for this change in dissolution profile might be due to existence of a threshold value for viscosity of the polymer. The decrease in drug release percentage in formulations using HPMC K100M might be due to thick gel formation by polymer when it comes in contact with water and hindered the drug diffusion greatly. While in formulation with lower polymer viscosity showed increase in drug release percentage it might be due to enhanced polymer relaxation and with the decrease in viscosity the strength of gel layer is diminished and the drug release is accompanied by some surface erosion of the polymer matrix [4, 8].

The dissolution profile of two formulations ASR02 and ASR05 with 9% i.e. 20mg of polymer were studied and found that the formulation with higher viscosity grade retards the drug release or shows greater sustained release effect as shown in figure 7.

***In vitro* dissolution studies of two marketed products:** The dissolution studies of two reference products coded as MSR01 and MSR02 was carried

out in 900 ml of phosphate buffer pH 7.2. The dissolution profiles obtained is shown in figure 9.When dissolution profiles between two marketed products were compared it was found that MSR01 showed better sustained release profile than MSR02.

**Similarity and dissimilarity factor with marketed product MS01:** The similarity and difference factor of all the formulations was obtained with the marketed product MSR01 as in table 8. It showed that the greatest similarity factor (69.55) and lowest difference factor (5.72) with marketed product was of ASR01. So, this formulation was considered optimized formulation and correlation of dissolution of this formulation was carried with marketed product which showed good correlation with $R^2$ value=0.969 in figure 11. When the drug release profiles were analyzed by one way ANOVA it showed there was not a significant difference in release rates between marketed and optimized formulations with $p>0.05$($p= 0.000$) and with good correlation in the dissolution profiles ($R^2$adj=0.961) as shown by figure 10.

**Study on Kinetic models of formulated and marketed products:** The drug release profile was fitted in different mathematical models which showed that all formulations followed either Higuchi or Peppas model and some formulations followed zero order (table 7). This showed that most drug followed diffusion controlled drug release which is in coherence with available literatures [4, 9, and 10]. When data analyzed using power law drug release kinetics of all formulation and MSR01 followed Fickian diffusion whereas MSR02 followed Super Case-II transport.

## CONCLUSIONS

Aceclofenac sustained release tablets were formulated by direct compression with varying grades and concentration of HPMC, a hydrophilic polymer. The drug release was found to vary with viscosity and concentration of polymer. The formulated tablets were compared with marketed formulation in terms of similarity and difference factor which showed good similarity. Therefore, sustained release Aceclofenac tablets can be prepared by using HPMC of varying viscosity and concentration to be used once daily in conditions associated with pain and inflammation

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Table 1: Composition of formulated products

| Formulation no./composition (mg) | ASR01 | ASR02 | ASR03 | ASR04 | ASR05 | ASR06 |
|---|---|---|---|---|---|---|
| Aceclofenac | 200 | 200 | 200 | 200 | 200 | 200 |
| HPMC K4M | 40 | 30 | 20 | | | |
| HPMC K100M | | | | 40 | 30 | 20 |
| Microcrystalline cellulose | 100 | 100 | 100 | 100 | 100 | 100 |
| Crosprovidone | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 |
| Magnesium stearate | 3 | 3 | 3 | 3 | 3 | 3 |
| Talc | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 | 3.5 |
| Total weight | 350 | 340 | 330 | 350 | 340 | 330 |

Table 2: The absorbance of various concentrations of Aceclofenac RS in phosphate buffer pH 7.2

| Concentration(µg/ml) | Absorbance | | | |
|---|---|---|---|---|
| | Solution 1 | Solution 2 | Solution 3 | Mean ± SD |
| 10 | 0.272 | 0.274 | 0.275 | 0.276±0.001 |
| 15 | 0.498 | 0.497 | 0.498 | 0.497±0.0005 |
| 20 | 0.664 | 0.665 | 0.667 | 0.665±0.001 |
| 25 | 0.783 | 0.785 | 0.787 | 0.785±0.002 |
| 30 | 0.939 | 0.942 | 0.944 | 0.941±0.002 |

Table 3: The absorbance of various concentrations of Aceclofenac RS in Methanol

| Concentration(µg/ml) | Absorbance | | | |
|---|---|---|---|---|
| | Solution 1 | Solution 2 | Solution 3 | Mean ± SD |
| 10 | 0.392 | 0.394 | 0.392 | 0.392±0.001 |
| 15 | 0.563 | 0.566 | 0.564 | 0.564±0.001 |
| 20 | 0.728 | 0.726 | 0.725 | 0.726±0.001 |
| 25 | 0.919 | 0.919 | 0.92 | 0.919±0.005 |
| 30 | 1.046 | 1.046 | 1.044 | 1.045±0.001 |

Table 4: Weight variations and Thickness of marketed and formulated products

| Formulation no. | Weight variations Average(mg)± std.dev (n=20) | Thickness Average(mm)±std.dev (n=10) |
|---|---|---|
| ASR01 | 354.54±0.001 | 3.516±0.005 |
| ASR02 | 345.10±0.001 | 3.372±0.037 |
| ASR03 | 333.16±0.001 | 3.207±0.021 |
| ASR04 | 354.05±0.002 | 3.36±0.026 |
| ASR05 | 345.03±0.002 | 3.305±0.035 |
| ASR06 | 334.70±0.002 | 3.24±0.046 |
| MSR01 | 358.20±0.004 | 4.23±0.008 |
| MSR02 | 371.18±0.0 | 4.35±0.008 |

Table 5: Hardness, Friability, Diameter and Assay of marketed and formulated products

| Formulation no. | Hardness($kg/cm^2$) Average± Std. dev (n=20) | Friability (%) (n=20) | Assay (%) Average± Std. dev (n=3) |
|---|---|---|---|
| ASR01 | 14.43±0.18 | 0.13 | 100.66±0.67 |
| ASR02 | 14.39±0.16 | 0.33 | 104.29±0.87 |
| ASR03 | 14.26±0.21 | 0.18 | 97.93±0.13 |
| ASR04 | 14.31±0.11 | 0.15 | 99.88±1.10 |
| ASR05 | 14.40±0.12 | 0.41 | 100.84±0.57 |
| ASR06 | 14.36±0.08 | 0.13 | 98.87±0.64 |
| MSR01 | 15.10±0.21 | 0.06 | 100.42±0.76 |
| MSR02 | 12.20±0.17 | 0.09 | 104.32±1.06 |

Table 6: The dissolution profile of marketed and formulated products

| **Time (hrs)** | **Average drug release %** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | ASR01 | ASR02 | ASR03 | ASR04 | ASR05 | ASR06 | MSR01 | MSR02 |
| 1 | 40.28 | 40.58 | 67.23 | 27.29 | 32.06 | 51.11 | 44.79 | 4.21 |
| 2 | 49.22 | 52.35 | 73.11 | 38.04 | 40.03 | 60.14 | 47.9 | 13.74 |
| 3 | 52.11 | 61.85 | 80.83 | 46.21 | 49.08 | 71.29 | 51.93 | 25.37 |
| 6 | 66.9 | 73.95 | 90.92 | 58.81 | 60.03 | 80.75 | 60.36 | 74.92 |
| 8 | 73.32 | 81.71 | 95.10 | 68.97 | 72.12 | 85.07 | 69.7 | 99.57 |
| 10 | 79.63 | 83.21 | 95.16 | 72.32 | 78.03 | 94.81 | 75.75 | 111.75 |

Table 7: Kinetic Models

| Formulations | Zero order | | First order | | Higuchi | | Peppas | |
|---|---|---|---|---|---|---|---|---|
| | $R^2$ | K | $R^2$ | K | $R^2$ | K | $R^2$ | n |
| ASR01 | .9819 | 4.252 | .9523 | .0718 | .9964 | 18.06 | .9893 | .3087 |
| ASR02 | .916 | 4.563 | .8604 | .0732 | .9727 | 19.83 | .9372 | .3222 |
| ASR03 | .9053 | 3.158 | .8857 | .0384 | .9638 | 13.74 | .9529 | .1682 |
| ASR04 | .9565 | 4.869 | .8914 | .0996 | .9915 | 20.93 | .9571 | .4352 |
| ASR05 | .9796 | 5.008 | .9386 | .0936 | .9926 | 21.23 | .9822 | .4038 |
| ASR06 | .9420 | 4.415 | .9015 | .0613 | .9726 | 18.96 | .9573 | .2664 |
| MSR01 | .9956 | 3.460 | .9948 | .0507 | .9727 | 14.42 | .9887 | .2467 |
| MSR02 | .9846 | 12.868 | .8639 | .3379 | .9799 | 54.15 | .9408 | 1.487 |

Table 8: Similarity and dissimilarity factor of formulated batch with marketed product MSR01

| Formulation | Similarity factor | Dissimilarity factor |
|---|---|---|
| ASR01 | 69.55 | 5.72 |
| ASR02 | 51.41 | 14.73 |
| ASR03 | 29.57 | 43.35 |
| ASR04 | 52.95 | 11.069 |
| ASR05 | 59.53 | 8.127 |
| ASR06 | 39.44 | 26.46 |

Table 9: Similarity and dissimilarity factor of formulated products with marketed product MSR01

| Formulation | Similarity factor | Dissimilarity factor |
|---|---|---|
| ASR01 | 69.55 | 5.72 |
| ASR02 | 51.41 | 14.73 |
| ASR03 | 29.57 | 43.35 |
| ASR04 | 52.95 | 11.069 |
| ASR05 | 59.53 | 8.127 |
| ASR06 | 39.44 | 26.46 |

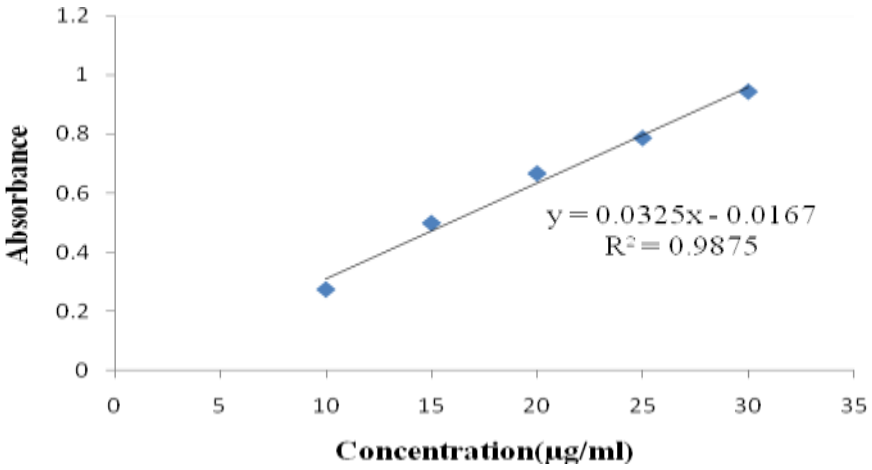


Figure 1: Calibration curve for Aceclofenac in phosphate buffer pH 7.2

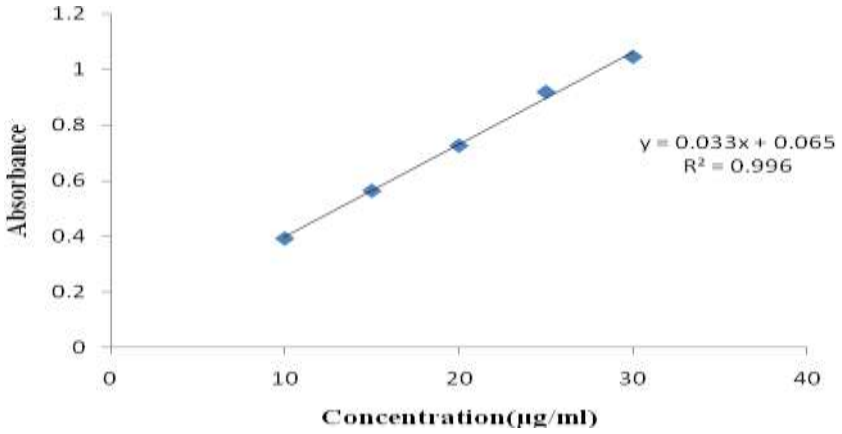


Figure 2: Calibration curve for Aceclofenac in methanol as medium

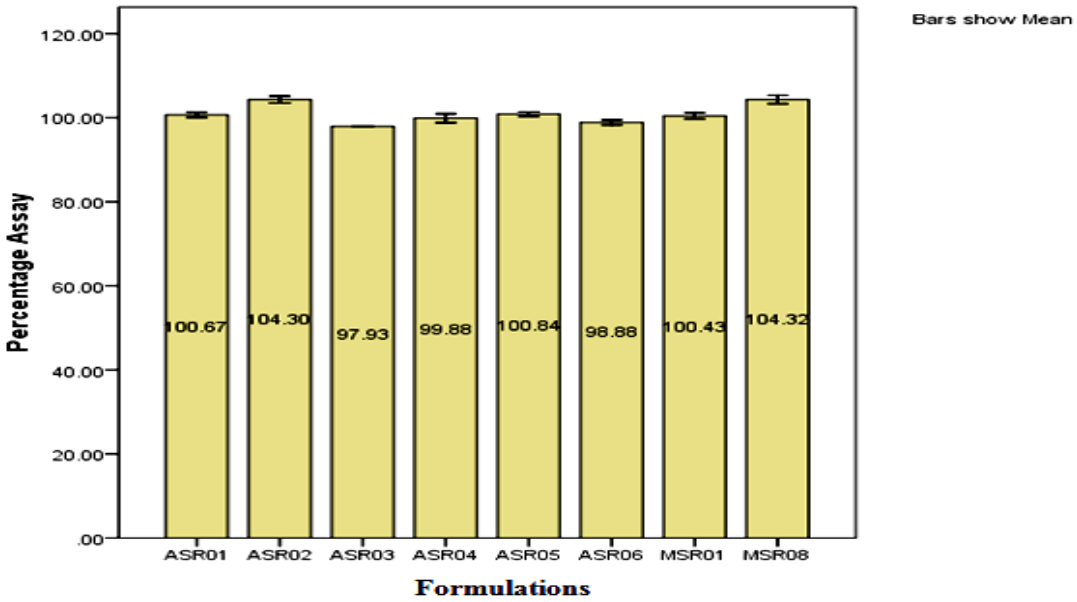


Figure 3: Bar diagram of Assay percentage of various formulated and marketed product

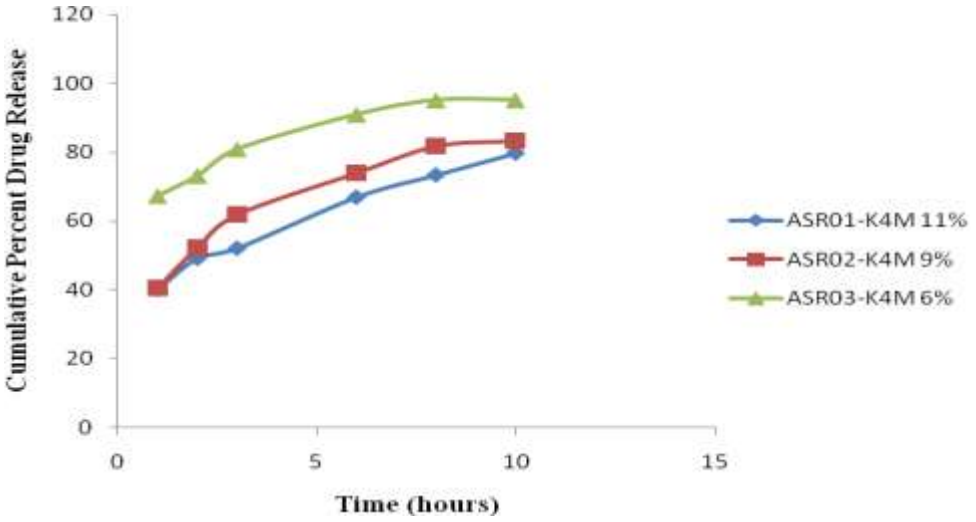


Figure 4: Effect of level of HPMC K4M concentration on dissolution profile

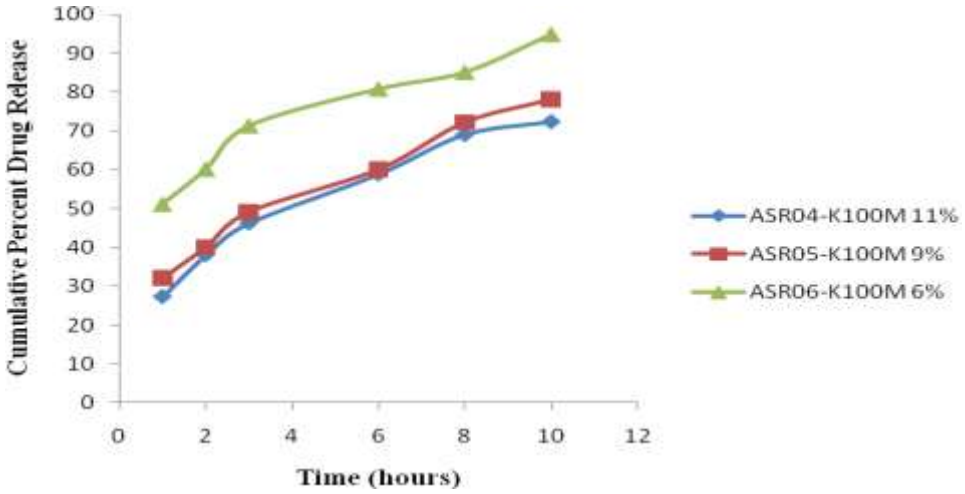


Figure 5: Effect of level of HPMC K100M concentration on dissolution profile

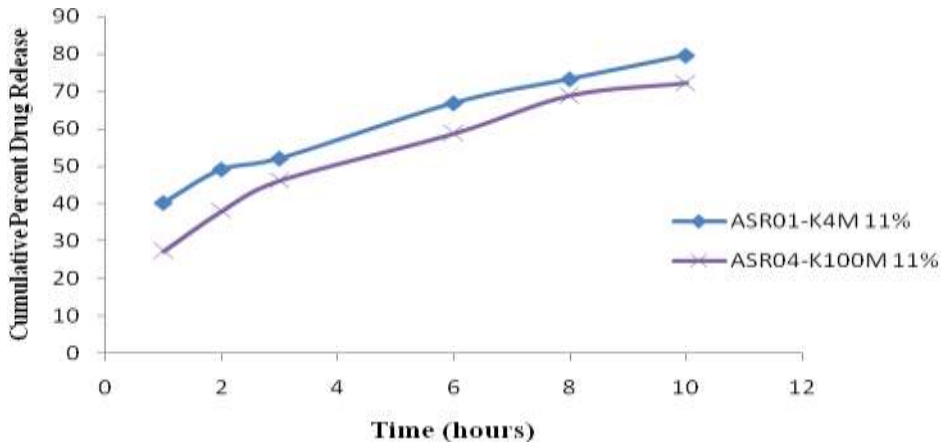


Figure 6: Effect of level of polymer viscosity in dissolution profile with 11% of polymer

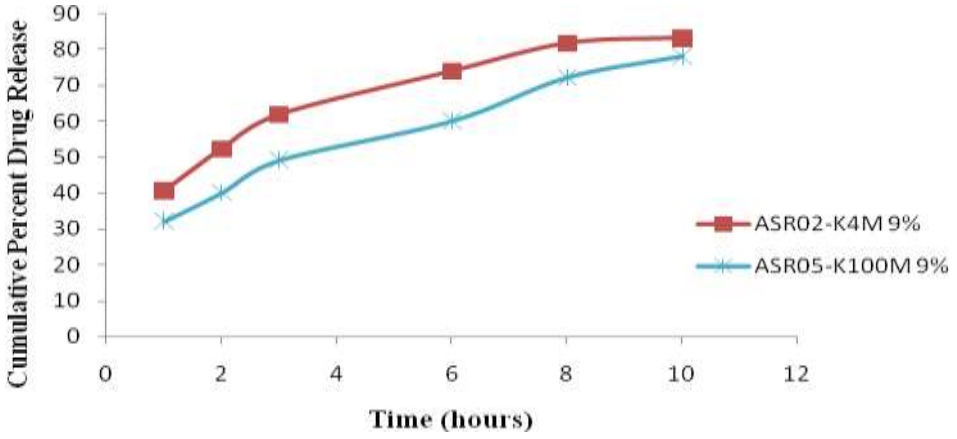


Figure 7: Effect of level of polymer viscosity in dissolution profile with 9% of polymer

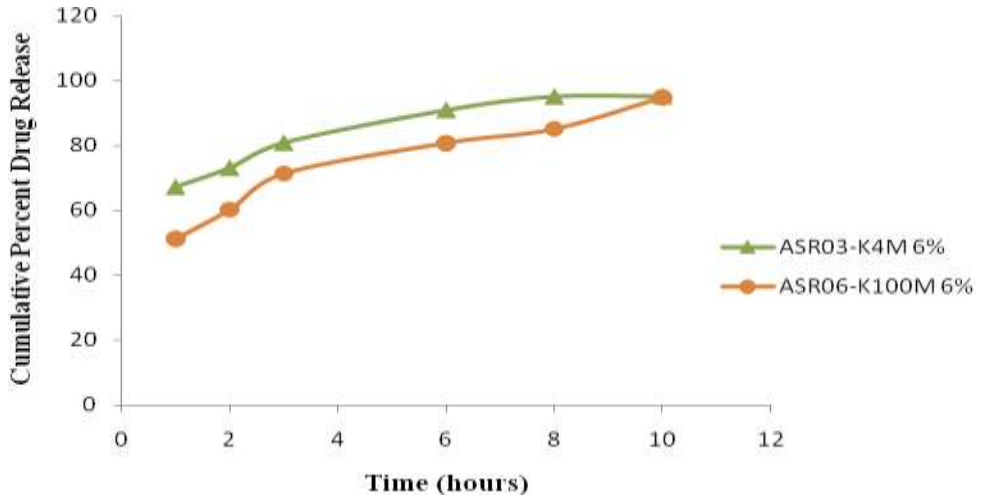


Figure 8: Effect of level of polymer viscosity in dissolution profile with 6% of polymer

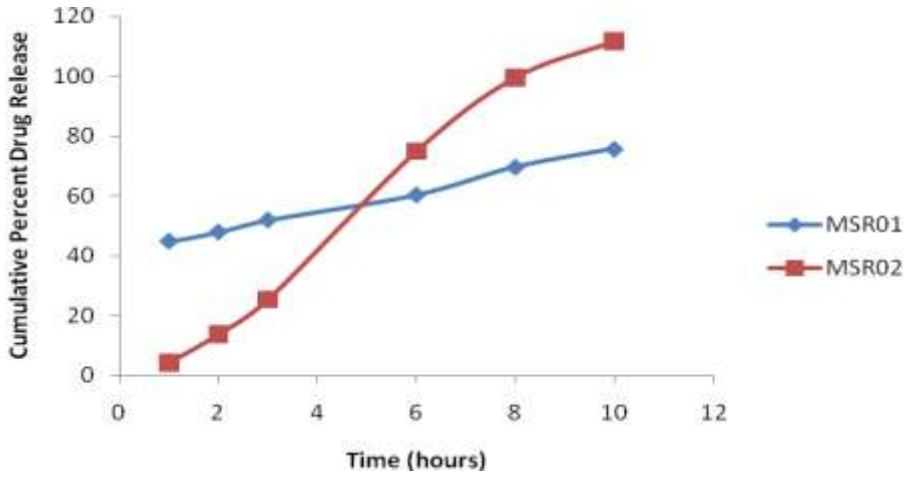


Figure 9: Dissolution profiles of two marketed products

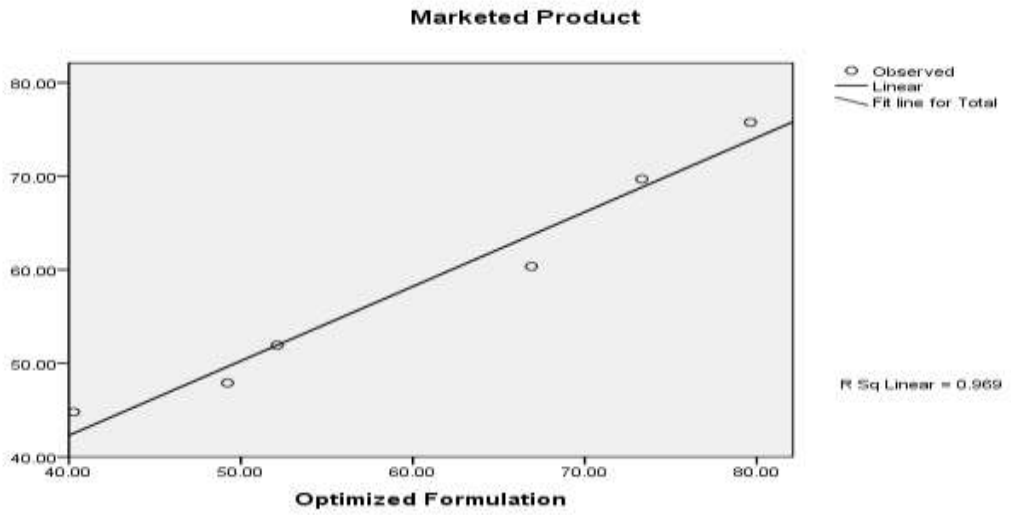


Figure 10: Comparison between marketed product with optimized formulation

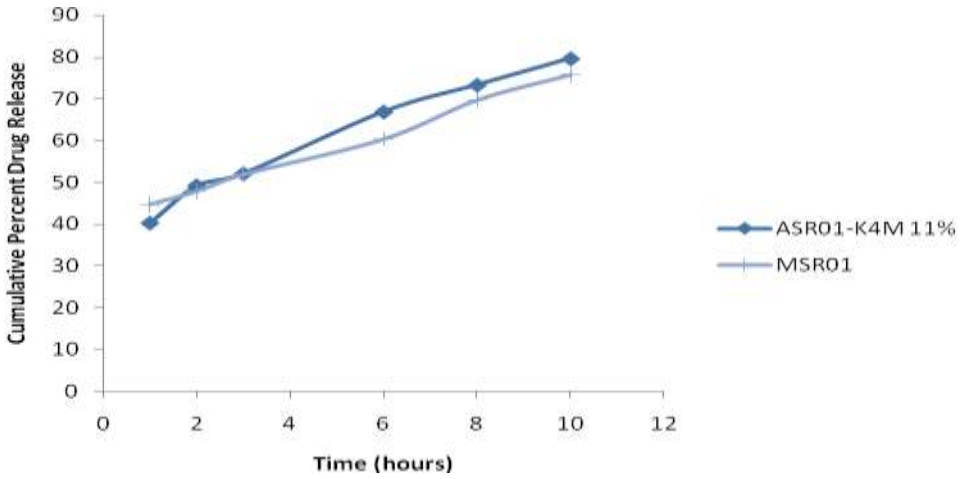


Figure 11: Dissolution profiles of marketed and optimized product

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