PROLONG RELEASE BIOADHESIVE VAGINAL FILM OF ANTI-HIV DRUG (ZIDOVUDINE): FORMULATION AND IN-VITRO EVALUATION

Arkendu Chatterjee*, Benoy Brata Bhowmik and Deepak Awasthi

Department of Pharmaceutics, Himalayan Pharmacy Institute, Majhitar, Rangpo, East Sikkim, India

ABSTRACT

The present study concerned with the development and characterization of bioadhesive vaginal film (VF). Zidovudine containing VF were prepared by solvent casting method using different ratios of Acrycoat S 100 (AC) or Ethyl cellulose (EC) to Hydroxy propyl methyl cellulose (HPMC) and di butyl phthalate(DBP) as a plasticizer. The optimized films were found to be transparent, flexible and soft and evaluated for mechanical properties by modified instrument, drug content, folding endurance, in vitro drug release with release kinetic and % moisture content bioadhesive strength by modified pan balance method. The films were found higher drug content and flexible. The VF10 (containing AC: HPMC 4:1) was selected. In vitro drug was found of Zidovudine over 11 hr obeying zero order followed by Higuchi kinetics and Case II non-Fickian (anomalous) diffusion control, indicating the rate of drug release is due to the combined effect of drug diffusion and polymer relaxation with a sufficient bio adhesion quality with good mechanical properties. The results were compared statistically and found with satisfactory correlation. Thus in conclusion preparation protocol of VFs studied may be adopted for a successful development of newer drug delivery system for treatment and prevention for AIDS.

Keywords: AIDS, Zidovudine, Bioadhesive, Film

*Correspondence for Author
Arkendu Chatterjee
Department of Pharmaceutics, Himalayan Pharmacy Institute, Majhitar, Rangpo, East- Sikkam, India
E-mail:- arkendu2001@yahoo.co.in

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INTRODUCTION: UN global summary of the AIDS pandemic 2007 revealed, women (15.4 million) account for approximately 50% of people (33.2 million) infected and living with HIV. More than 20 million people have died of AIDS and about 14,000 are newly infected every day. HIV is affecting women and girls increasing in numbers. As researchers, these statistics emphasize the responsibility and a challenge that includes understanding personal risks of our young people, to make healthy choices about their sexuality as well as a course for future action in designing safe, effective, acceptable and affordable vaginal microbicide to reduce the risk of STD transmission, particularly HIV, specifically for women.

Access to a safe and effective microbicide would benefit both women and men. Although somewhat neglected in clinical studies, pharmaceutical characterization of vaginal polymeric films, is an important step in order to optimize safety, efficacy and acceptability. Vagina is explored as an effective site for local and systemic drug delivery due certain unique features such as presence of dense network of blood vessels, lacking of GI and liver first pass effect. The primary objective of this study was to develop VF of Zidovudine. The VF were targeted to control the release of Zidovudine in a predetermined manner for a prolong time through vagina. We had prepared VF of Zidovudine by solvent casting method with reduced initial burst, increased prolonged cumulative release in vitro to achieve controlled release over a period of 11 hr and improved vaginal bio adhesive strengths in goat vagina ex- vivo. The film also possessed aesthetic appeal such as good appearance, softness, flexibility and free from any sharp edge to avoid mechanical injuries during insertion for ease of administration and user convenience after administration.

MATERIALS AND METHODS:

Materials: Zidovudine was obtained as a gift sample from Aurobindo Pharma Ltd, A.P, India and EC (ethoxy content- 47.5% by weight and viscosity [η] of 22 cps in a 5% concentration by a weight in toluene: ethanol 80:20 at 25°C), HPMC (K4M,4000 cps 2% aqueous solution) and AC were obtained from S.D. Fine Chem., Mumbai, India. All other chemicals and reagents used were of analytical grade and used as received.

Methods: VF of Zidovudine was prepared by solvent casting method containing different ratios of AC or EC and HPMC in di-butyl phthalate or glycerol or sorbitol or PEG 400 as a plasticizer. 40 % w/w of polymeric solution was allowed to stir for 1 h. After that, drug and plasticizer were added with constant stirring and this solution was allowed to stir until we got clear solution. The solution was allowed to stand overnight to remove all the air bubbles. The solution was then casted onto a petri dish and dried in the oven at 60°C until complete drying. The film was carefully removed from the petri dish, checked for any imperfections and cut according to the size required for testing. The films thus prepared, were wrapped in a aluminum foil and kept in a desiccators for further study. Each formulation was replicated three times.

Morphological characterization: Films were analyzed in Scanning Electron
Microscopy (LEO, 435 VP, UK) to reveal the surface morphology of the films. The films were placed on double-sided tape attached onto graphite surface. The samples were coated with gold using an ion sputter. Coating was provided at 20 mA for 4 min. Observation was performed at 15 kV and ~ X550 magnification.  

**Measurement of mechanical properties:**
Mechanical properties of the films were evaluated using a modified instrument based on the similar working principle as reported by Kok Khiang Peh et al. Film strip in dimension of 50x10 mm and free from air bubbles or physical imperfections, were held between two clamps positioned at a distance of 3 cm. A cardboard was attached on the surface of the clamp via a double-sided tape to prevent the film from being cut by the grooves of the clamp. One clamp remains fixed and another one is movable.

During measurement, the strips were pulled by the movable clamp at a rate of 2.0 mm/s to a distance of 5 mm before returning to the starting point. The force and elongation were measured when the films broke. Results from film samples, which did not broke at between the clamps, were not included in calculations. Measurements were triplicate for each film. The following equations were used to calculate the mechanical properties of the films:

\[
\text{Tensile strength (kg/mm}^2\) = \frac{\text{Force at break (kg)}}{\text{Initial cross-sectional area of the sample (mm}^2\)} - (1)
\]

\[
\text{Elastic modulus (kg/mm}^2\) = \frac{\text{Force at corresponding strain (kg)}}{\text{Cross-sectional area of the sample (mm}^2\)} \times \frac{1}{\text{Corresponding strain}} - (2)
\]

\[
\text{Elongation break (mm/mm}^2\) = \frac{\text{Increase in length (mm)}}{\text{Original length (mm)}} \times \frac{100}{\text{Cross sectional area (mm}^2\)} - (3)
\]

\[
\text{Strain} = \frac{\text{Tensile strength}}{\text{Elastic modulus of the sample}} - (4)
\]

**Estimation of drug content:** Zidovudine content in film was estimated by UV-Visible spectrophotometric method in simulated vaginal fluid (SVF, phosphate buffer I.P., pH 4.7). The accurately weighed film strip in dimension of 50x10 mm, were dissolved first in solvent (2ml methanol) so that polymer get dissolved to release drug into the solution. Then volume was made up to 25 ml with SVF and kept for 1 hr under stirring. Similarly, a blank was carried out using drug free film. The solution was filtered and absorbance was measured at 267nm (λmax) using UV-Visible spectrophotometer (UV-1700, Shimadzu, Japan).  

**Estimation of moisture Content:** The prepared films were cut into 50 ×10 mm strips. The films were weighed individually and kept in a desiccator containing Calcium Chloride as desiccant at 37°C for
24hr. The films were reweighed individually until a constant weight was obtained. Percentage of moisture content was then calculated based on the change in the weight with respect to the initial weight of the film.\(^\text{12, 13}\)

**Determination of swelling index:** Each film sample was weighed and placed in SVF for 25 min. The swelling index of film was calculated using following formula.\(^\text{10}\)

\[
\text{Swelling index} = \frac{W_t - W_0}{W_0} \times 100\%
\]

Where \(W_t\) = weight of film at time \(t\), \(W_0\) = initial weight of film

**In vitro drug release and release kinetics of VFs:** *In vitro* drug diffusion studies were carried out by using K.C. cell with a semi permeable barrier. Cellophane membrane was soaked in SVF. Film of specified diameter was placed on the surface of processed cellophane membrane and was fixed to one end of the cylindrical donor compartment by cyanoacrylate adhesives, such that the lower end just touched the surface of SVF medium. Also 0.5 ml of SVF was placed and maintained at same level throughout the study in donor compartment. Temperature was maintained at 37 ± 2°C with constant stirring at 50 ± 10 rpm. A quantity of 5 ml sample was withdrawn from the receptor compartment at definite time interval and replaced with 5 ml of SVF to maintain sink condition. The drug was estimated by using UV-Visible spectrophotometer at 267 nm (\(\lambda_{\text{max}}\)).\(^\text{11, 14}\) In order to investigate the mechanism of Zidovudine release from different VFs, the release data was analyzed with the following mathematical model, zero order kinetic equation (\(Q_t = K_0 t\)), first order kinetic equation (\(\ln Q_t = \ln Q_0 - K_1 t\)) and Higuchi kinetic equation (\(Q_t = K_H t^{1/2}\)), where \(Q_t\) is the percent of drug released form VF at time \(t\), \(Q_0\) is the initial amount of drug present in VF. \(K_0\), \(K_1\) and \(K_H\) are the constants of the equations. Further to confirm the mechanism of drug release, drug release was fitted in Korsmeyer Peppa’s model, \(\frac{M_t}{M_\infty} = K_p t^n\), where \(\frac{M_t}{M_\infty}\) is the fraction of drug release at time \(t\) and \(K_p\) is the power law constant and \(n\) is the release exponent.

The power law is valid only for the first 60% of the release profile. The \(n\) value is used to characterize different release mechanisms and was calculated from the slope of the plot of \(\log \frac{M_t}{M_\infty}\) vs. \(\log\) of time (\(t\)). The criterion for selecting the most appropriate model was chosen on the basis of goodness of fit test.\(^\text{15, 16}\)

**Bioadhesion strength in goat vaginal mucosa:** Isolated goat vaginal tissue (*Capra hircus*, local breed, obtained immediately after sacrifice of animals at a slaughter house) was cleaned, separated from the supporting muscular and connective tissues taking care to maintain integrity of mucosa, and kept at 0°C till further use. Before experiments, goat vaginal tissue was thawed in SVF medium. The bio adhesion measurement was performed by using a modified balance method intact with goat vaginal tissue. The two pans of physical balance were removed. Right side pan was replaced with a 100 ml beaker and on left side, a glass slide was hanged. For balancing the assembly a weight of 20g was hanged on left side. Another glass slide was placed below the hanged slide. Portions of vaginal membranes were attached with
both slides. The height of this set up was so adjusted, leaving a space of about 0.2 cm between two vaginal membrane faces. One film was placed between two vaginal membrane faces. Little pressure was applied to form bio adhesion bond, and then slowly drop of water was added on right side beaker, till the VF was separated from one face of vaginal membranes attached. Volume of water added was converted to mass. This gave the bioadhesive strength of film in gm. An initial investigation examined the reproducibility of the system using five same formulations. Then the study was carried out for all formulations 17.

Statistical analyses: Statistical data analyses were performed by using Mystat statistical software. One way ANOVA was performed and was considered significant (p < 0.05) at 5 % level.

RESULTS AND DISCUSSION: Antiretroviral drug, Zidovudine, a nucleoside reverse transcriptase inhibitor, is taken up by the host cells where it is converted into its tri-phosphate form. Subsequently, by competitive inhibition, it inhibits the reverse transcriptase, therefore, viral replication stops. Also it is incorporated into the viral DNA chain which is growing (during replication) and terminates the lengthening of the viral DNA chain, thereby stops viral replication. Zidovudine was chosen as a model drug of choice due to its short half life of about 1 hour, high oral dose, low systemic bioavailability (only 64%) due to rapid hepatic first-pass metabolism. Thin and soft transparent Bioadhesive vaginal film released drug in a predetermined manner. Film has advantages among bioadhesive vaginal formulations with better dispersion throughout vagina, better aesthetic appeal, more comfortable, less interference during intercourse, dose removal possibility in emergency situations, suitability for a wide variety of drugs and excellent drug content uniformity. The formulation code and composition of VF were presented in (Table 1).

Physical characteristics of films: Physical characteristics of different VF were shown in column 4 and 5 of (Table 1) to optimize plasticizers. Films containing PEG 400 and sorbitol as plasticizers could not be removed from glass plate after drying. Film containing Glycerol as a plasticizer, was appeared transparent and easily removed from plate but was brittle. Films containing DBP as a plasticizer appeared transparent, easily removed from plate and were soft. So for such composition of Film, DBP was selected as plasticizer of choice.

Table 1: Composition and plasticizer of Bio-adhesive vaginal films

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Polymer</th>
<th>Drug: Polymer</th>
</tr>
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<tbody>
<tr>
<td>VF 05</td>
<td>EC: HPMC</td>
<td>1: 5</td>
</tr>
<tr>
<td></td>
<td>(4: 1)</td>
<td></td>
</tr>
<tr>
<td>VF 08</td>
<td>EC: HPMC</td>
<td>1: 5</td>
</tr>
<tr>
<td></td>
<td>(1: 4)</td>
<td></td>
</tr>
<tr>
<td>VF 10</td>
<td>AC: HPMC</td>
<td>1: 5</td>
</tr>
<tr>
<td></td>
<td>(4: 1)</td>
<td></td>
</tr>
<tr>
<td>VF 13</td>
<td>AC: HPMC</td>
<td>1: 5</td>
</tr>
<tr>
<td></td>
<td>(1: 4)</td>
<td></td>
</tr>
</tbody>
</table>
Morphological Characterization: SEM photographs of blank and drug loaded films were shown in (Figures 1a and 1b) accordingly. Films appeared to be homogenous and continuous. Drug was distributed on the surface, over the drug loaded film.

Measurement of mechanical properties: The tensile testing is an indication of the strength and elasticity of the film, reflected by the parameters, tensile strength (TS), elastic modulus (EM) and elongation at break (E/B). A soft and weak film is distinguished by a low TS, EM and E/B; a hard and brittle film is defined by a moderate TS, high EM and low E/B; a soft and tough polymer is characterized by a moderate TS, low EM and high E/B; whereas a hard and tough polymer is characterized by a high TS, EM and E/B. Another parameter, Strain has been used as an indicator of the overall mechanical quality of the film. A high strain value indicates that the film is strong and elastic. Hence, it is suggested that a suitable vaginal film should have a relatively high TS, E/B and Strain but a low EM. (Table 2) showed mechanical properties of different formulations. For EC film, decrease HPMC content TS and EM decreases, E/B increases but no significant difference in case of strain. For AC film, decrease TS, EM and strain, E/B increases.

These results indicated that HPMC generally increase the strength while decreased the softness, elasticity and flexibility of both EC as well as AC films. The greater elasticity exhibited by films containing lower HPMC content. From Table 2, VF 8 (EC:HPMC=1:4) with moderate TS and EM with low B/Band low strain indicated that film were soft & weak nature, while formulation VF10(AC: HPMC=4:1) with low TS, low EM, high E/B with high strain was found indicated film were soft, strong and elastic; while Formulation VF 05 (EC: HPMC= 4: 1) with low TS ,low EM and high E/B with low strain indicated soft & weak film ,whereas formulation VF13(AC:HPMC=1:4) high TS and high EM, with low E/Band low strain indicated that film was hard ,brittle elastic nature. These results indicated that AC generally reduced the strength while increased the softness, elasticity and flexibility of both EC as well as AC films. The greater elasticity exhibited by films containing higher AC content could be related to its conformation and configuration, which is highly cross linked. In comparison, the mean TS values of
both EC and AC films were closely comparable for similar compositions. Increase in AC content rendered the HPMC films more elastic than EC films.

Table 2: Mechanical properties of different vaginal formulations

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Tensile Strength</th>
<th>Elastic Modulus</th>
<th>Elongation Break</th>
<th>Strain</th>
</tr>
</thead>
<tbody>
<tr>
<td>VF 05</td>
<td>1.23 ± 0.17</td>
<td>3.41 ± 0.23</td>
<td>12.57 ± 0.20</td>
<td>0.36 ± 0.09</td>
</tr>
<tr>
<td>VF 08</td>
<td>2.45 ± 0.65</td>
<td>5.83 ± 0.32</td>
<td>10.99 ± 0.09</td>
<td>0.42 ± 0.09</td>
</tr>
<tr>
<td>VF 10</td>
<td>1.24 ± 0.18</td>
<td>2.88 ± 0.21</td>
<td>12.54 ± 0.08</td>
<td>0.43 ± 0.05</td>
</tr>
<tr>
<td>VF 13</td>
<td>2.71 ± 0.32</td>
<td>6.15 ± 0.42</td>
<td>11.67 ± 0.14</td>
<td>0.44 ± 0.12</td>
</tr>
</tbody>
</table>

Each value represents as mean ± standard deviation (n=3)

Estimation of drug content: The drug content of all the prepared VFs was found to be satisfactory and each formulation demonstrated high drug contents, as summarized in column 2 of (Table 3). The drug contents of the prepared VFs were found to be in the range of 77.87(VF 05) - 97.65% (VF 13). The formulation VF 13 showed highest drug contents among all the formulations. Further, as shown in (Table 3), the drug content analysis of the prepared films showed that the process used to prepare the films in this investigation is capable of giving optimum drug content and minimum batch variability.

Folding endurance: Evaluation of folding endurance involves determining the folding capacity of the films subjected to frequent extreme conditions of folding. The column 4 of (Table 3) showed folding endurance of different formulations. The folding endurance the prepared VFs were found to be 296-324 numbers of times for all formulation indicating that all formulations were flexible and soft. This also gives an indication of brittleness; less folding endurance indicates more brittleness.

Table 3: % Drug content, moisture content, folding endurance, bioadhesive strength and swelling index of different formulations

<table>
<thead>
<tr>
<th>Formulation</th>
<th>% w/w Drug Content</th>
<th>% Moisture Content*</th>
<th>Folding Endurance *(no. of times)</th>
<th>*Bioadhesive Strength</th>
<th>*Swelling Index (Upto 25 mins.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VF 05</td>
<td>77.87 ± 0.74</td>
<td>2.94 ± 0.65</td>
<td>308 ± 21</td>
<td>5.1 ± 3.2</td>
<td>19.72 ± 0.83</td>
</tr>
<tr>
<td>VF 08</td>
<td>87.75 ± 0.75</td>
<td>4.13 ± 0.95</td>
<td>324 ± 15</td>
<td>17.5 ± 2.9</td>
<td>56.56 ± 77</td>
</tr>
<tr>
<td>VF 10</td>
<td>87.44 ± 0.45</td>
<td>1.23 ± 1.11</td>
<td>321 ± 23</td>
<td>4.4 ± 1.8</td>
<td>17.08 ± 67</td>
</tr>
<tr>
<td>VF 13</td>
<td>97.65 ± 1.32</td>
<td>3.43 ± 0.84</td>
<td>296 ± 76</td>
<td>14.6 ± 2.6</td>
<td>51.32 ± 1.56</td>
</tr>
</tbody>
</table>

*Each value represents as mean ± standard deviation (n=3)

% Moisture content: The column 3 of (Table 3) showed % moisture content of different formulation. The moisture content in the formulations was found to increase with the increasing concentration of drug and hydrophilic polymer HPMC. Formulation containing EC and HPMC showed higher % moisture content than formulation containing AC and HPMC. Formulation VF 8 showed highest (4.13 %) moisture content and Formulation VF 10 showed lowest (1.231%) moisture content indicating that as ratio of HPMC increases % moisture content increases and vice-versa.
Table 4: Drug release profile and kinetics of different formulations

<table>
<thead>
<tr>
<th>Formulation</th>
<th>% Cumulative Drug Release (11 hr study)</th>
<th>Zero Order Eq.</th>
<th>First order Eq.</th>
<th>Higuchi Square Root Eq.</th>
<th>Korsmeyer and Peppas Eq.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VF 05</td>
<td>21.30 ± 0.96</td>
<td>0.991</td>
<td>2.055</td>
<td>0.99</td>
<td>0.928</td>
</tr>
<tr>
<td>VF 08</td>
<td>59.30 ± 0.84</td>
<td>0.873</td>
<td>5.185</td>
<td>0.91</td>
<td>0.952</td>
</tr>
<tr>
<td>VF 10</td>
<td>13.54 ± 1.12</td>
<td>0.981</td>
<td>1.229</td>
<td>0.97</td>
<td>0.889</td>
</tr>
<tr>
<td>VF 13</td>
<td>44.86 ± 1.11</td>
<td>0.823</td>
<td>3.015</td>
<td>0.99</td>
<td>0.960</td>
</tr>
</tbody>
</table>

Each value represents as mean ± SD. n=3

In- vitro drug release of prepared Film: The in- vitro drug releases of acquired films were shown in column 2 of (Table 4) and (Fig. 2).

Effect of swelling index on Zidovudine release: In all the cases, the release rate was increased with increased proportion of hydrophilic polymer (HPMC) due to more swelling. Initially, the diffusion coefficient of drug in the dehydrated polymer will be less and increases significantly as the polymer imbibes more and more water, and forms a gel, as the time progresses. The hydration rate of the polymer and thereby the gel formation significantly depended on polymer proportion. The overall effect of polymer was observed as follows. Formulation VF 8 (EC: HPMC= 1:4) with highest swelling index (56.56 ± 0.77), showed highest % cumulative drug release (59.30 ± 0.84% up to 11th hr) while formulation VF10 (AC: HPMC= 4: 1) with lowest swelling index (17.08 ± 0.67), was found to release the drug only about 13.54± 1.12% upto 11 hrs. Formulation VF 05 (EC: HPMC= 4:1) with swelling index of 19.72 ± 0.77, showed 21.30 ± 0.96% % cumulative drug release up to 11th hr whereas formulation VF13 (AC:HPMC=1:4) with swelling index of 51.32 ± 1.56, was found to release the drug only about 44.86± 1.11% upto11hrs. This finding can be attributed to the higher water repelling property of AC, thus concluded that AC was a better rate controlling polymer to sustain the release of drug for longer period of time when compared to formulations containing EC as a rate controlling polymer.

Different kinetic models (zero- order, first-order and Higuchi’s) were applied to interpret the release profile from VFs. The best fit with higher correlation ($r^2> 0.9$) was found with the Higuchi’s equation. The rate constants were calculated from the slope of the respective plots. The best fit with the highest correlation coefficient was shown in Higuchi followed by first order and zero-order equations as given in Table 4. The drug release was proportional to square root of time, indicating that the drug release from...
VFs was diffusion controlled. However, two factors diminish the applicability of Higuchi’s equation to matrix systems as this model fails to allow the influence of swelling of the matrix (upon hydration) and gradual erosion of the matrix. Therefore, the dissolution data were also fitted according to the well-known power law equation (Korsmeyer Peppas’ equation). The drug release mechanism of all VFs was found to be predominately influenced by the different bioadhesive polymer added. The mechanism of drug release from hydrophilic-hydrophobic polymeric films involves solvent penetration, hydration and swelling of the polymers, diffusion of the dissolved drug in the matrix and erosion of the gel layer. Form (Table 4 and Figure 2), the \( n \) values for all the formulations ranged from 0.304 to 0.979 indicating different release patterns viz. Case I Fickian release (\( n = 0.5 \)), Case II non-Fickian (anomalous) release (\( 0.5 \leq n \leq 0.89 \)), super case II type of release (\( \geq 0.89 \)). It was observed that the VF 13 (\( n = 0.304 \)) films underwent Case I Fickian diffusion control, during the diffusion study. In case of Case I Fickian release mechanism, the rate of drug release is much lesser than that of polymer relaxation (swelling/erosion). So the drug release was chiefly dependent on the diffusion through the films.

Also it was observed that the formulations VF 8 (\( n = 0.766 \)) and VF10 (\( n = 0.785 \)), underwent Case II non-Fickian (anomalous) diffusion control, indicating the rate of drug release is due to the combined effect of drug diffusion and polymer relaxation. Further VF 05 (\( n = 0.979 \)) endured super case II release, denoting polymer relaxation had a significant role in the drug release mechanism. Super Case II release generally refers to the polymer relaxation. The overall effect of polymer on release (VF 04- VF 13) was also significantly different (\( P < 0.05 \), single factor ANOVA). It means null hypothesis is nullified and alternative hypothesis is accepted i.e. the variation in formulations in polymeric type and content (VF4-VF13) have significant effect on release profile.

**Selection of Film-Forming Polymer:** Combination of hydrophobic (EC or AC S 100) and hydrophilic (HPMC or PVP) polymer was experimented with different plasticizer (DBP, glycerol, sorbitol, PEG 400) for film formation. Solvent casting techniques was employed for the preparation of VF. From the results of the present study it appears that the release of Zidovudine was significantly influenced by the characteristics of the polymer used AC and HPMC (4:1) shown greater rate retarding property in comparison with EC and HPMC (4:1). Thus we chosen AC and HPMC (1:4) as a film forming polymers.

**Vaginal bioadhesion measurements:** (Figure 3 and column 2 of Table 4), indicates the vaginal bioadhesive properties of the prepared VF (VF 04- F 13) in goat vagina and the result showed that all vaginal bioadhesive strengths were found in the following order VF 08 >VF 13 >VF 05 >VF10. It was
concluded that Bioadhesive strength proportional to the proportion of HPMC in formulation VF 08 (EC: HPMC 1: 4) showed the highest bioadhesive property.

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