**IJPSR (2022), Volume 13, Issue 9** **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 03 January 2022; received in revised form, 08 July 2022; accepted, 17 August 2022; published 01 September 2022

# FORMULATION AND EVALUATION OF MUCOADHESIVE MATRIX TABLET OF ACYCLOVIR

Ashwini Madgulkar, Mangesh Bhalekar, Tejinder Kaur and Nisha Thange *

Department of Pharmaceutics, AISSMS College of Pharmacy, Near RTO, Kennedy Road, Pune - 411001, Maharashtra, India.

**Keywords:**

Acyclovir, Mucoadhesive Matrix Tablet, Chitosan, Evaluation, HPMC $K_4M$

**Correspondence to Author:**
**Ms. Nisha Thange**

Research Scholar,
Department of Pharmaceutics,
AISSMS College of Pharmacy, Near RTO, Kennedy Road, Pune - 411001, Maharashtra, India.

**E-mail:** nishathange8@gmail.com

**ABSTRACT:** The binding capacity of mucoadhesive polymers with gastric mucin prolongs the gastric residence time, increasing bioavailability. In the present research work, an attempt was made to formulate and evaluate sustain release mucoadhesive matrix tablet of Acyclovir. In the present work, an effort has been made to evaluate the effect of mucoadhesive polymers on the release characteristics of mucoadhesive matrix tablets of Acyclovir. Matrix tablets were prepared by wet granulation method using different types and levels of polymers *viz.* Chitosan and HPMC $K_4M$. Tablets were evaluated for thickness, friability, hardness, uniformity of weight, the content of active ingredients, mucoadhesive strength, and *in-vitro* dissolution studies. The studies indicated that the drug release can be modulated by varying the concentrations of polymers. It was observed from the optimization studies that the F3 formulation has exhibited the best release profile of the drug and can sustain the drug release for 8 h with optimum mucoadhesive strength.

**INTRODUCTION:** The systemic delivery of drugs through novel administration methods is one area in which significant changes and improvements have been made. Consequently, precise control of drug input into the body by various routes is now possible. Controlled and sustained-release formulations have been developed and are gaining in popularity and medical acceptance. Sustained release dosage forms are designed to release a drug at a predetermined rate to maintain a constant drug concentration for a specific period with minimum side effects.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(9).3525-34

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(9).3525-34

The advantage of administering a single dose of a drug that is released over an extended period to maintain the uniform blood level of a drug often translates into better patient compliance and enhanced clinical efficacy of the drug for its intended use [1]. Acyclovir is an antiviral drug; it is given in conventional dosage form five times a day; hence, frequent administration is its major problem. Moreover, the major absorption site is from the stomach and the upper part of the intestine.

The challenging task of drugs with a narrow absorption window in the gastrointestinal tract or acting locally in the stomach is to prolong drug release and retain the dosage form in the upper gastrointestinal tract. This result in higher bioavailability, a reduced time interval for drug administration, and thus better patient compliance. Matrix technologies have often proven popular among the oral controlled drug delivery

technologies because of their simplicity, ease in manufacturing, high level of reproducibility, stability of the raw materials and dosage form, ease of scale-up, and process validation.

The primary goal of a mucoadhesive controlled drug delivery system is to localize a delivery device with the body to enhance the drug absorption process in a specific manner and to facilitate intimate contact of the dosage form with the underlying absorption surface to improve and enhance the bioavailability of drugs [2].

In the present study, an attempt was made to develop a sustainable release mucoadhesive matrix tablet of Acyclovir using polymers like Chitosan and HPMC $K_4M$, thereby enhancing the bioavailability of selected drug and optimizing the process variables and additives for the preparation of matrix tablets with desirable physicochemical and *in-vitro* release characteristic.

The term mucoadhesion refers to forming a bond between mucus and polymer. The mucoadhesive system has many advantages, such as bioavailability enhancement, increased residence time, and utility in local and systemic therapy.

The interest in mucoadhesion has been bolstered by developing novel bioadhesive polymers for mucosal delivery [3]. There are two stages of the Mucoadhesion contact stage and consolidation stage.

In the contact stage, there is intimate contact between a bioadhesive material and the membrane, either from a good wetting of the bioadhesive surface or from the swelling of the bioadhesive is established. In the consolidation stage, there is the interpenetration of a chain of the bioadhesive with the mucus. In molecular terms, mucoadhesion can be explained based on molecular interactions such as attraction and repulsion. Attractive interaction occurs from hydrogen bonding, electrostatic attraction, van der waals forces, and hydrophobic interaction. Repulsive interaction arises due to electrostatic and steric repulsion. For mucoadhesion to occur, the attractive interactions should be greater than nonspecific repulsion. Several Mucoadhesion theories contribute to forming mucoadhesive/bioadhesive bonds [4, 5].

**Theories of Mucoadhesion [5]:** The phenomenon of mucoadhesion is well explained by six general theories of adhesion [3, 6, 7].

- **Electronic Theory:** According to this theory, mucoadhesion occurs by electron transfer upon contact of adhering surfaces due to differences in their electronic structure, which results in forming an electronic double layer at the interface.

- **Adsorption Theory:** The adsorption theory suggests that hydrogen bonding and van der waal's forces are responsible for mucoadhesion. Also, secondary surface force such as hydrophobic interactions is involved.

- **Wetting Theory:** According to wetting theory, mucoadhesion occurs when the liquid spreads spontaneously onto a surface. The techniques such as contact angle goniometry to measure the contact angle of the liquid on the surface are used to determine a liquid's affinity for a surface.

  Lower the contact angle, the greater the affinity of the liquid to the solid. Greater the individual surface energies of the solid and liquid relative to the interfacial energy, the greater the work of adhesion.

- **Diffusion Theory:** The diffusion theory suggests an inter-diffusion of the chain of the polymer across an adhesive interface. The concentration gradient controls the process and is influenced by the available molecular chain lengths and their mobilities. The sufficient depth of the penetration creates the semi-permanent adhesive bond.

- **Mechanical Theory:** According to mechanical theory, mucoadhesion involves the interlocking of an adhesive onto a surface. In the adhesion process, the increased surface for interaction and enhanced viscoelastic and plastic energy dissipation during joint failure is more important than a mechanical effect [7].

- **Fracture Theory:** Fracture theory relates the adhesive strength to the forces required to detach the two involved surfaces after adhesion.

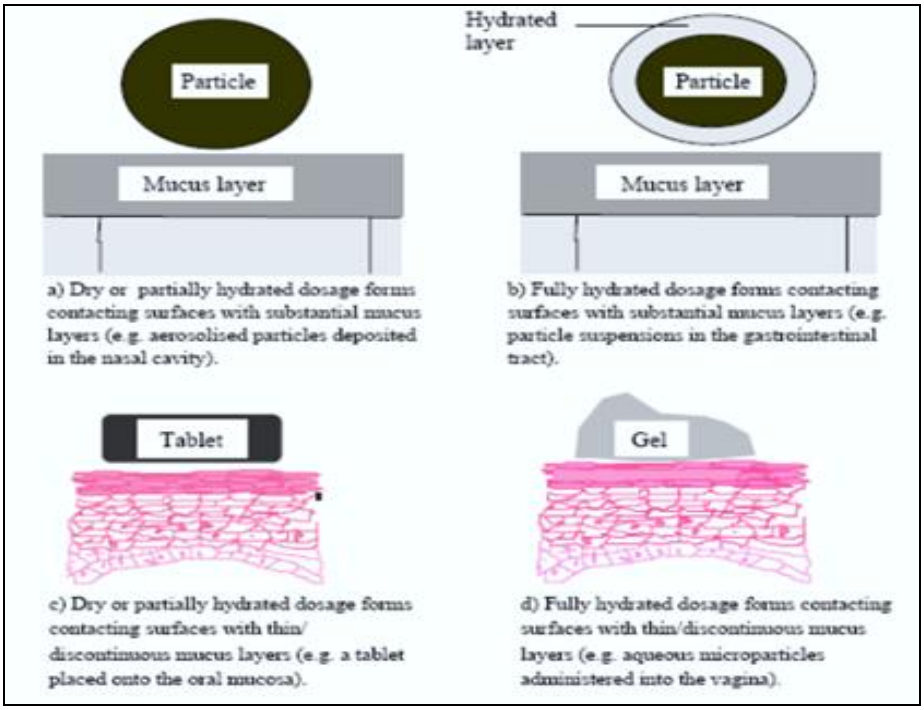


**FIG. 1: DIAGRAMMATIC REPRESENTATION OF TABLET AND GEL**

**Classification of Mucoadhesive Polymers:**

- ✓ **Hydrophilic Polymer:** Hydrophilic polymers are water-loving polymers. They swell when they come in contact with water and undergo complete dissolution. The systems coated with these polymers give high mucoadhesion to the mucosa in a dry state, but bioadhesive nature starts deteriorating as they start to dissolve. So that, their mucoadhesiveness is for a short time. Such polymers include hydroxyl propyl methyl cellulose (HPMC), polyacrylic acid, and poly (methacrylates).

- ✓ **Hydrogel polymers:** Hydrogel polymers swell upon contact with water. The degree of cross-linking determines the extent of swelling. Examples include chitosan, carbopol, polyox, polycarbophil, and PAA-cysteine. This polymer consists of various carboxyl groups. These polymers adhere to the mucosa and interact through hydrogen bonding at the wet mucosal surface. As these polymers hydrate into a hydrogel, a bioadhesive bond becomes over-extended, resulting in reduced mucoadhesion. Due to this reason, hydrophilic polymers are widely used in the case of buccal, nasal, ophthalmic, and vaginal delivery.

- ✓ **Thermoplastic Polymers:** These are hydrophobic polymers that contains both bio-erodible and non-bio-erodible polymers. Examples include poly (methyl vinyl ether-co-malic anhydride), polyesters, and poly anhydride polymer that is spheres. These rapidly degrading polymers regenerate a new polymer surface rich in carboxylic acid end groups, these groups can form hydrogen bonds with the surrounding mucin strands, which in turn penetrate into newly created surfaces [8].

**TABLE 1: VARIOUS MUCOADHESIVE POLYMERS USED IN MUCOADHESIVE DELIVERY SYSTEMS**

| Polymers | Mucoadhesive strength |
|---|---|
| Carboxy Methylcellulose | +++ |
| Hydroxy Ethylcellulose | +++ |
| Tragacanth | +++ |
| Carbopol 934 | +++ |
| Poly (acrylic acid/ divinyl benzene) | +++ |
| Polycarbophil | +++ |
| **Polymers** | **Mucoadhesive strength** |
| Sodium alginate | +++ |
| Gelatin | ++ |
| Guar gum | ++ |
| Gum karaya | ++ |
| Pectin | + |
| Acacia | + |
| Amberlite-200 | + |
| Hydroxyl-propyl cellulose | + |
| Thermally modified starch | + |
| Chitosan | + |
| Hydroxyl Ethyl Metharylate | + |

## MATERIALS AND METHOD:

**Material:** Acyclovir was obtained as a gift sample from Emcure Pharmaceuticals, Bangalore. Chitosan was purchased from Loba Chemie, Mumbai. HPMC K4M, Micro crystalline cellulose, PVP K30 were procured from Lobachemie, Mumbai. All reagents used were of analytical grade.

**Method:**

**Calibration Curve by UV Analytical Method:** A series of solutions of Acyclovir in methanol of concentrations 1-20 µg/ml was prepared. The absorbance of all the solutions was measured using methanol as blank at 256 nm using double beam spectrophotometer. A standard plot of absorbance v/s concentration of drug in µg/ml was plotted. Coefficient and regression equations were obtained from the calibration curve.

**UV Spectroscopy (Determination of ƛmax):** About 10 mg acyclovir was accurately weighed and dissolved in 10 ml of methanol to make concentration 1 mg/ml. This solution was then suitably diluted with methanol to get a final concentration of 10 µg/ml. UV spectrum was recorded over the wavelength range 200-400 nm.

**FTIR Spectroscopy:** The infra-red spectrum of the Acyclovir was recorded using a Fourier Transform Infra-Red spectrophotometer over wavelength ranging from 400 to 4000 cm-1 (Jasco 460 plus).

**Drug Excipient Compatibility Studies:** FT-IR spectra matching method was used to detect any possible chemical interaction between the Acyclovir and polymers. The samples were ground, mixed thoroughly with KBr, and compressed at a pressure of 15 tons / $cm^2$. Samples were prepared for Acyclovir, polymers such as Chitosan, HPMC K4M, and the physical mixtures of drugs with polymers. The spectra obtained were compared and interpreted for the functional group peaks.

**Pre-formulation Studies:** The flow properties of granules were determined in terms of angle of repose, Car's index, and Hausners ratio. The bulk density and tapped density were determined, and from this data Car's index, and Hausners ratio were calculated [9].

**Formulation of Mucoadhesive Matrix Tablets of Acyclovir**

**Optimization Study:** A response surface statistical experimental design was used to optimize the effect of different independent factors on dependent variables. The variables were investigated using a $3^2$ full factorial designs using Design-expert software® 11 (Stat-Ease, Inc., USA).

This design was based on a $3^2$ factorial design, three replicates of the central run, leading to 9 sets of possible combinations, allowing each experimental response to be optimized. Different batches were prepared with different independent factors at different levels and responses.

The experiments were designed to study the effect of two independent variables: the mucoadhesive strength and % drug release for 8 hrs.

**TABLE 2: FORMULATION COMBINATION AS PER THE $3^2$ FULL FACTORIAL DESIGNS**

| Ingredients(mg) | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| Drug | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 | 200 |
| Chitosan | 150 | 50 | 150 | 100 | 50 | 150 | 50 | 100 | 100 |
| HPMC K4 M | 150 | 50 | 50 | 150 | 150 | 100 | 100 | 100 | 50 |
| **Ingredients(mg)** | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
| Microcrystalline cellulose | 170 | 20 | 70 | 120 | 170 | 120 | 220 | 120 | 70 |
| PVP K30 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Magnesium stearate | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Talc | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Total weight | 525 | 525 | 525 | 525 | 525 | 525 | 525 | 525 | 525 |

The coefficient of determination R2 expressed the quality of the fitted model, and its statistical significance was checked by an F-test (analysis of variance) at the 5% significance level. The statistical significance of the regression coefficients was determined by using the t-test (only significant coefficients with p-value < 0.05 are included). The optimum processing conditions were obtained using graphical and numerical analysis based on the desirability function and response surface criteria.

**Preparation of Mucoadhesive Matrix Tablets:** Different batches of matrix tablets containing 200 mg of ACV were prepared using wet granulation. First, all necessary components were previously sieved through a mesh size of 16mm. In every case, the ingredients included in Table 1 (ACV, HPMC K4M, and MCC) were mixed homogeneously. A known quantity of PVP was dissolved in enough amount of ethanol to achieve a damp mass, and this solution was gradually added and mixed continuously to the previous mixture to form a damp mass, that was forced through a mesh size of 16 mm, and the granules obtained were dried at 40°C for 12 h. Dried granules were lubricated with 1% Magnesium stearate (w/w). Tablets with an average weight of 525 mg and a diameter of 12 mm were obtained by compressing the lubricated granules using a Rimek tablet punching machine, fitted with a 10 mm diameter flat and circular punch and applying the maximum compression force accepted by the formulation [9, 10].

**Characterization of Matrix Tablets:**

**a) Thickness:** Five randomly selected tablets from each batch were used for thickness determination. The thickness of each tablet was measured using Digital Vernier Caliper; their values were reported in millimeters. The mean and SD were calculated and reported.

**b) Weight Variation Test:** Twenty tablets were randomly selected from each batch and individually weighed using an electronic balance (Shimadzu). The average weight was calculated. The percentage deviation from average weight was reported.

**c) Hardness:** The resistance of the tablet to chipping, abrasion or breakage under storage conditions, transportation, and handling before usage depends on its hardness. The hardness of six randomly selected tablets from each batch was measured using Monsanto Hardness tester and expressed in $Kg/cm^2$. The average mean and SD were calculated.

**d) Friability:** Friability of tablets was performed by using Roche friabilator. The tablets should be carefully dedusted prior to testing.

Six tablets were randomly selected from each batch and accurately weighed the tablet sample, and place the tablets in the drum. Rotate the drum 100 times and remove the tablets, re-weighed and percentage loss was determined.

**e) Drug Content Estimation:** Twenty tablets were weighed individually and average was calculated and powdered. A quantity equivalent to 200 mg of Acyclovir was extracted with 100 ml of 0.1 N HCl. The solution was filtered through a filter paper (Whatman 044 µmpore size), properly diluted with 0.1 N HCl and drug content was determined by UV spectrophotometer at a wavelength of 256 nm and the percentage drug content was calculated.

**f) *In-vitro* Drug-release Studies:** The drug release study was performed using dissolution test apparatus (Lab India) for all the combinations of formulation. Dissolution was carried out in 0.1 N HCl at 50 rpm and temperature 37±1°C using USP II paddle system. Aliquots of 5ml were withdrawn periodically and the sample volume was replaced with an equal volume of fresh dissolution medium. All samples were analyzed by UV-spectrophotometer at 256nm [9].

**g) Measurement of Mucoadhesive Strength:** Mucoadhesive strength was evaluated using a texture analyzer (CEB Texture Analyzer, Make-Brookfield Engineering Labs, Inc., Model Texture Pro CT V1.4 Build 17). Fresh goatgastric mucosa was obtained from a local slaughter house and was used within 2 h of slaughtering. The mucosal membrane was washed with distilled water and then with 0.1N HCl subsequently it was fixed in between two plates and placed it in beaker. The tablet carefully attached to a 10-mm cylindrical probe (TA 3/100probe) by a bioadhesive tape. The probe attached with tablet was moved downward toward mucosa at a constant speed of 1mm/s until a predetermined compressive force of 0.5 N with holding time 60 s and load cell 1000gm. The probe was then removed with return speed of 1 mm/s to a distance of 15 mm and maximum detachment weight was determined for each sample. For each new sample, a different mucosa sample was used.

**RESULTS AND DISCUSSIONS:**

**Calibration Curve by UV Analytical Method:** Calibration curve was done in 0.1 N HCl. The

Regression Coefficients of 0.996 was obtained with the Equation Y= 0.066x-0.002

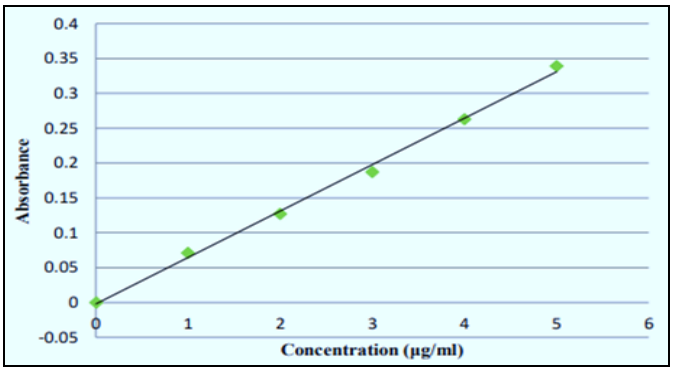


**FIG. 2: CALIBRATION CURVE OF ACYCLOVIR IN 0.1 N HCL**

**3.1 UV Spectroscopy (Determination of λmax):** The dilution of the drug in different solutions was done, and the UV spectrum was obtained, as shown in **Fig. 3**.

The absorption maximum was obtained at 256nm. Therefore, all further analysis was done at 256nm.

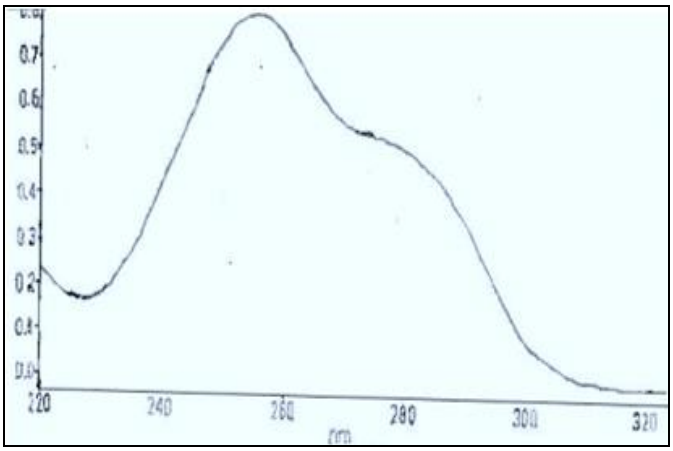


**FIG. 3: UV SPECTRA OF ACYCLOVIR IN 0.1N HCL**

**3.2 FTIR Spectroscopy:** The IR spectrum of the drug was recorded, and the interpretations of the functional groups were done as per the structure.

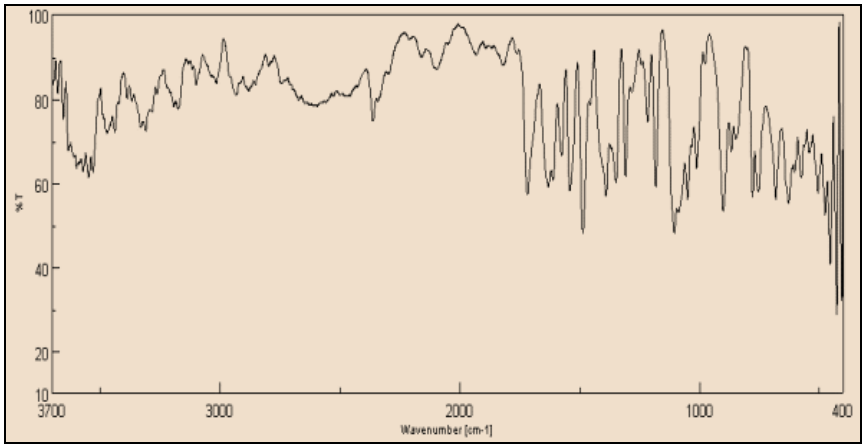


**FIG. 4: FTIR SPECTRUM OF ACYCLOVIR**

**TABLE 3: INTERPRETATION OF PEAKS OBTAINED IN THE IR SPECTRA OF ACYCLOVIR**

| Wave number ($cm^{-1}$) | Functional Group |
|---|---|
| 3359 | NH2 stretch |
| 3307 | N-H stretch |
| 3456 | O-H stretch |
| 1757 – 1671 | Carbonyl group band |
| 1668 | C-O stretch |
| 1450 | C=C stretch |
| 1265,1157 | C-O-C stretch |

**3.3 Drug Excipient Compatibility Studies:** The results showed that the principal IR peak of pure drug and its physical mixture with polymer was almost similar, indicating no interaction between drug and polymer during the formulation of tablets.

**3.4 Pre-formulation Studies of Powders:** The prepared powders were characterized for the angle of repose, bulk density, tapped density, Hausners factor and Car's compressibility index and the values were reported in **Table 4.**

The angle of repose of the different batches of powders was determined as per the method mentioned earlier, and results ranged between 21.07° to 26.17°. The bulk densities of powder ranged from 0.590 $g/cm^3$to 0.693 $g/cm^3$. Tapped density ranged between 0.763 $g/cm^3$ to 0.890 $g/cm^3$. The percentage compressibility, an indirect method of measuring powder flow property, was calculated, and it is in good agreement with the results of angle of repose and Hausner's ratio. All these results indicated that the powder possesses excellent flow properties and compressibility.

**TABLE 4: PHYSICAL PROPERTIES OF ACYCLOVIR BLEND WITH DIFFERENT EXCIPIENTS**

| Parameters/ batches | Bulk density | Tapped density | Hausners ratio | Car's index | Angle of repose(θ) |
|---|---|---|---|---|---|
| F1 | 0.590 | 0.879 | 1.14 | 12.41 | 24.50 |
| F2 | 0.683 | 0.781 | 1.12 | 11.88 | 22.98 |
| F3 | 0.650 | 0.778 | 1.13 | 10.89 | 22.35 |
| F4 | 0.675 | 0.769 | 1.13 | 10.87 | 25.38 |
| F5 | 0.687 | 0.789 | 1.15 | 11.93 | 22.81 |
| F6 | 0.629 | 0.767 | 1.12 | 12.33 | 21.07 |
| F7 | 0.680 | 0.763 | 1.14 | 11.87 | 23.46 |
| F8 | 0.627 | 0.890 | 1.11 | 12.78 | 26.17 |
| F9 | 0.693 | 0.798 | 1.14 | 13.40 | 25.41 |

**Formulation of Mucoadhesive Matrix Tablets:**

- **Optimization Study:** The design of experiment (DOE) is an approach in which process variables are first screened and then optimized to determine best settings for the variables. The full factorial design is a quadratic design that requires 3 levels (-1, 0, +1) for each factor. The concentration of Chitosan and HPMC K4M was selected as the independent variables, whereas Drug release and mucoadhesive strength were selected as the dependent variables. The interactions between the factors were demonstrated using 3-D graphs. The experimental values obtained were compared with those predicted by the mathematical models. The data generated is given in **Table 5,** which was analyzed using Design Expert software version 11.0, and polynomial equations were obtained for the same.

**TABLE 5: $3^2$ EXPERIMENTAL DESIGNS WITH RESPONSE**

| S. no. | Concentration of Chitosan (mg) | Concentration of HPMC K4M (mg) | *In-vitro* drug release (%) | Mucoadhesive strength (gm) |
|---|---|---|---|---|
| F1. | 150 | 150 | 63.12 | 78.01 |
| F2. | 50 | 50 | 65.31 | 57.12 |
| F3. | 150 | 50 | 87.11 | 80 |
| F4. | 100 | 150 | 66 | 64 |
| F5. | 50 | 150 | 60.02 | 56.02 |
| F6. | 150 | 100 | 79.10 | 74.05 |
| F7. | 50 | 100 | 71.05 | 59.07 |
| F8. | 100 | 100 | 81.21 | 68 |
| F9. | 100 | 50 | 89.33 | 72.04 |

**Response Surface Plots:**

**1. *In-vitro* Drug Release:**

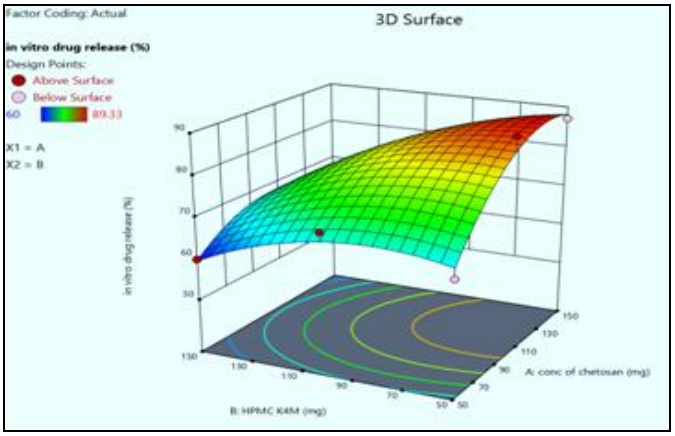


**FIG. 5: RESPONSE SURFACE FOR *IN-VITRO* DRUG RELEASE**

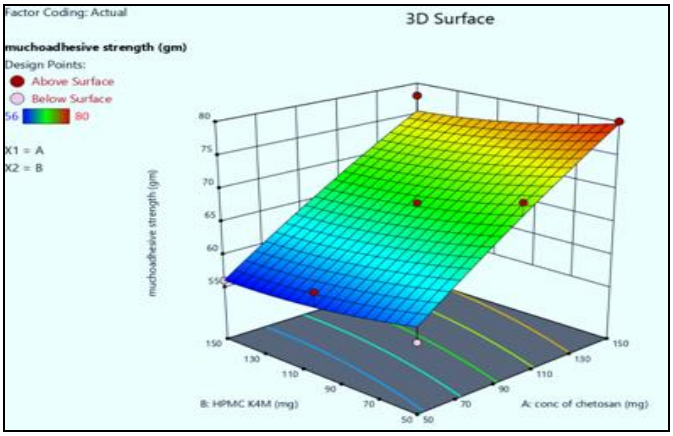


**FIG. 6: RESPONSE SURFACE FOR MUCOADHESIVE STRENGTH**

**2. Mucoadhesive Strength:** A $3^2$ factorial design that revealed the effect of process parameters on the responses as well as any interaction within was selected.

The negative sign of the coefficient of B, i.e., factor code for HPMC K4 M concentration that indicates

HPMC K4 M concentration has a dominant influence on *In-vitro* drug release, Eq.1. Drug release was performed at different concentrations of chitosan and HPMC K4 M ranging from 50-150mg. The drug release was lowest at low chitosan concentration and highest at high HPMC K4 M concentration. Still, the increase in chitosan at low HPMC K4 M concentration caused drug release to rise and subsequently decline. The negative sign of the coefficient of B i.e., factor code for HPMC K4 M indicates HPMC K4 M has a dominant influence on mucoadhesive strength. Eq.2. The mucoadhesive strength was mainly influenced by the chitosan, and HPMC K4 M had negligible effect, however, at higher HPMC K4 M, better mucoadhesive strength was seen as the chitosan increased.

The equation for *In-vitro* drug release:

*In-vitro* drug release = +82.28+5.52*A-8.74*B-4.78*AB-7.93*$A^2$-5.26*$B^2$…. Equation (1).

The equation for Mucoadhesive strength:

Mucoadhesive strength = +67.46+9.99*A-1.83*B-0.2500*AB-0.6550*$A^2$+0.8100*$B^2$…. Equation (2)

Analysis of variance (ANOVA) has been designed to determine the contribution and interaction of each variable to the model. The F distribution is a forecast proportion used by the analysis of the distribution of variances. The value of F would equate to one if they are equal. The F value of the ANOVA is the model mean square (MS) to the corresponding model mean square error. The higher the ratio, the higher the F value, and the more likely the variance that the model contributes is significantly higher than a random error.

The conclusion is based on the analysis of variance that the selected design sufficiently represents the statistics formulation of a sustained-release mucoadhesive drug delivery system. The ANOVA analysis of the linear model indicated that the model was significant ($p<0.05$), also endorsed by the large F value, and with the adequate Precision (ratio>4) observed, as shown in **Table 4.**

**TABLE 6: ANOVA STUDIES**

| S. no. | Outcomes | *In-vitro* drug release | Mucoadhesive strength |
|---|---|---|---|
| 1 | Models | Quadratic | Quadratic |
| 2 | $R^2$ VALUE | 0.9618 | 0.9483 |
| 3 | F – VALUE | 15.10 | 11.01 |
| 4 | P – VALUE | 0.0245 | 0.0350 |
| 5 | Adequate Precision | 10.0420 | 8.6217 |

**TABLE 7: DESIRABILITY FUNCTION OF OPTIMIZED FORMULATION**

| Formulation code | Chitosan (mg) | HPMC K4M (mg) | Desirability |
|---|---|---|---|
| F3 | 150 | 50 | 1 |

The optimized batch was obtained from statistical analysis of response plots using design expert software version 12. In the software, the criterion was selected in the range for % drug release and mucoadhesive strength; the desirability was found to be 1.000. The desirability concentration of Chitosan 150 (mg) and HPMC K4 M was found to be 50 (mg).

### 3.6 Evaluation of Matrix Tablets:

- **Thickness and Weight Variation test:** The thickness and weight variation results were represented in **Table 8.** The thickness of the prepared tablets was uniform and ranged between 3.24±0.065 mm to 3.84±0.064 mm. Also, it was observed that increasing the polymer concentrations resulted in a slight decrease in the tablet formulations' thickness. The weights of the prepared tablets ranged from 510±1.92 mg to 526±1.90 mg.

- **Hardness, Friability, and Drug Content Estimation:** The hardness, friability and drug content estimation results were reported in **Table 8.** The hardness of the tablets fell into the range of 5.30±0.13 kg/$cm^2$to 6.45±0.13 kg/$cm^2$.

  For all the formulations, friability ranged from 0.40% to 0.53%, indicating that the friability is within the prescribed limit of 1%. The percentage drug content of matrix tablets from each batch was found to be uniform and ranged from 96.32 ± 0.95 % to 101.11 ± 0.33%.

- ***In-vitro* Dissolution Study:** The dissolution studies of the batches (F1-F9) are given in **Fig. 7.** Dissolution studies of all batches were done. *In-vitro* drug release from matrix systems depends on several factors, such as the manufacturing process, the type of excipients, drug solubility, polymer concentration, and pH of the dissolution medium. It was found that the drug release from the tablets varied concerning the proportion of polymers. Increased polymer concentration reduced the diffusion of the drug from the matrix. If the viscosity increases, the entrapment of the drug is tightly bound in between the cross-links of the polymer; the drug will take time to release from the patches. From the results, it can be concluded that there was an increase in the duration of drug release with an increase in polymer concentration in the formula.

**TABLE 8: POST-COMPRESSION PARAMETERS OF MUCOADHESIVE MATRIX TABLET OF ACYCLOVIR**

| Batches | Thickness* | Hardness* (kg/sq.cm) | Friability (%) | Weight variation (mg) | Drug content* (%) |
|---|---|---|---|---|---|
| F1 | 3.53±0.24 | 5.65±0.12 | 0.40 | 515±2.30 | 96.32±0.95 |
| F2 | 3.48±0.027 | 6.16±0.14 | 0.50 | 526±1.90 | 100.95±0.45 |
| F3 | 3.24±0.065 | 6.00±0.14 | 0.45 | 525±2.03 | 97.56±0.39 |
| F4 | 3.84±0.064 | 5.30±0.13 | 0.41 | 515±2.35 | 97.20±0.81 |
| F5 | 3.44±0.039 | 5.89±0.11 | 0.53 | 513±2.12 | 101.11±0.33 |
| F6 | 3.54±0.051 | 5.67±0.16 | 0.50 | 528±1.92 | 97.99±0.77 |
| F7 | 3.52±0.039 | 5.81±0.14 | 0.43 | 522±2.13 | 99.14±0.91 |
| F8 | 3.57±0.053 | 6.45±0.13 | 0.46 | 510±1.92 | 99.15±0.95 |
| F9 | 3.51±0.046 | 5.94±0.20 | 0.49 | 525±2.02 | 100.11±0.27 |

* All values expressed in mean ± SD, n=3

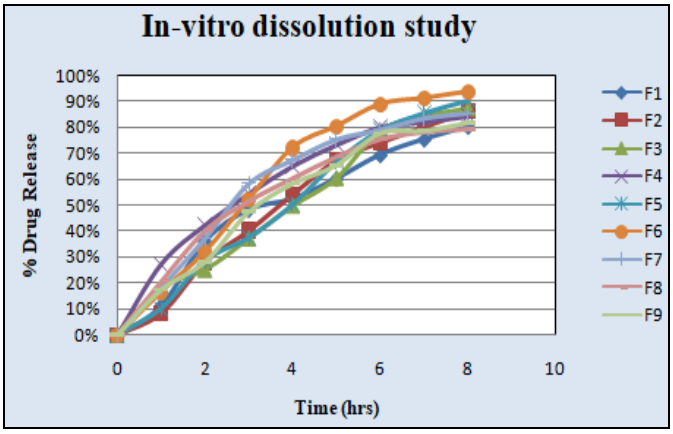


**FIG. 7: *IN-VITRO* DRUG RELEASE**

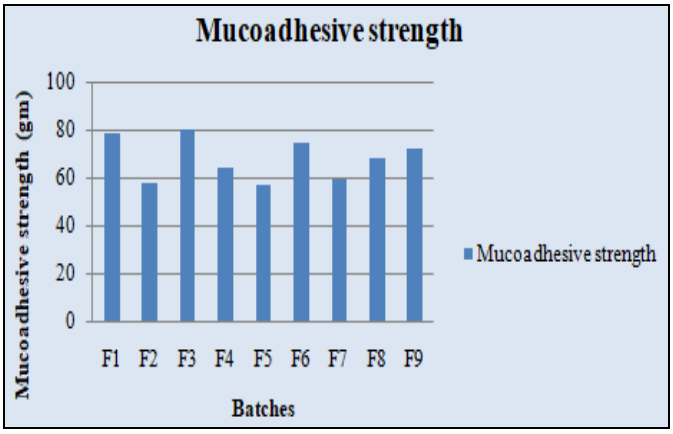


**FIG. 8: MUCOADHESIVE STRENGTH**

**Measurement of Mucoadhesive Strength:** The mucoadhesive strength for F1 to F9 batches was determined using the mucosal surface adhesion model. The mucoadhesive strength of the tablet was dependent on the property of the bioadhesive polymers, which on hydration, adhere to the mucosal surface, and also on the concentration of polymer used. Bioadhesive force values ranged from 56.02 gm to 80gm. The in-vitro retention time is one of the important physical parameters of mucoadhesive tablets recorded as per the procedure mentioned above. Retention time values ranged from 3.5 h to 8.5 h. The result showed that, as the concentration of mucoadhesive polymer increased, the retention time also increased.

**CONCLUSION:** According to this study, the polymers HPMC K4M can create a regulated drug release pattern in the acyclovir tablets that have been manufactured. Due to this formulation's strong mucoadhesive strength, it is likely to spend more time in the digestive system, raising the bioavailability level. However, a correct balance between the various amounts of the polymers is required to achieve optimal release and mucoadhesion. Complete drug release can be achieved before the absorption window by creating mucoadhesive Acyclovir tablets. As a result, the issue of incomplete drug release and unpredictable absorption can be resolved by lengthening the retention time of the medication in the GIT.

**ACKNOWLEDGMENT:** Authors express their sincere gratitude to Faculty members of AISSMS College of Pharmacy, Pune, for continuous motivation, support, and guidance for research activity and for providing all required facilities to accomplish the entitled work.

**CONFLICTS OF INTEREST:** The authors declare that they have no competing interests.

## REFERENCES:

1. Modi SA, Gaikwad PD, Banker VH and Pawar SP: Sustained release drug delivery system: A review. Int J of Pharm Res &Deve 2012; 4(3): 147-156.
2. Fahan JA, Sushma D, Smriti K and Sheveta B: Development and evaluation of floating matrix tablets of Acyclovir. Res J Pharma Bio Che Sci 2011; 2(4): 547-553.
3. Chickering DE and Mathiowitz E: Definitions, Mechanisms and Theories of Bioadhesion. In DE Chickering E. Mathiowitz, CM. Lehr. Bioadhesive Drug Delivery Systems: Fundamentals, Novel Approaches and Development. New York Marcel Dekker 1999; 1-10.
4. Chowdary KPR and Srinivas L: Mucoadhesive drug delivery systems: A review of current status. Indian Drug 2000; 37(9): 400−406.
5. Lee WJ, Park JH and Robinson JR: Bioadhesive dosage form: The next generation. J Pharm Sci 2000; 89: 850−864.
6. Ahuja RP and Khar J. Ali: Mucoadhesive drug delivery systems. Drug Dev Ind Pharm 1997; 23: 489– 515.
7. Peppas NA and Sahlin JJ: Hydrogels as mucoadhesive and bioadhesive materials: a review. Bioma 1996; 17: 1553-61.
8. Nangia A: Bioadhesives for targeted oral drug delivery. Drug Delivery Report Spring/Sumer 2006; 12: 134-142.
9. Lachman L, Lieberman HA and Kanig JL: The theory and practice of industrial pharmacy. 3rd ed. Delhi: Varghese Publishing House 2008; 293-342.
10. Senyigit Z, Vetter A, Guneri T and Bernkop-Schnurch A: A comprehensive *in-vitro* and *in-vivo* evaluation of thiolated matrix tablets as a gastroretentive delivery system. Drug Delivery 2011; 18(6): 405-414.

**How to cite this article:**
Madgulkar A, Bhalekar M, Kaur T and Thange N: Formulation and evaluation of mucoadhesive matrix tablet of acyclovir. Int J Pharm Sci & Res 2022; 13(9): 3525-34. doi: 10.13040/IJPSR.0975-8232.13(9).3525-34.