PREPARATION AND EVALUATION OF ACYCLOVIR LOADED FAST DISSOLVING BUCCAL PATCHES

Abstract

Acyclovir, an anti-retroviral agent, is utilized for treating HIV-1 infection. The aim of this study was to fabricate and evaluate Acyclovir loaded fast dissolving mucoadhesive buccal patches. The buccal patches of Acyclovir were produced using the solvent casting technique. The resulting films were subjected to various evaluation tests like weight variation, thickness, swelling index, surface pH, folding endurance, and In-vitro drug release study. All formulations displayed positive outcomes for physicochemical characteristics. In the In-vitro drug release studies, the patches exhibited rapid release within 5 hours. Formulation F1, which contained HPMC and croscarmellose, did not cause irritation on the buccal mucosa. It was found that the composition of superdisintegrants significantly influenced the drug release. Therefore, it is possible to determine that a stable dosage form for fast release of Acyclovir can be developed using buccal patches.

Keywords: Fast dissolving Buccal patches, Acyclovir, superdisintegrants, % Cumulative drug release

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I. INTRODUCTION

Oral route has been the commonly adopted and most convenient route for drug delivery. Oral administration has been received more attention in the pharmaceutical sector because of the more flexibility in the designing of dosage form than drug delivery design for other routes, administration convenience as well as traditional belief that by oral administration the drug is fine immersed as the food stuffs that are ingested daily [1,2] Rich blood supply, robust nature, short recovery times after stress or damage, lower enzymatic activity of saliva, facile removal of formulation, better patient acceptability and compliance are some other significant benefits of mucoadhesive systems.

Acyclovir is the most effective antiviral drug against HIV. Acyclovir oral absorption is dosage dependent and highly variable, with bioavailability ranging from 15% to 30%. Acyclovir has limited percutaneous absorption. [3] The main disadvantages of this medication include stomach discomfort, first pass metabolism, and limited oral bioavailability. Stinging and burning sensations are common side effects of medication topical administration. However, the medicine is well tolerated when taken orally. Rashes, sweating, and emesis are noted after intravenous injection. As a result, an oral delivery strategy for acyclovir that enhances systemic distribution, bypass of first pass metabolism, and increased bioavailability is required.

The current research aims to develop rapid dissolving mucoadhesive buccal patches loaded with acyclovir that will operate as transmucosal drug delivery systems to improve oral bioavailability.

II. MATERIALS AND METHODOLOGY

Acyclovir was purchased from yarrow chemicals Mumbai, Glycerol, HPMC K4M, Croscarmellose, Crospovidone, Sodium Starch Glycolate, Citric acid, Sodium Lauryl Sulphate, Methanol, Ethanol, Chloroform was procured from yarrow chem. Ltd. All other materials used and received were of analytical quality.

III. METHODOLOGY

1. **Drug-polymer-excipient compatibility studies:** Infrared light absorption spectroscopy (IR) was utilized to perform this task. The infrared spectra of the pure drug and the mixture of formulations were obtained by dispersing the drug and formulation mixture in an appropriate material (KBr) using a Fourier Transform Infrared Spectrophotometer (FTIR). Following a baseline correction with dried KBr, the FTIR spectrum of the dehydrated blend of drugs and formulation mixture, and KBr were recorded.

2. **Preparation method for buccal patches:** The mucoadhesive buccal patches were developed using the solvent casting technique. In this process, the required amount of mucoadhesive polymers is mixed with a solvent, and the polymers swell after vigorous mixing. A measured quantity of plasticizer is then added to the polymer mixture and mixed again. The necessary amount of the drug is liquefied in a small volume of solvent system and added to the polymer solution, ensuring thorough mixing. The solution is then placed into a petri dish containing glycerin and left to dry overnight, allowing the solvents to evaporate. Finally, the dried patches are collected.

Table 1: Formulation table of Acyclovir mucoadhesive buccal patches

Ingredients	F1	F2	F3	F4	F5	F6
Acyclovir (mg)	50	50	50	50	50	50
Glycerol(mg)	200	194	200	194	200	194
HPMC(mg)	400	400	400	400	400	400
Croscarmellose(mg)	20	26	-	-	-	-
Crospovidone(mg)	-	-	20	26	-	-
SSG(mg)	-	-	-	-	20	26
Citric acid (mg)	6	6	6	6	6	6
SLS(mg)	1	1	1	1	1	1
Orange spirit(mg)	5	5	5	5	5	5
Methanol:Ethanol:Chloroform(solvents)	6:9:12	6:9:12	6:9:12	6:9:12	6:9:12	6:9:12

IV. EVALUATION TESTS FOR PATCHES

1. **Weight Variation:** The patches were cut in the required sizes and weights were calculated individually.

2. **Thickness:** The each patch thickness was assessed by employing a screw gauge at various positions across the film, and the average thickness was subsequently computed.

3. **Moisture Absorption:**The patches were initially weighed (w1) and placed inside desiccators containing anhydrous Aluminum chloride. After duration of 3 days, the patches were weigh again (w2). The % moisture absorption was determined using the following calculation:

$$\% \text{ Moisture absorption} = \frac{\text{Final weight} - \text{initial weight}}{\text{initial weight}} \text{ X } 100$$

4. **Moisture Loss:** The patches were weighed initially (w1) and the patches were subsequently put into desiccators with anhydrous calcium chloride. After an age of 3 days, the patches were weighed again (w2). The % moisture absorption was determined by utilizing the following calculation:

$$\% \text{ Moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{initial weight}} \text{X } 100$$

5. **Folding Endurance:** The folding endurance of the patches was evaluated by repetitively folding a 20mm diameter patch at the same location until it fractured. The folding endurance rating was measured by the numeral of times the patch might be folded at the identical location without breaking.

6. **Drug content uniformity:** Drug content uniformity of the films was assessed by taking a 1 cm^2-sized film, which was then positioned in a beaker containing 100 ml of phosphate buffer with a pH of 6.8. The films were permitted to dissolve in the solution, and the contents were subsequently transferred to a volumetric flask. The absorbance of the solution was analyzed using spectrophotometric analysis (UV-Visible) to determine the absorbance at the wavelength (λmax) of 252 nm.

7. **Surface p^H:** To determine the surface pH, the patches were permissible to swell in 6.8 pH phosphate buffer for duration of 2 hours. pH paper was then placed on the plane of the patches to measure the surface pH. The mean value of three readings was recorded.

8. **Swelling Index:** A film containing the drug, measuring 1 cm2, was weighed and subsequently immersed in 50 ml of phosphate buffer with a pH of 6.8. After a period of 2 hours, the patch was taken out and again weighed. The disparity between the final and initial weights provided the outcome of the weight increase caused by water absorption and film swelling.

$$\text{Swelling index} = \frac{\text{Final weight} - \text{initial weight}}{\text{initial weight}} X\ 100$$

9. **Disintegration time:** It serves as a crucial factor in the formulation of the dosage form. It denotes the duration needed for the dosage form to disintegrate into granules of a specific size under precisely defined conditions.

10. **Diffusion Studies:** The fabricated patches were sliced to meet the required dimensions and then affixed to the open end of a glass test tube. The tube was subsequently positioned inside a beaker filled with a phosphate buffer solution having a pH of 6.8. The beaker was placed on a magnetic stirrer, and the temperature was maintained at 37±0.50°C. At regular intervals of 1 minute, a specific volume of samples was extracted, and an alike quantity of fresh medium was added in its place. The absorbance of the solution was measured using UV-Visible spectrophotometric analysis to determine the absorbance at the wavelength of 252 nm (λmax).

11. **Kinetic study:** The matrix systems were found to exhibit a release rate that adheres to zero-order kinetics and follows a diffusion mechanism for drug release. To examine the release mechanism and kinetics of the dosage form, the collected data was analyzed using different models like First order, Zero order, Higuchi, and Peppa's model. By comparing the obtained r^2 values, the most suitable model was chosen as the best fit.

V. RESULTS AND DISCUSSION

1. **Drug polymer compatibility studies:** The infrared (IR) spectrum of the pure drug displayed a resemblance to the standard spectrum of Acyclovir. The frequencies of the following groups are observed in the spectrum of Acyclovir shown in 1037, 1330, 1412, 1586, 2923, 3108 cm^{-1}.

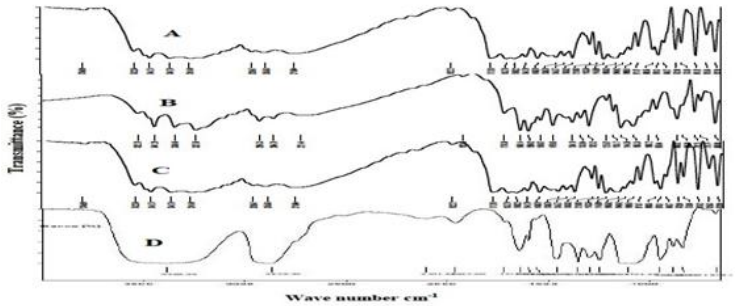

Figure 1: A) FTIR Spectrum of Acyclovir B) FTIR Spectrum of Acyclovir with HPMCK4M C) FTIR Spectrum of Acyclovir with crospovidone D) FTIR Spectrum of Acyclovir with SSG

2. **Preparation of fast dissolving mucoadhesive Buccal patches:** Buccal patches acyclovir is prepared by solvent evaporation method.

Figure 2: Acyclovir fast dissolving mucoadhesive Buccal patches

3. **Evaluation Results of Prepared Acyclovir Buccal Patches:**

- **Weight variation:** A weight variation test was conducted, and the weights of the patches ranged from 0.30 gm to 0.35 gm. As a result, all patch formulations successfully met the weight variation requirements. The results are presented in Table 2.

- **Thickness:** The thickness of the formulations from F1-F9 ranged from 0.21 mm to 0.28 mm. The corresponding results can be found in Table 2.

- **Percentage moisture absorption:** The % of moisture absorption for all formulations ranged from 6.45% to 14.70%. The specific results can be found in Table 2.

- **Percentage Moisture loss:** The formulations exhibited a percentage of moisture loss ranging from 9.09% to 16.12%. The results can be found in Table 2.

- **Folding endurance:** The folding endurance, which indicates the fragility of the strip, was determined by counting the numeral of times the strip might be folded at the identical spot without breaking. For the prepared films, the folding endurance was measured manually. The results of this test can be found in Table 2.

- **Drug content:** The drug content percentage for all formulations ranged from 85.34% to 96.73%. The corresponding results can be found in Table 2.

- **Surface pH:** The surface pH of the prepared inserts fell within the range of 6.7 to 7. These indicate that the inserts would not cause any pH changes in the tear fluid of the eye. The results can be found in Table 2.

- **Swelling index:**The swelling index for all formulations ranged from 0.52% to 0.86%. The results can be found in Table 2.

- **Disintegration time:**The disintegration time of every formulation ranged from 32 to 59. The corresponding results can be found in Table 2.

Table 2: Evaluation studies of formulated buccal patches

Formula No.	Weight variation (mg)	Thickness (mm)	% of Moisture absorption	% of Moisture loss	Folding endurance	Drug content (%)	Surface pH	Swelling Index (%)	Disintegration Time (sec)
F1	0.30	0.21	9.10	9.09	295	98.34	7.0	0.86	32
F2	0.33	0.26	15.23	15.74	267	96.73	6.8	0.65	34
F3	0.33	0.23	14.60	11.87	285	91.63	6.7	0.61	40
F4	0.31	0.24	10.52	16.48	191	88.16	6.8	0.69	46
F5	0.35	0.28	12.35	12.20	199	94.49	6.9	0.84	59
F6	0.34	0.23	6.45	16.12	205	91.54	7.0	0.86	54

4. In vitro drug release studies:

Table 3: % Cumulative drug release studies for all formulations

Time in min	F 1	F 2	F 3	F 4	F 5	F 6
0	0	0	0	0	0	0
0.5	25.12	22.43	23.37	19.46	24.45	24.36
1	41.49	37.63	33.65	24.63	34.42	35.42
1.5	50.17	49.47	49.34	39.58	43.67	45.43
2	69.38	65.14	57.48	64.45	58.62	65.88
3	77.64	74.63	68.36	71.31	69.71	75.43
4	87.73	83.63	79.49	80.41	84.97	85.66
5	97.14	92.15	94.59	87.98	95.67	96.74

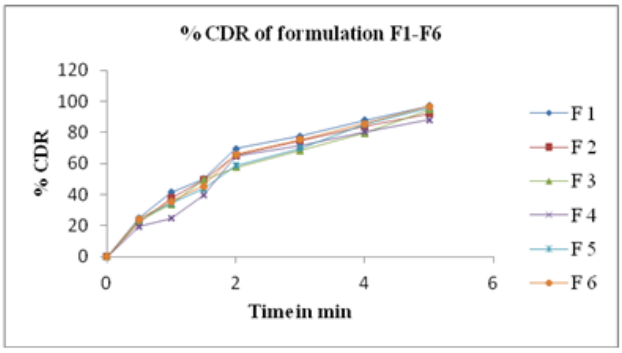

Figure 3: Percentage cumulative drug release of F-F6

Amongst all formulations, the one prepared with croscarmellose demonstrated superior drug release compared to the other five formulations (F2, F3, F4, F5, and F6). In the case of formulation F1, 97.14% of the drug was released within 5 minutes. On the other hand, formulations F2, F3, F4, F5, and F6 exhibited release percentages of 92.15%, 94.59%, 87.98%, 95.67%, and 96.74% respectively.

5. In vitro release kinetics:

Table 4*: In vitro* Drug release kinetics of F1 formulation

Formulation code	Zero order		First order		Higuchi model		Korsmeyer-peppas		Release Mechanism transport
	Slope	R^2	Slope	R^2	Slope	R^2	n	R^2	
F1	17.97	0.899	-0.279	0.949	45.22	0.986	1.072	0.314	Super case II Transport

The best formulation, F1, was analyzed using four different models: First order, Zero order, Higuchi order, and Peppas model equations. Among these models, the Higuchi model provided the best fit for all formulations. The diffusional exponent (n) values ranged from 0 to 98.57, indicating that the drug release from the formulation occurred primarily through diffusion followed by an erosion mechanism.

VI. CONCLUSION

These results indicated that F1 (drug 50 mg) with croscarmellose of Acyclovir buccal patches has achieved the objective of considerable influence on the physio chemical characteristics and releasing property. The concentration of Croscarmellose in the formulation determines the drug release from the patches. As the concentration of Croscarmellose increases, drug release also increases. So, finally the best concentration of Croscarmellose was found to be 20 mg and formulation F1 gave the best results.

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