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Research Article

Effect of Polymer Type, Concentration and Formulation Technique on Mucoadhesive Strength and Swelling Index of Clarithromycin Tablets

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Abstract

This study aims to evaluate the effect of polymer type, concentration, and formulation technique on mucoadhesion and the Swelling Index of matrix tablets. Tablets were formulated by wet-granulation, solid dispersions, and direct compression techniques using different polymers in different concentrations (D:P 5:1, 5:2, and 5:3). Swelling Index and Mucoadhesive strength were analyzed for all the formulations (F1-15). The physicochemical parameters of the tablets were found to be within the acceptable limit. The swelling index for matrix tablets (F1-15) prepared by wet-granulations technique was found to be ranging from 33.81±2.42 - 67.36±0.77; by solid dispersions technique ranging from 34.02±1.32 - 65.09±1.08; by direct compression technique ranging from 36.82±2.02 - 68.35±1.73, after 6 hours. Mucoadhesive strength ranged from 13.673 ± 1.542 to 40.378 ± 2.345N, increasing with an increase in the polymer concentrations. The study helped to find the drug's optimum formulation with excellent bio adhesive strength.

Keywords: Clarithromycin, hydrophobic polymers, tablets, mucoadhesiveness, Swelling Index

1. Introduction

The oral route of drug administration is the ideal, convenient, and preferred route (Hwang *et al*., 1998. Conventional oral drug administration does not generally offer target specificity or rate-controlled release. In controlled release drug delivery systems (CRDDSs), an active therapeutic agent is incorporated in the structural network of the polymer in such a way that the drug is released in a predefined controlled manner (Misra et al. 2008). Prolonging gastric residence time (GRT) is the most important objective of CRDDSs, as short GRT is the major hindrance in the development of CRDDSs. The prolonged residence time of the drug in the body is believed to prolong its duration of action(Deshpande et al. 1996, Wilding 2000). Mucoadhesive controlled drug delivery systems (MCDDSs) offer several advantages over other CR systems since they provide a controlled drug release over time, target, and localize the dosage form to a specific site (Rajput et al. 2010). Mucoadhesive drug delivery devices can be applied to any mucosal tissue in the body, including the gastrointestinal, ocular, respiratory, buccal, nasal, rectal, urethral, and vaginal path (Lee, Park, and Robinson 2000, Peppas et al. 2000). Since a mucus layer covers the gastrointestinal (GI) tract, localization of an MCDDS at a specific site is very beneficial. Depending upon the drug delivery system, the drug release time may vary from a few hours to months or even several years. Gastroretentive drug delivery techniques (GRDDTs) are principally CRDDSs that increase GRT and, subsequently, increases absorption of drug for the projected time duration. Diverse

Table I. The composition of various Clarithromycin formulations fabricated by different techniques

Formulation code	Polymer	D:P	Drug (mg)	Polymer (mg)	Lactose (mg)	Talc (mg)	Mag Stearate (mg)
F1	Methocel®	5:1	500	100	360	30	10
F2		5:2	500	200	260	30	10
F3		5:3	500	300	160	30	10
F4	Carbopol	5:1	500	100	360	30	10
F5		5:2	500	200	260	30	10
F6		5:3	500	300	160	30	10
F7	Ethocel®	5:1	500	100	360	30	10
F8		5:2	500	200	260	30	10
F9		5:3	500	300	160	30	10
F10	CMC	5:1	500	100	360	30	10
F11		5:2	500	200	260	30	10
F12		5:3	500	300	160	30	10
F13	Eudragit	5:1	500	100	360	30	10
F14		5:2	500	200	260	30	10
F15		5:3	500	300	160	30	10
Control	------	----	500	----	460	30	10

means for preparation of gastroretentive drug delivery formulations include mucoadhesive systems, floating systems, swellable and expandable systems, high-density systems, altered shape systems, gel-forming solution or suspension systems, and sachet systems (Streubel, Siepmann, and Bodmeier 2006a, b). Mucoadhesion has been an extensively adapted approach for achieving site-specific drug delivery by amalgamating mucoadhesive polymers in pharmaceutical formulations and the active pharmaceutical ingredient (API). Mucoadhesive materials are hydrophilic macromolecules containing numerous hydrogen-bond-forming groups. The mechanism by which mucoadhesion takes place has been said to have two stages; first, the contact (wetting) stage, followed by the consolidation stage (the establishment of the adhesive interactions) (Smart 2005).

Clarithromycin belongs to the macrolide group of antibiotics. Its molecular formula is $C_{38}H_{69}NO_{13}$. The difference between Clarithromycin and erythromycin is the methylation of the hydroxyl group at position No. 6. Clarithromycin is more effective than erythromycin against the strains of *Staphylococci* and *Streptococci*. It has modest activity against *H. influenzae* and *N. gonorrhea*. It has good activity against *M. catarrhalis, Chlamydia spp., L. pneumophila, B. burgdorferi,* and *Mycoplasma pneumoniae.* It is used at 250 mg twice daily for children over 12 years and adults with mild to moderate infection. For severe infections, higher doses are required. Extended-release tablets are prescribed as two 500 mg tablets once daily. It is bacteriostatic because it inhibits protein synthesis by binding reversibly to 50 S ribosomal subunits of the microorganism. It prevents the translation of peptides. Clarithromycin and erythromycin have similar antibacterial spectrums (Alfered, 1996).

The current study aimed to formulate and evaluate once daily controlled release mucoadhesive tablets of Clarithromycin. The prepared batches were evaluated for tablet parametric tests (diameter, thickness, hardness, friability, and tensile strength), Swelling Index, mucoadhesive strength (using a texture analyzer), and *in-vitro* drug release studies.

Table 2. Swelling index of matrix tablets prepared by wet granulation technique

Formulation code	Swelling Index (%), (n=3, mean±SD)					
	1 hr	2 hrs	3 hrs	4 hrs	5 hrs	6 hrs
F1	32.97±1.00	38.46±3.61	39.01±1.89	38.36±2.81	35.72±2.35	33.81±2.42
F2	32.17±0.59	38.06±1.10	41.11±0.56	43.26±1.32	44.21±1.24	45.88±0.93
F3	33.02±1.33	44.16±0.31	46.62±0.61	47.42±0.75	48.27±0.87	49.53±1.03
F4	41.08±3.03	53.44±2.49	58.03±2.44	60.88±1.65	62.65±1.21	64.82±0.27
F5	39.66±0.79	50.02±1.98	55.89±2.24	59.25±1.07	62.26±0.50	64.59±0.43
F6	41.24±0.89	47.81±1.01	56.01±1.29	62.20±1.18	65.46±1.37	67.36±0.77
F7	44.36±1.33	49.84±1.71	53.32±0.27	52.97±0.75	49.95±1.10	48.49±1.87
F8	42.19±3.17	48.88±2.36	48.05±3.11	47.21±2.58	46.52±2.89	45.42±2.59
F9	42.41±3.36	51.08±2.93	51.03±3.07	48.59±1.35	45.25±2.61	43.01±3.12
F10	61.74±2.01	66.04±1.88	65.29±1.93	64.78±1.86	62.48±1.37	61.37±1.72
F11	63.26±3.12	61.72±2.10	61.49±2.29	60.54±2.60	60.61±2.25	60.68±2.49
F12	63.31±1.09	66.55±0.90	67.85±1.54	67.12±0.46	65.23±1.27	66.66±1.92
F13	41.09±0.87	47.52±2.34	46.09±1.95	40.61±0.64	40.76±3.79	36.86±2.04
F14	48.81±1.04	54.43±2.09	51.45±2.90	43.27±1.59	41.58±.075	36.76±2.68
F15	44.36±1.01	51.86±2.08	53.62±1.84	48.07±0.93	46.02±0.20	42.08±2.10
Control	37.29±2.07	36.17±2.46	26.55±3.07	24.33±1.57	21.94±2.92	13.65±0.38

2. Materials & Methods

2.1 Materials

Clarithromycin was gifted by Feroze Sons laboratories (Pvt Ltd) Nowshera, Pak. Methocel®, Ethocel® 7FP (Dow Chemicals, Midland, USA), carboxymethylcellulose (CMC), sodium hydroxide, potassium phosphate (monobasic), disodium hydrogen phosphate (Merck, Germany), magnesium stearate (Solomon Enterprise, Karachi), lactose (BDH Chemical Limited, Pool, England), HPLC grade water (Fisher, England), and sample tubes (Eppendrof Netheler Hinz GmbH, Hamburg, Germany). All chemicals used were of analytical grade.

2.2. Preparation and Fabrication of Matrix Tablets

2.2.1. Wet Granulation

A Specified quantity of Clarithromycin was mixed with polymer and lactose, as shown in **Table 1.** The physical mixture was mixed thoroughly and passed through sieve number 30. Then the suitable quantity of distilled water was mixed with a physical mixture until a doughy mass was formed. Then these prepared dough granules were sieved through mesh ≠ 10. These sieved wet granules were then placed in a tray dryer and dried at a temperature of 50 °C. The dried mass was again passed through mesh ≠ 30. Then added the required excipients, such as talcum and magnesium stearate. After that, the mixture was thoroughly blended, and the final granules were compressed using flat 13 mm punches in the tableting compression machine (Erweka, AR 400 GMBH, Germany) (Akhlaq et al. 2014).

2.2.2. Solid Dispersions

Solid dispersions of Clarithromycin matrix tablets with different polymers were prepared (Shivakumar, Desai, and Deshmukh 2008). Clarithromycin was dissolved in chloroform with different polymers, drug-to-polymer ratios (D:P), and lactose. It was stirred with the help of a magnetic stirrer for 4 hrs at room temperature. Then the organic solvent was evaporated with the help of a water bath. The mixture was further dried using a rotary evaporator until the solvent disappeared completely. The residue was then placed in the vacuum drier for 24 hrs. at the temperature of 40 °C. The samples were then passed through a mesh # 100 to get the granules of uniform particle size. The samples were then

Table 3. Swelling index of matrix tablets prepared by solid dispersions technique.

Formulation code	Swelling Index (%), (n=3, mean±SD)					
	1 hr	2 hrs	3 hrs	4 hrs	5 hrs	6 hrs
F1	24.92±1.01	25.46±3.32	29.01±1.00	31.32±2.81	33.32±1.33	34.02±1.00
F2	32.13±0.52	34.06±1.13	38.11±0.32	40.01±1.30	45.01±1.32	46.83±0.84
F3	36.03±1.21	42.16±0.34	43.62±0.38	45.33±0.72	47.24±0.20	50.52±1.00
F4	42.05±3.10	54.44±2.45	59.03±2.01	60.01±1.68	63.27±1.01	65.80±0.07
F5	42.61±0.32	52.02±1.93	55.89±2.22	58.10±1.04	61.01±0.92	63.55±0.23
F6	41.23±0.21	48.81±1.04	57.01±1.24	61.18±1.18	64.27±1.00	64.10±0.08
F7	44.30±1.55	50.84±1.76	53.32±0.01	46.53±0.32	48.18±1.39	49.33±1.04
F8	45.11±3.63	51.88±2.37	48.05±2.12	46.32±1.83	44.01±1.33	44.02±1.39
F9	43.19±3.10	55.08±2.92	54.03±2.46	49.47±1.03	46.17±1.60	42.88±1.10
F10	64.92±2.14	66.04±1.86	65.29±1.03	63.82±1.32	61.23±1.32	60.09±1.12
F11	67.23±3.01	63.72±2.19	64.49±2.01	61.10±1.60	60.01±2.02	59.20±0.19
F12	63.32±1.11	66.55±0.91	67.85±1.32	67.01±0.09	64.10±1.00	67.83±1.02
F13	45.05±0.73	51.52±2.00	47.09±1.44	39.43±0.32	39.24±3.43	35.01±1.09
F14	50.84±1.11	54.43±2.23	52.45±2.28	43.01±1.73	40.19±.029	38.32±0.64
F15	42.38±1.93	55.86±2.06	55.62±1.02	47.19±1.90	45.32±0.01	43.19±1.43
Control	37.31±2.10	38.17±2.22	28.55±3.17	23.32±0.57	20.72±1.43	15.35±0.98

stored in an air-tight amber-colored glass jar. Then talcum and magnesium stearate were mixed in each batch thoroughly. Finally, these granules were compressed to form matrix tablets using 13 mm flat punches. The compression machine used was Erweka, AR 400 GMBH, Germany **(table 1)**.

2.2.3. Direct Compression

A specified quantity of Clarithromycin was mixed with different polymers, in different D:P, and other excipients, including lactose, talcum, and magnesium stearate. This mixture was then thoroughly mixed and screened through mesh ≠ 20 in order to obtain a powder mixture of uniform particle size. The mixture was compressed (by Erweka, AR 400 GMBH, Germany) to form the matrix tablets (see Table 1)

2.3. Post-Compression Evaluation of Matrix Tablets

Various physiochemical tests, including hardness, friability, dimensional studies (thickness and diameter), weight variation, and content uniformity, were performed on the test batches of Clarithromycin tablets (Akhlaq et al. 2014). The values were taken in triplicate, and the means and standard deviation were calculated.

2.3.1. Swelling Index

The extent of swelling is measured as the percentage weight of the tablet increased. To determine this, 3 tablets were taken from each formulation. Each tablet was weighed and placed in a petri dish containing buffer solution (25 ml / 1.2 pH). The readings were taken at one-hour intervals for a period of 6 hrs. After each time interval, the tablet was taken out of the buffer solution, removed excess water with absorbing tissue, and then the tablet was weighed again. The procedure for estimating the swelling index was performed in triplicate, then the average of these three readings was calculated, and the results were reported in the form of mean±SD. The following was used to measure the swelling index of the test-formulated tablets (Singh et al. 2012)

$$\% \quad \text{Swelling} \quad \text{Index} = W_1 - W_2 \Big/ W_2 \times 100 \qquad (1)$$

Where "W_1" represents the weight of the tablets after a specific interval of time, and "W_2" represents the weight of the tablet before swelling i.e. the initial weight.

Table 4. Swelling index of matrix tablets prepared by direct compression technique

Formulation code	Swelling Index (%), (n=3, mean±SD)					
	1 hr	2 hrs	3 hrs	4 hrs	5 hrs	6 hrs
F1	31.92±3.02	38.45±2.60	37.05±1.83	39.52±2.80	34.74±2.35	38.03±1.00
F2	32.14±1.54	38.03±0.13	40.13±0.52	41.56±1.31	45.25±1.23	46.84±0.32
F3	34.03±3.32	44.16±0.34	47.63±0.65	44.2±0.71	45.25±0.80	44.54±1.11
F4	40.04±2.02	53.43±2.45	59.03±2.41	61.38±1.62	66.66±1.25	64.85±0.21
F5	42.63±1.74	50.01±1.96	56.85±2.22	55.55±1.03	62.25±0.50	63.56±0.32
F6	42.25±0.86	47.86±1.06	55.05±1.24	61.40±1.15	65.44±1.33	65.97±0.51
F7	43.36±2.32	49.81±0.74	52.36±0.25	50.57±0.75	49.96±1.15	46.48±1.84
F8	44.13±2.15	48.84±2.36	49.06±3.10	46.41±2.56	46.57±2.86	47.43±2.54
F9	45.43±3.37	51.02±2.95	50.07±3.05	45.59±1.35	45.27±2.65	47.02±3.11
F10	60.75±1.02	66.02±2.86	64.22±1.94	63.48±1.86	61.43±1.35	68.35±1.73
F11	62.26±3.19	61.74±1.15	60.44±2.23	61.64±2.65	62.65±2.24	61.66±2.46
F12	61.36±1.04	66.52±3.93	66.82±1.54	65.42±0.46	64.24±1.25	64.67±1.90
F13	40.05±0.85	47.54±2.33	45.04±1.93	41.11±0.64	42.76±3.75	36.82±2.02
F14	46.86±1.03	54.40±2.05	50.41±2.92	42.47±1.59	41.52±.075	37.75±2.01
F15	40.36±1.07	51.82±1.04	52.60±1.81	47.27±0.95	45.06±0.26	48.05±2.11
Control	35.25±2.06	36.12±1.46	25.52±3.09	23.33±1.53	20.91±2.95	14.84±2.32

2.3.2. Mucoadhesive Force

The mucoadhesive force was measured by a reported method (Shaikh, Pawar, and Kumbhar 2012) with slight modifications. The left plate of the balance was used for placing the weight needed to determine the adhesive strength. A sheep's intestinal mucosa was used as a model membrane. The mucosal membrane was incised, and the underlying adipose and connective tissues were removed. It was placed in the phosphate buffer, having a pH of 1.2. It was equilibrated at the temperature of 37± °C. The tablet was attached to the lower side of the right plate of the balance with the help of double-sided sticking tape. The tablet was then lowered onto the mucosa and placed on a platform. The tablet was pressed against the mucosa by a constant weight of 5 grams for a period of 5 minutes. The mucoadhesive strength was then assessed by weight (in grams) at which the tablets detached from the mucous membrane. The mucoadhesive force (force of adhesion) was calculated with the help of equation 2. The values were taken in triplicate, and the means and standard deviation were calculated.

Mucoadhesive force (N) = Mucoadhesive Strength (gm)/1000 × 9.81 (2)

3. Results

3.1. Post-Compression Evaluation of Matrix Tablets

The parametric tests were performed on formulated tablets using different polymers, including hydroxypropylmethylcellulose (Methocel®), Carbopol, ethylcellulose (Ethocel®), carboxymethylecellulose and Eudragit over the 5:1, 5:2, 5:3 (drug-to-polymer ratios) using wet granulation, solid dispersions, and direct compression technique.

All the test formulations had hardness within the acceptable range. The hardness of the control formulation was found to be 7.8±0.25 kg. The hardness for the test formulations (F1-15) prepared with wet granulation technique ranged from 9.1±0.03 - 8.5±0.06, solid dispersion method tablets' ranged from 7.8±0.03 - 8.1±0.01, and with direct compression ranged from 7.1±0.07 - 7.9±0.03. The friability of the control formulation was found to be 0.6±0.12. The friabilities for the test formulations (F1-15) prepared with wet granulation technique ranged from 0.1±0.14 -

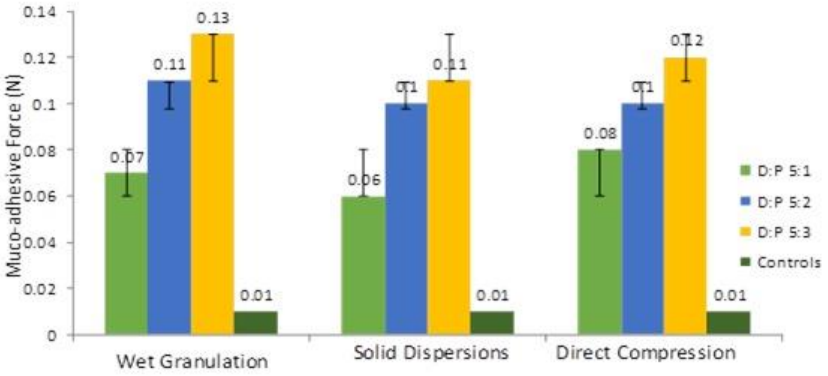

Figure 1. Influence of D:P proportion and formulation techniques on muco-adhesive force using Methocel® as release controlling agent.

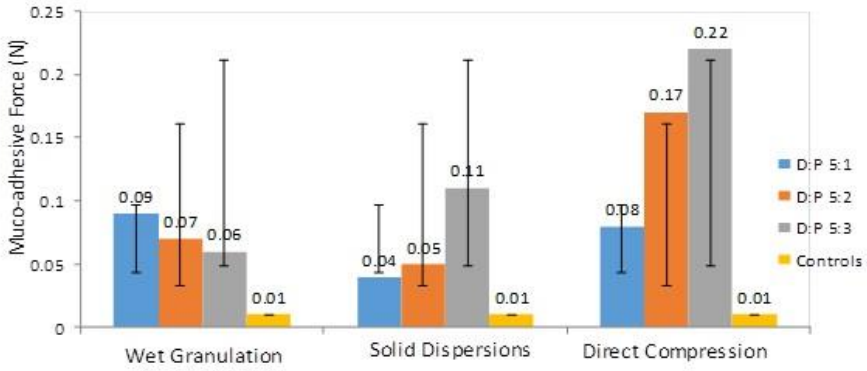

Figure 2. Influence of D:P proportion and formulation technique on muco-adhesive force using Carbopol as release controlling agent.

6.5±0.03, with solid dispersions ranged from 0.8±0.06 - 0.9±0.00, and with direct compression ranged from 0.5±0.04 - 0.8±0.02.

Thickness and diameter of the control formulation were found to be 4.52 ± 0.01 and 14.6 ± 0.05 mm, respectively. While thickness and diameter of test formulations (F1-15) prepared with wet granulation technique ranged from 4.52 ± 0.01 – 4.70 ± 0.04, 14.6 ± 0.03 - 14.8 ± 0.01 mm, for those prepared with solid dispersions technique ranged from 4.49 ± 0.11 - 4.80 ± 0.02 and 14.5 ± 0.07 – 14.7 ± 0.04 mm, and of those prepared with direct compression technique ranged from 4.50 ± 0.07 - 4.69 ± 0.02 and 14.5 ± 0.11 - 14.4 ± 0.02 mm, respectively.

The average weights and the variation of the control formulations were found to be 102±0.52 - 105±0.35. The average weights and the variation of the test formulations (F1-15) prepared with wet granulation technique ranged from 100±0.03 - 103±0.21, with solid dispersions ranging from 102±0.11 - 104±0.01, prepared with direct compression technique ranged from 103±0.01 - 104±0.09, respectively.

Drug contents of control formulations were found to be in the range of 100%±0.52 - 103%±0.05. While drug contents of test formulations (F1-15) prepared with wet granulation technique ranged from 101%±0.62 - 103%±0.10, with solid dispersions technique ranged from 102%±0.11 - 103%±0.14, with direct compression technique ranged from 100%±0.09 - 104%±0.04, respectively.

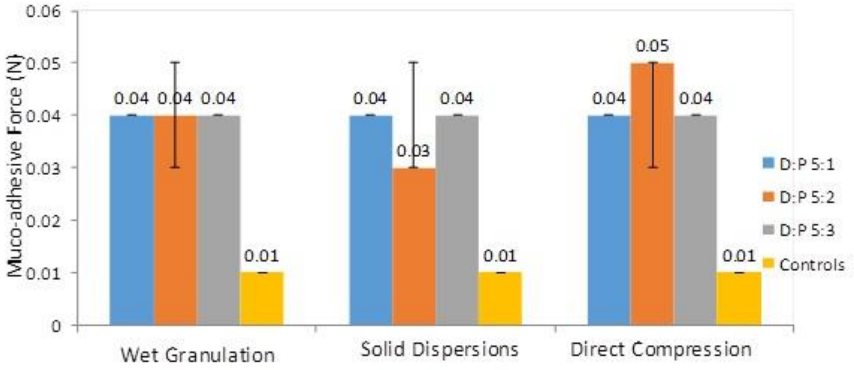

Figure 3. Influence of D:P proportion and formulation technique on mucoadhesive force using Ethocel® as release controlling agent

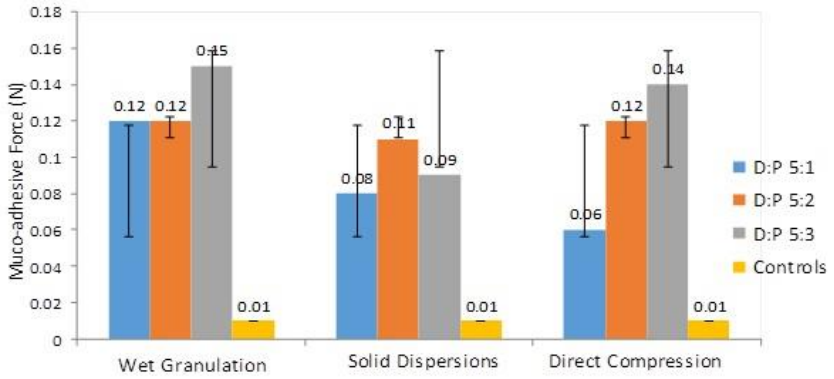

Figure 4. Influence of D:P proportion and formulation technique on mucoadhesive force using CMC as release controlling agent

3.2. Swelling Index

The results of the swelling index of the control and the test formulations prepared by wet granulation, solid dispersions, and direct compression techniques are shown in **Tables 2-4.** The swelling index of the control formulations prepared by wet granulation, solid dispersions, and direct compression techniques were found to be 13.65±0.38, 15.35±0.98, and 14.84±2.32 after six hours, respectively.

The swelling index for matrix tablets (F1-15) prepared by wet granulations technique was found to be ranging from 33.81±2.42 - 67.36±0.77 after 6 hrs, and those prepared by solid dispersions technique were found to be ranging from 34.02±1.32 - 65.09±1.08 after 6 hrs, prepared by direct compression technique were found to be ranging from 36.82±2.02 - 68.35±1.73 after 6 hrs.

3.3. Mucoadhesive Force

3.3.1. Effect of Methocel®

It was observed that there was a direct relationship between the concentration of the release-controlling polymer and the magnitude of the mucoadhesive force. This increase in the mucoadhesive force was observed in all formulation techniques used in the study, i.e., wet granulation, solid dispersions, and direct compression. When the tablets were formulated by using the wet granulation technique, F1(D:P 5:1), F2 (D:P 5:2), and F3 (D:P 5:3), they showed adhesive force of 0.07, 0.11 and 0.13N *Newton?*, respectively. In case of solid dispersions technique, F1 (D:P 5:1), F2 (D:P 5:2), and 3 (D:P 5:3), had adhesive forces of 0.06N, 0.1N

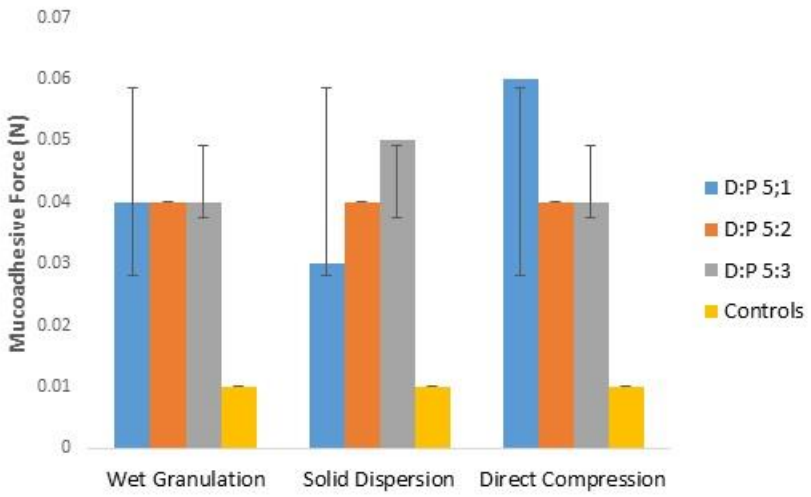

Figure 5. Influence of D:P proportion and formulation technique on muco-adhesive force using Eudragit as release controlling agent

and 0.11N, respectively. F1 (D:P 5:1), F2 (D:P 5:2), and 3 (D:P 5:3) had adhesive forces of 0.08, 0.01, and 0.12N when formulated with the direct compression technique **(figure 1).**

3.3.2. Effect of Carbopol:

The effect of Carbopol polymer was evaluated on the mucoadhesive strength of the tablets using three different techniques. F4 (D:P 5:1), F5 (D:P 5:2) and F6 (D:P 5:3) showed adhesive force of 0.09N, 0.07N, and 0.06N, respectively when prepared by wet granulation technique**.** When solid dispersions technique was used, F4 (D:P 5:1), F5 (D:P 5:2) and F6 (D:P 5:3) presented adhesive force of 0.04N, 0.05N and 0.11N, respectively. In case of direct compression technique, F4 (D:P 5:1), F5 (D:P 5:2) and F6 (D:P 5:3) displayed adhesive force of 0.08N, 0.17N, and 0.22N, respectively **(figure 2)**.

3.3.3. Effcet of Ethocel®

It was observed that the polymer concentration in the tablets with D:P 5:1 and 5:3 did not affect the value of mucoadhesive force (F7, F8, and F9 have adhesive force of 0.04 N). Similarly, in the case of formulation techniques (wet granulation, solid dispersions, and direct compression), no effect on the values of adhesive force was observed. Only in case D:P 5:2, tablets manufactured by direct compression method exhibited maximum values (F8 0.05 N), while the formulations prepared by solid dispersions had the lowest values of mucoadhesive force (F8 0.03) **(figure 3)**.

3.3.4. Effcet of CMC

In the case of D:P 5:1, the formulations prepared by the wet granulation technique had the highest values of mucoadhesive force (F10, 0.12 N), whereas the matrix tablets manufactured by the direct compression method had the lowest adhesive force (F10, 0.06N). In case when D:P 5:3 is used, the formulations prepared by wet granulation technique have higher adhesive force (F12, 0.15N), while the tablets made by solid dispersions have the lowest values of mucoadhesive force (F12, 0.09N). In case when D:P is 5:2, the difference in the magnitude of the mucoadhesive force is nonsignificant (F9) displayed adhesive forces of 0.12N, 0.11N, and 0.12N for wet granulation, solid dispersions, and direct compression techniques, respectively) **(figure 4).**

3.3.5. Effects of Eudragit

It was observed that the adhesive force of matrix tablets formulated by wet granulation techniques was not affected by the variation in the concentration polymer (F13, F14, and F15 all showed an adhesive force of 0.04N). In the case of the formulations prepared with solid dispersions, an increase in adhesive force was observed when the quantity of matrix forming agent was

increased, with an adhesive force of 0.03N, 0.04N, and 0.05N, respectively. When direct compression was used as a formulation technique, only D:P 5:3 showed a higher value (F15, 0.06N), while the other two D:P (i.e., 5:2 and 5:1) possessed the same adhesive force value (F13 and F14 displayed 0.04N) **(figure 5)**.

4. Discussion

In the present study, post-compression tests were applied to the formulated and fabricated tablets. The results displayed for hardness, friability, dimensional analysis, weight variation, and content uniformity tests showed that the tablet was efficient enough to comply with the reported acceptable limits. The types of polymer concentration used to prepare the tablets supported making a quality product when combined with the excipients. Though different polymers were used with different physicochemical natures, the formulated tablets presented acceptable post-compression results, making the tablets suitable for further analysis.

The results for the swelling index could be important for the current study, as the swelling of the polymer matrix might be taken as an important factor for the extent of the drug to be released from the polymer matrix. The more the swelling of the tablet, the more will be the release of the drug. When the tablets come in contact with water, they swell up. This swelling of tablets results in weight gain, also the volume of the tablets is increased. The mechanism of this water uptake is due to the sucking and saturation of the fine capillary network present in the core of the matrix tablets. The hydration process of the macromolecules also augments this swelling. Water absorbed through the small pores binds to the large molecules, breaking the hydrogen binding and swelling particles. The results indicate that almost all of the polymers displayed proper swelling of the matrix tablets after coming in contact with the dissolution medium, but the polymers Methocel and CMC revealed rather more swelling of the polymer matrix. The effect might be attributed to their hydrophilic natures. The Ethocel and Carbopol might be considered more hydrophobic as compared to Methocel and CMC. The nature of Eudragit could be taken as both hydrophilic as well as hydrophobic. Hence depending upon the other factors like compression force, binding agent, lubricant, and diluent, it could be interpreted that almost all of the polymers played a significant role in designing the most feasible tablet formulations.

The effect of polymer type, concentration, and formulation technique on the mucoadhesive strength was determined for various formulations (F1-15). It could be seen in the results that as the amount of the polymer increased from 5:1 to 5:2 and 5:3, the mucoadhesive strength is also increased **(figure 1-5)**. This rise in mucoadhesive strength by increasing the polymer quantity may provide more adhesive sites and polymer chains for interpenetration with mucin, resulting in the augmentation of bioadhesive strength. Moreover, an appropriate rise in tensile strength with the polymer concentration was sufficient to keep the formulation intact for sufficient mucoadhesion. This mucoadhesive strength is instrumental in developing gastroretentive mucoadhesive controlled release formulations. It was observed from the results of the mucoadhesive tendency of the matrix tablets that it was significantly influenced by changing the type of polymer, D:P in the total formula as well as the change in the fabrication techniques used to prepare the matrix tablets. Considering the formulation technique, when the D:P is kept constant, it might be observed that the matrix tablets manufactured by wet granulation technique displayed slightly higher values of the adhesive force than those made by solid dispersions and direct compression.

5. Conclusions

Once-daily controlled released matrix tablets of Clarithromycin were designed, formulated, and evaluated successfully using different polymers,

i.e., Methocel®, Carbopol, Ethocel®, CMC, and Eudragit with different D: P. The polymer concentration, type, and formulation technique played an effective role in the mucoadhesive strength of the tablets. The tablets presented proper adhesion to the mucous membrane, showing a well-controlled release of Clarithromycin by diffusion and erosion mechanism.

Conflict of Interest

The authors declare no conflict of interest.

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Study Approval

This study was approved by the Faculty of Pharmacy, Gomal University, Dera Ismail Khan, Pakistan.

Consent Forms

NA.

Data Availability

All the data related to this study is available with the authors.

Authors Contribution

MR conceptualized the study and wrote the final manuscript, AH & HS helped in experimentation and writing the first draft, MR, AH, and HS did the literature search and analysis, and MR supervised the whole project.

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