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Development, Optimization and Evaluation of Mucoadhesive Microspheres of Amoxicillin for the Treatment of *H.Pylori* by Full Factorial Design

Bhawna Sharma*, Dr. Anand Chaurasia, Dr. Naveen Gupta, Dr. Dharmendra Singh Rajput

Patel College of Pharmacy, Madhyanchal Professional University, Ratibad, Bhopal, MP. India

***Correspondence Author:**
Bhawna Sharma
Affiliation: Ph.D. Research Scholar, Patel College of Pharmacy, Madhyanchal Professional University, Ratibad, Bhopal, MP. India.
Email: officialbhawna56@gmail.com
ORCID ID: https://orcid.org/0009-0009-8954-6328

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Abstract

Objective: This work is aimed to formulate and evaluate Mucoadhesive Microspheres contain Amoxicillin for the effective use in the treatment of *H.Pylori*.

Methods: Microspheres were prepared using Emulsification-cross linking technique. To this guar gum (GG) and sodium alginate (SA) was dissolved in 200 ml of water and allowed to swell for 24 h at room temperature. And separately chitosan (CH) was dissolved in 2% (v/v) glacial acetic acid and this also kept for 24 h to swell or dissolve properly. After 24 h this swelled mixture was mixed under magnetic stirrer (Remi, India) at specific stirring rate for 1 h in order to find homogeneous mass of both the gum. Then slurry of chitosan also was homogenized for half an hour. The drug, Amoxicillin (1g) was then added to the chitosan solution and mixed homogeneously.

Results: The aim of the study was to formulate and evaluate microspheres, for SR of the chosen drug. The particle size of microspheres was in the range of 200-500 μ, maximum mucoadhesive property observed was 57.41% for Optimized formulation F-9, Drug release 68.52% till 8 h, and the maximum entrapment was 94.87% for F-9 formulation. The work also aims to study various parameters affecting the behavior of microspheres in oral dosage form.

Conclusion: Drugs with short half life that are absorbed from the gastrointestinal tract (GIT) are eliminated rapidly from the blood flow. To avoid this, the oral SR was developed as this formulation released the drug slowly into the GIT and maintained a stable drug concentration in the serum for a longer duration of time.

Keywords Amoxicillin, Sodium alginate, Guar gum, Chitosan, Sustained release microspheres, In-vitro activity

Introduction

Helicobacter pylori (*H.Pylori*) illness is a major public health problem that affects a lot of people around the world. This gram-negative bacteria settles on the lining of the stomach and can cause chronic gastritis, peptic sores, and in the worst cases, gastric cancer. Most

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of the time, medicines and proton pump inhibitors are used together to treat *H.Pylori*. But antibiotic resistance is growing and patients don't always follow through with standard treatments. This means that better and more specific drug delivery methods are needed. A common drug called amoxicillin has been shown to work against *H.Pylori*. However, its healing ability is often limited by how quickly it is cleared out of the stomach and broken down in the acidic environment of the stomach. Mucoadhesive drug administration methods have become a hopeful way to deal with these problems. These systems can stick to the lining of the stomach, which makes the drug stay there longer and release it slowly over time. This improves the effectiveness of the therapy and lowers the number of times it needs to be taken. A new and useful way to get amoxicillin straight to the site of an illness is through Mucoadhesive nanoparticles. These microspheres can stick to the stomach wall because they contain the drug in a Mucoadhesive polymer structure. This keeps the drug from breaking down and allows for a controlled release. This focused delivery method not only makes Amoxicillin more bioavailable, but it also keeps systemic side effects to a minimum [1].

The main goal of this study is on creating, improving, and testing *in-vitro* Mucoadhesive nanoparticles that contain amoxicillin to treat *H.Pylori* infections. Using a planned method, we want to find the best formulation factors that will allow for the most drug loading, long-lasting mucoadhesion, and controlled drug release. The in-vitro test will check how well the created microspheres stick to mucosa, how they release drugs, and how well they kill microbes. This will give us a full picture of their promise as a specific treatment for *H.Pylori* infection. The study shows a lot of potential for improving the problems with current *H.Pylori* treatments and creating a new, better, and more patient-friendly option. We want to make treatment work better and improve the quality of life for people with diseases linked to *H.Pylori* by creating amoxicillin pellets that stick to mucosa [2].

Material and method

Material

Amoxicillin was a kind gift sample from Torrent Research Centre (Ahmedabad, India). Sodium alginate, chitosan, guar gum, n-octanol, calcium chloride and Span 80 were procured from Oxford Fine Chemicals (Mumbai, India). All other chemicals and reagents used in the study were of analytical grade [3].

Method

Microspheres were prepared using emulsification-cross linking technique. To this guar gum (GG) and sodium alginate (SA) was dissolved in 200 ml of water and allowed to swell for 24 h at room temperature. And separately chitosan (CH) was dissolved in 2% (v/v) glacial acetic acid and this also kept for 24 h to swell or dissolve properly. After 24 h this swelled mixture was mixed under magnetic stirrer (Remi, India) at specific stirring rate for 1 h in order to find homogeneous mass of both the gum. Similarly, slurry of chitosan also was homogenized for half an hour. The drug, Amoxicillin (1g) was then added to the chitosan solution and mixed homogeneously. This dispersion is sonicated for 30 min to remove the entrapped air bubbles. Then the gas forming agent sodium bicarbonate with alginate was mixed. The gum slurry of SA and GG was added in CH solution and mixed properly at an appropriate stirring rate by using magnetic stirrer as shown in Table 6.1. Cross linking solution containing 1.5 g span 80 which was stirred first using a mechanical stirrer at 300 rpm. And 0.1 ml of concentrated sulphuric acid and 0.75 ml of glutaraldehyde was poured into a separate beaker. This above solution was added into the span 80. This cross-linking solution were added to the dispersion through a disposable syringe-needle (24G size), followed by stirring at constant speed 3000 rpm for 4 h at 50ºc. the microspheres formed and collected by sedimentation, followed by decantation of oil, were then washed with several fractions of isopropyl alcohol. The residual glutaraldehyde was removed by the reaction with sodium bisulfate. The microspheres were filtered and dried. The dried microspheres were kept for 24 h using vacuum desiccators at room temperature.

Experimental design

Experiment design (DOE) is a systematic method of determining the relationship between the factors that affect a process and the output of that process. DOE is a tool for developing a plan for exploration that maximizes learning using a minimum of resources. Experimental design techniques in such cases are becoming increasingly important in developing new products and processes in a cost-effective and confident manner [2].

Microsponges were formulated using 2^3 full factorial designs and eight experimental formulations were prepared by varying both, the amount of guar gum, sodium alginate and the concentration of chitosan at two different levels. The quantity of drug was kept constant in all experimental formulations [4]. Three

factors were designated as independent variables and the particle size, % entrapment efficiency, % buoyancy and % cumulative drug release were designated as dependent variables. There were three factors and two level so according to factorial design formula: L^f (Level ^{factor}) are shown in Fig: 1 and formulation table are shown in Table No. 1 [13].

$L^f = 2^3 = 8$ so there were eight formulation prepared.

Three Factors are = A= Guar gum, **B=** Sodium alginate, **C=** Chitosan.
Two Levels are I= 1:1:1, **II=** 2:2:2 **(g)**

Evaluation of Mucoadhesive microspheres

Particle size

Particle size analysis of drug-loaded microspheres was performed by optical microscopy using a compound microscope. A small amount of dry microspheres was suspended in glycerin. A small drop of suspension thus obtained was placed on a clean glass slide. The slide was mounted on the stage of the microscope and diameter of at least 100 particles was measured using a calibrated ocular micrometer. The process was repeated for each batch prepared [5].

Swelling index

The swelling ability of the microspheres in physiological media was determined by swelling them to their equilibrium. For estimating the swelling index, the microspheres (100) were suspended in 5ml of simulated gastric fluid USP (pH 1.2) for 24 h. The following formula was used for the calculation of degree of swelling:

DEGREE OF SWELLING= $\alpha = W_s - W_0 / Ws$
Where W_s= weight of microspheres after swelling
W_0= initial weight of microspheres
Swelling index= Final weight-initial weight / Final weight

Percentage yield (%yield)

The dried microspheres were weighed and percentage yield of the prepared microspheres was calculated by using following formula [12].

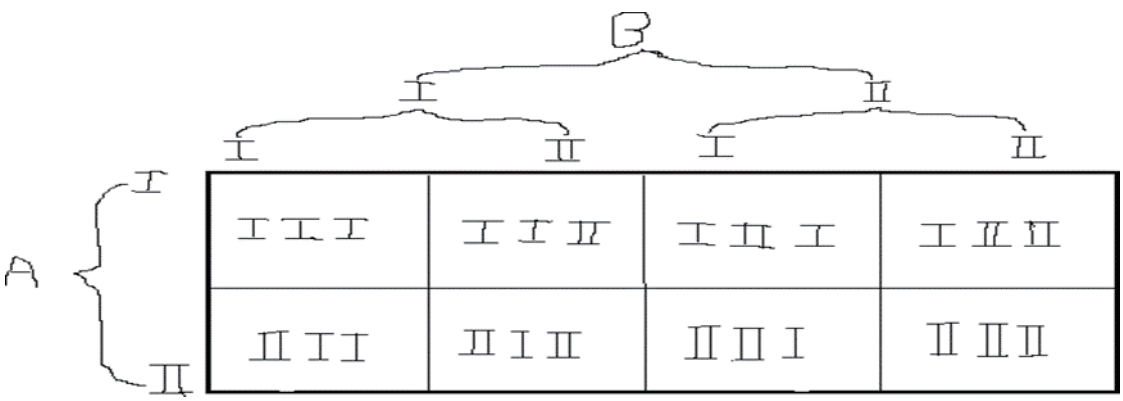

Figure 1: Experimental design using Factorial design

Table 1: Formulation of Amoxicillin Loaded Mucoadhesive Microspheres

Formulation batches	Composition of factor with their level according to factorial design			Stirring speed(rpm)
	A	B	C	
F1	1	1	1	2000
F2	2	1	1	2000
F3	1	2	1	2000
F4	2	2	1	2000
F5	1	1	2	2000
F6	2	1	2	2000
F7	1	2	2	2000
F8	2	2	2	2000

Percentage yield= Actual weight of microspheres / Total weight of polymer + drug × 100

Percentage drug entrapment efficiency (%EE), drug content (%DC)

The amount of drug present in prepared Mucoadhesive microspheres was determined to check the drug entrapment efficiency and drug loading capacity. Microspheres were crushed into fine powder by using a mortar and pestle. Accurately weighed amount of crushed microspheres were suspended in 0.1 N HCl (pH 1.2), to extract the drug from microsphere. It was then shaken in mechanical shaker. After 24 h, the filtrate was analyzed spectrophotometrically at 293nm for drug content against 0.1 N HCl as blank [6].

% Drug entrapment efficiency= Practical drug content/Theoretical drug content × 100

In-vitro wash-off test

The mucoadhesive property of the microspheres was evaluated by an *in vitro* adhesion testing method known as the wash-off method. A 2×2-cm piece of stomach mucosa was tied onto a glass slide (3×1-inch) using thread. Microspheres were spread (100) onto the wet rinsed tissue specimen and the prepared slide was hung onto one groves of a USP tablet disintegrating test apparatus. The disintegrating test apparatus was operated such that the tissue specimen was given regular up and down movement in a beaker containing the simulated gastric fluid USP (pH 1.2). At the end of sixty minutes and hourly intervals upto 8 h, the no. of microspheres still adhering onto the tissue was counted [7].

Percent mucoadhesion was calculated by the using following formula.

% Mucoadhesion= No. of microspheres remains on stomach mucosa / No. of applied microspheres on stomach mucosa × 100

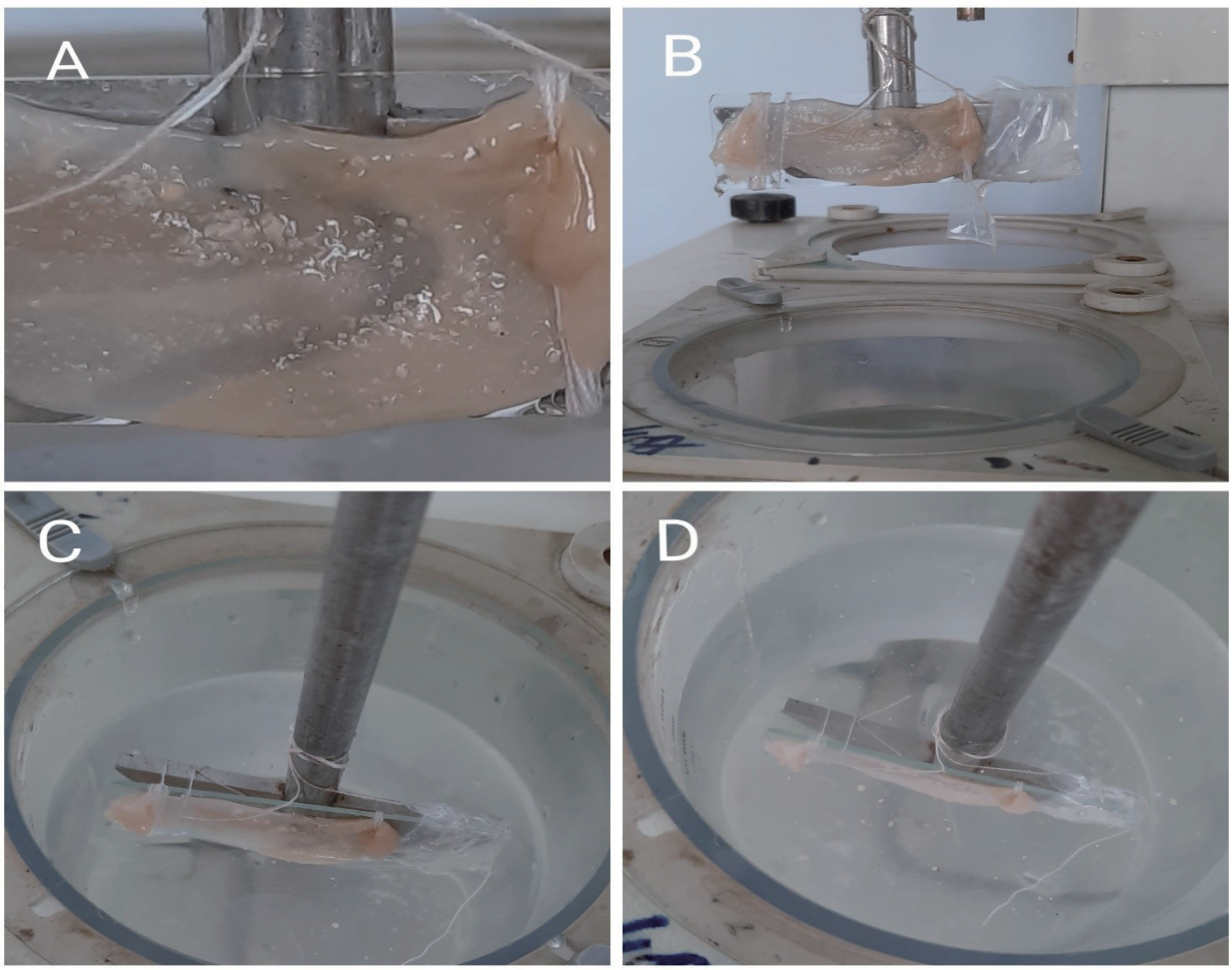

Figure 2: Images of different stages of Mucoadhesive test. (A) Stomach mucous. (B) Slide Tie with paddle. (C) Paddle dip in pH 1.2 media. (D) Rotate paddle.

In-vitro drug release study

The drug release study was performed using U.S.P. dissolution testing apparatus II (Basket type) at 37 ± 0.5ºc and at 100 rpm using 900 ml of 0.1 N (pH 1.2) HCl, as dissolution medium for 8 h. Mucoadhesive microspheres of Amoxicillin were used for the test. 5ml of sample solution was withdrawn at predetermined time intervals, filtered, diluted suitably, and analyzed spectrophotometrically at 293 nm. An equal amount of fresh dissolution medium was replaced immediately after withdrawal of the test sample to maintain sink condition [8].

Buoyancy study

Microspheres (200 mg) were spread over the surface of a dissolution apparatus type II filled with 900 ml of 0.1 N hydrochloric acid containing 0.02% tween 80. The medium was agitated with a paddle rotating at 100 rpm for 12 h. The floating and the settled portions of microspheres were recovered separately. The microspheres were dried and weighed. Buoyancy percentage was calculated as the ratio of the mass of the microspheres that remained floating and the total mass of the microspheres [9].

Buoyancy (%) = W_f / W_f + W_s x 100

Where W_f and W_s are the weight of floating and settled microsphere respectively.

Release kinetic study

This study was performed to determine which model was given best drug release. The release data was applied on various mathematical models [10] .

Result and Discussion

Development of Amoxicillin Mucoadhesive Microspheres

Amoxicillin loaded different Mucoadhesive microspheres were developed by an appropriate emulsification cross-linking technique. Microspheres were prepared by using different drug: polymer ratios (w/w). The volume of cross-linking agent, polymer to drug ratio and stirring speed had a significant effect on the microsphere's characteristics. The optimized stirring rate was found to be 2000 rpm for fabricating Amoxicillin loaded appropriate mucoadhesive microspheres, prepared Mucoadhesive microsphere are shown in Fig. 3 (A-B).

Figure 3: Images of different batch of prepared mucoadhesive microsphere (F1 to F8). (A) Prepared Microspheres which we have protect in transparent 15 ml glass vial. (B) Open Microspheres with different batches.

Particle Size Analysis

Particle size of the various batches of microspheres was found to be in the range of 26.27 ± 4.14µm to 53.10 ± 9.04µm. As, we know that if the particle size is fine so its surface area is higher which may facilitate the drug absorption from the formulations. And, it was observed that particle size of the microspheres significantly increased with increasing polymer concentration. Increase in polymer concentration was attributed to increase in viscosity, which resulted in formation of large droplets, thus increasing the size of microspheres. So, with keep in mind the above information we got the desire size i.e. fine (micron size). The particle size of the prepared microspheres is displayed in Table 2.

Percentage Yield (%Yield)

The percentage yield of microspheres prepared by emulsification techniques was found to be in between 56.6 to 92.02 %. It was observed that as the polymer ratio in the formulation was increased, the percentage yield was also increased. The low percentage yield in some formulations may be due to blocking of needle and wastage of the drug-polymer solution, and microspheres lost during the filtration, washing process which ultimately decreased the percentage yields of microspheres. The% yield of the microspheres is shown in Table 7.2.

Estimation of drug entrapment efficiency

Entrapment efficiency of the various batches of microspheres was found to be in the range of 56.74 ± 2.01% to 86.25 ± 1.16%. It was observed that entrapment efficiency of the microspheres was dependent on the concentration of the polymer. Among the various formulations the F2 showed. It may be due to an appropriate ratio of drug: polymer (w/w)

Table 2: Mean particle size of Mucoadhesive microspheres

Formulation code	Average Particle size in (µm)
F1	46.8 ± 9.42
F2	34.5 ± 3.36
F3	39.40 ± 7.53
F4	45.17 ± 9.18
F5	26.27 ± 4.14
F6	46.31 ± 7.62
F7	53.10 ± 9.04
F8	42.00 ± 12.64

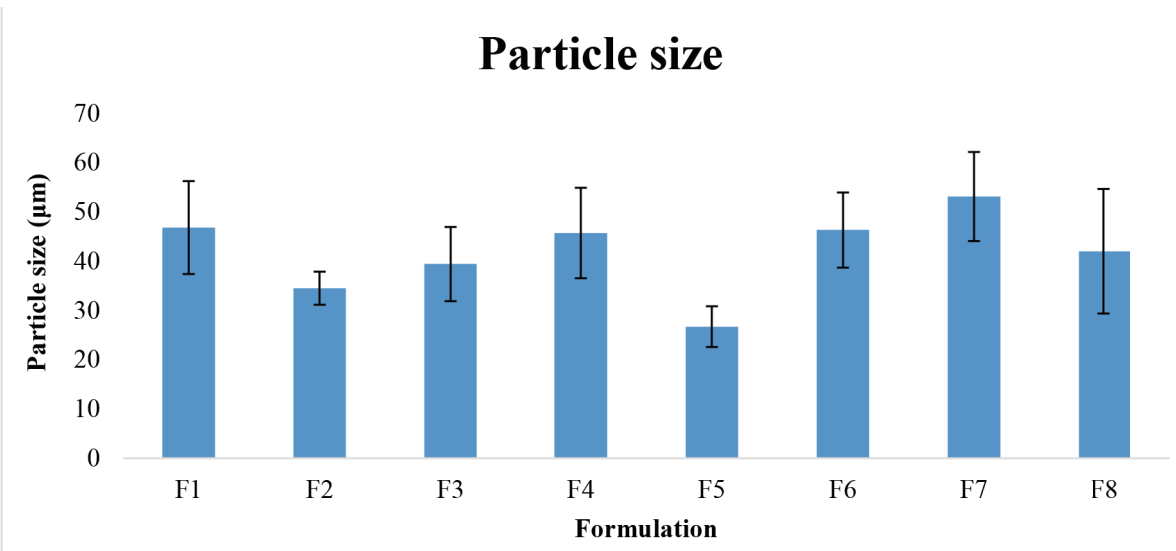

Figure 4: Mean particle size of Mucoadhesive microspheres

for development of microspheres at constant 2000 rpm. At this ratio % EE for Amoxicillin was found to be optimum. Therefore, the F5 formulation was chosen as an optimized formulation. The % drug entrapment efficiency of the prepared microspheres is displayed in Table 7.3.

Table 3: Percentage yield of Mucoadhesive microspheres

Formulation code	% Percentage Yield
F1	38.07
F2	89.06
F3	56.6
F4	74.3
F5	92.02
F6	70.54
F7	59.83
F8	75.01

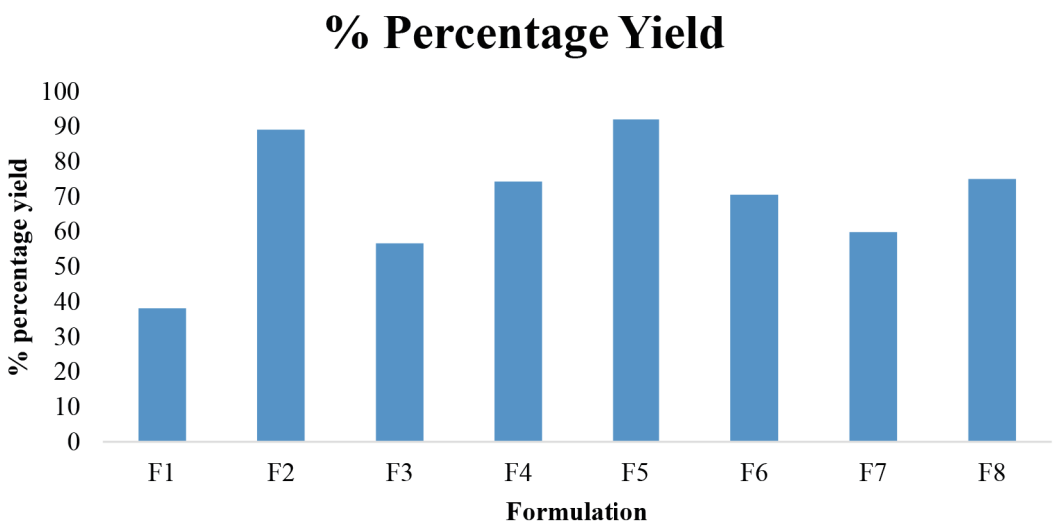

Figure 5: Percentage yield of Mucoadhesive microspheres

Table 4. Drug entrapment efficiency

Formulation code	% Drug entrapment efficiency
F1	65.51 ± 1.60
F2	82.22 ± 2.09
F3	56.74 ± 2.01
F4	73.75 ± 1.39
F5	86.25 ± 1.16
F6	67.31 ± 2.51
F7	64.09 ± 1.84
F8	62.09 ± 2.93

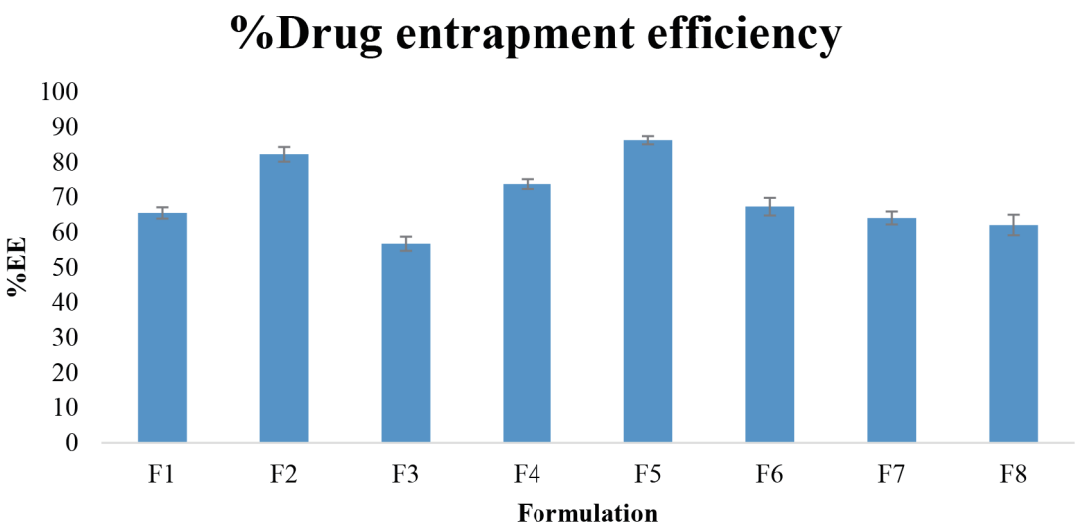

Figure 6: Drug entrapment efficiency

Swelling Index

Swelling properties of different formulations were performed in simulated gastric fluid USP (1.2 pH) and results were represented in table 7.5 in the range of. The best degree of swelling (1.38 ± 0.05) value was achieved with F5 for an extended period (24 h) among other formulations, which is suitable for retaining in stomach. It was found that by increasing the polymer concentration, swelling of all formulations were increases. The swelling index of the prepared microspheres after 24 h is displayed in Table 7.4.

In-Vitro Mucoadhesion Study

Prepared microspheres were found good mucoadhesion strength. Percent mucoadhesion of the all batches of microspheres were found to be in the range of 42 to 71%. It was observed that mucoadhesion of the microspheres significantly increased with increasing polymer concentration. Increase in concentration was attributed to increase in viscosity; produce stronger mucus gel network which helps to increase mucoadhesion. The percentage mucoadhesion of microspheres adhering to tissue after 8hrs is displayed in Table 6. The F5 batch showed highest % Mucoadhesion.

Buoyancy

Prepared microspheres were found good buoyancy strength. Percent buoyancy of the all batches of microspheres was found to be in the range of 52 to 82%. The percentage buoyancy of microspheres was float and reach to its targeted site. The F5 batch showed highest % buoyancy [14].

In-Vitro Release Study

In vitro drug release study of Amoxicillin loaded Mucoadhesive microspheres of optimized formulation of F5 was performed in 0.1 N HCl for 12 h. The sizes of microspheres of F5 were small and have a larger surface area exposed to dissolution medium, giving rise to faster drug release. The production yield of F5 was 92.02 % and particle size 160.7 ± 34.14(µm) which gives a greater total mass of microspheres as compared to other formulation which resulted in increased surface area of this batch releasing more drug release per unit time [5].

Statistical Analysis

On the basis of the data obtained from the formulation, a general statistical model can be depicted. Statistical analysis was done by Design expert software version 8.0.5.2 (Stat-Ease, Inc., Minneapolis, USA). Following second order polynomial equations were derived for the observed responses after application of one-way ANOVA after omitting non-significant ($p > 0.05$) coefficients. The transformed equations are, Analysis of variance table to predict EE of Amoxicillin microsphere. There result are show in Table No. 9-11 [2].

Final equation in term of actual factor

% Entrapment efficiency =+27.62 + 31.27A – 16.49B + 48.97C + 8.62AB -27.33AC - 5.07BC- **Equation 1**

% CDR = +109.82 – 19.68A -5.88B -38.05C +1.68AB

Table 5: Swelling index

Formulation code	Degree of Swelling
F1	0.99 ± 0.08
F2	1.26 ± 0.02
F3	0.81 ± 0.03
F4	1.11 ± 0.03
F5	1.38 ± 0.05
F6	1.03 ± 0.05
F7	0.92 ± 0.01
F8	0.85 ± 0.04

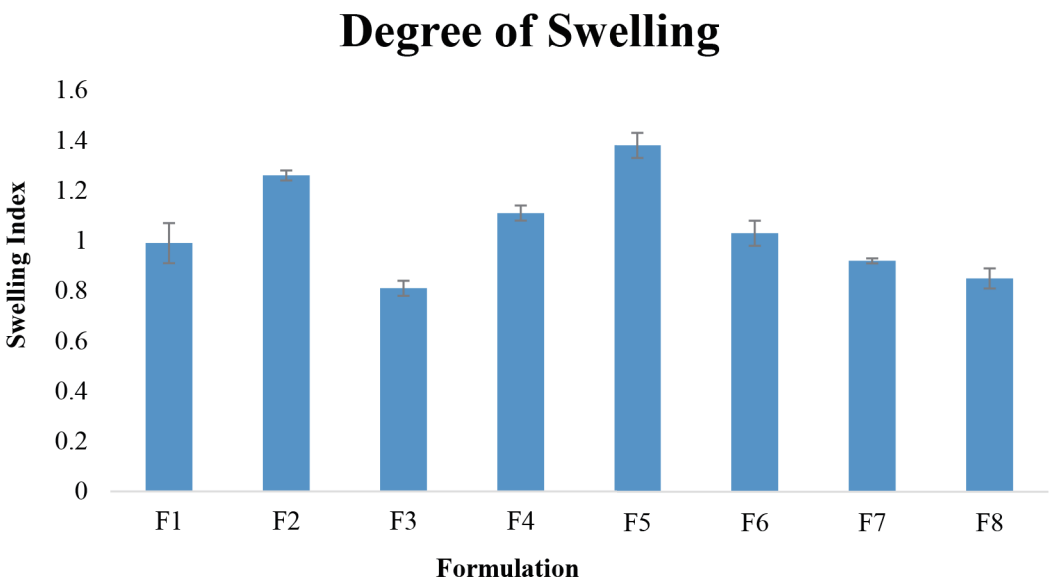

Figure 7: Swelling index

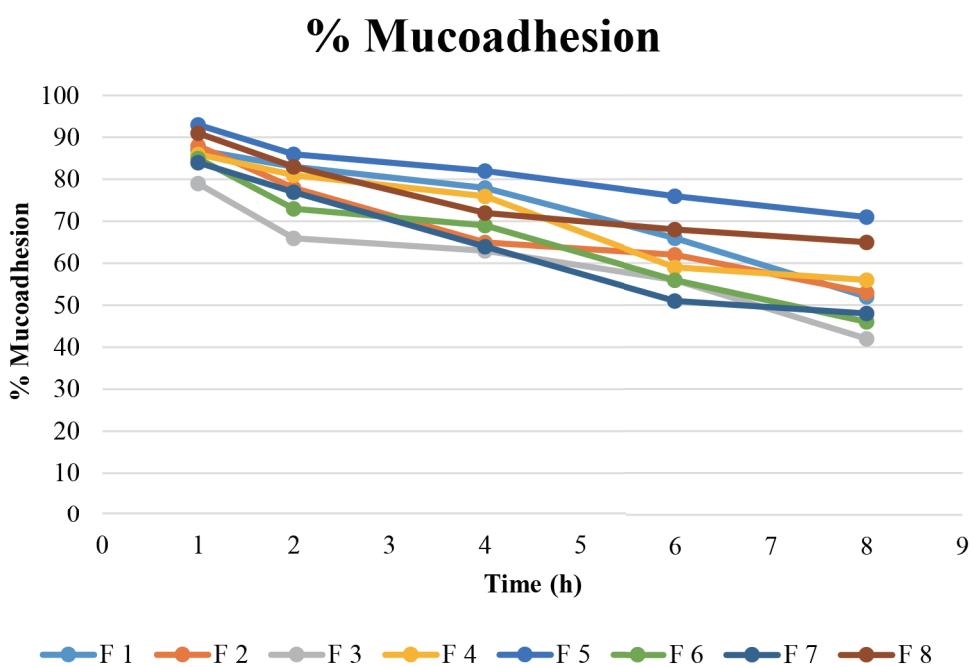

Figure 8: *In-vitro* Mucoadhesion study

Table 6: *In-vitro* mucoadhesion study

Time (h)	% Mucoadhesion							
	F 1	F2	F3	F4	F5	F6	F7	F8
1	87	88	79	86	93	85	84	91
2	83	78	66	81	86	73	77	83
4	78	65	63	76	82	69	64	72
6	66	62	56	59	76	56	51	68
8	52	53	42	56	71	46	48	65

Table 7: Percentage buoyancy study

Formulation code	Buoyancy %
F1	58.88534
F2	52.80545
F3	53.16456
F4	60.93703
F5	82.79849
F6	74.23787
F7	67.92676
F8	63.21785

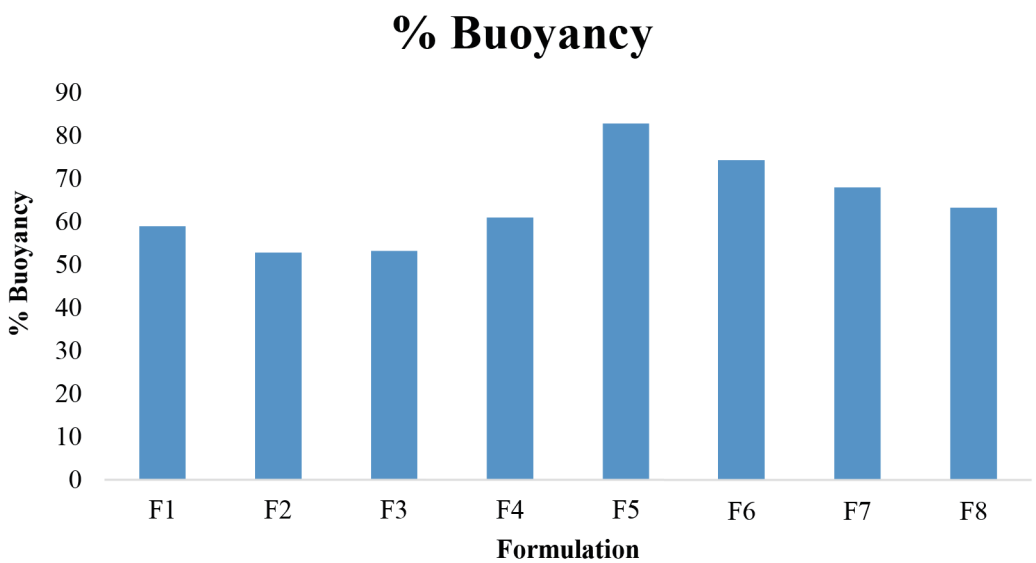

Figure 9: Percentage Buoyancy study

+17.52AC + 7.50BC- **Equation 2**

% Mucoadhesion = -12.63 +36.75A -4.25B +54.75C +1.50AB -28.50AC -1.50BC- **Equation 3**

i.e. Where, A= Guar gum, B= sodium alginate c= chitosan

The polynomial equations can be used to draw conclusions after considering the magnitude of coefficient and the mathematical sign it carries (i.e., positive or negative). A coefficient with positive sign represents a synergistic effect of the factor on the response, while a negative sign indicates an antagonistic effect. The mathematical relationship in the form of factor's coefficients, its corresponding P-values for the measured responses and correlation

Table 8: *In vitro* drug release

Time (h)	% Cumulative Drug Release (CR)							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	3.141635	8.130861	7.680452	6.021313	9.106422	4.215771	5.499146	8.152078
2	10.01759	15.38889	19.47554	16.18965	13.94987	13.02205	16.56301	14.56618
3	17.92723	24.10771	29.01854	29.09705	18.71575	19.00273	26.63739	27.38447
4	23.55747	31.67235	34.47578	39.98907	24.86218	28.05031	36.59209	30.50802
5	33.86452	36.65542	44.76273	54.81581	31.87572	40.34134	47.65206	46.59799
6	46.55115	43.52306	50.63654	60.93019	41.63647	51.10291	52.29248	64.26248
7	60.52405	53.81559	61.83849	66.92782	50.51274	68.94932	59.0588	72.04587
8	76.67496	68.6447	72.43902	81.15425	56.1029	80.66547	74.44259	85.60248

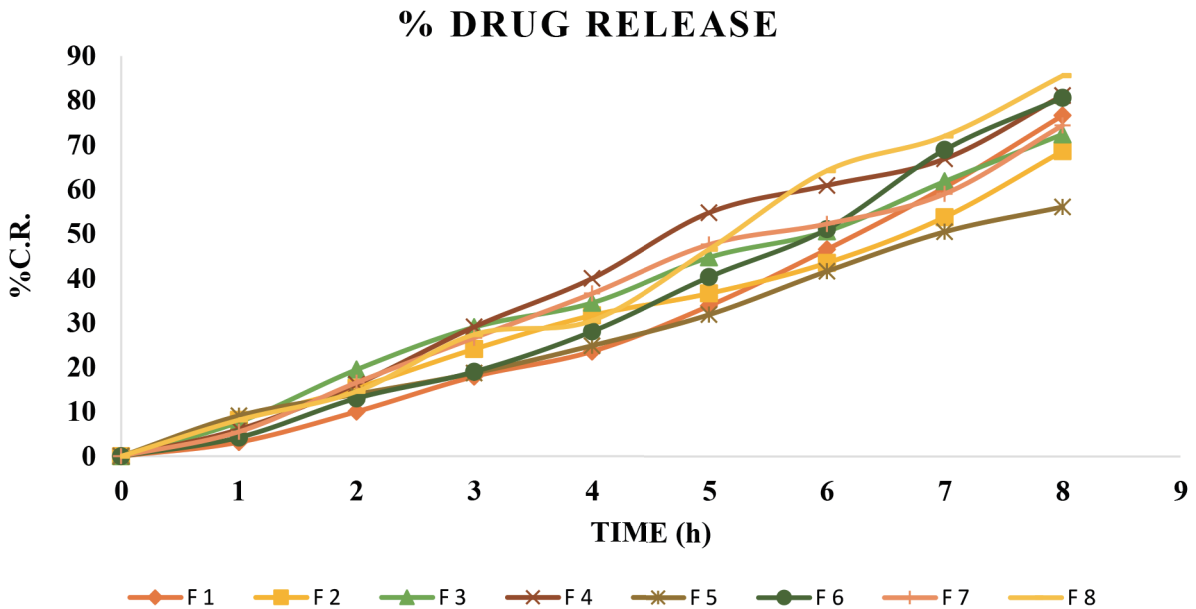

Figure 10: *In vitro* Drug release study of Mucoadhesive microsphereancy study

coefficient.

Concerning %EE, the results of multiple linear regression analysis showed that coefficients A and C bear a positive sign (R^2=0.9524). It can be concluded from the equation 1 that A showed the less positive effect compare to B. The coefficients A,B, AB, AC,BC were found to be non-significant at P >0 .05.

Concerning % CDR, the results of multiple linear regression analysis showed that coefficients combination of AB and AC show positive sign (R^2=0.996). It can be concluded from the equation 2 that combination of AB so less positive effect compares to BC then AC. The coefficients A, B, and C, AB, BC were found to be non-significant at p >0.05.

Concerning %Mucoadhesion, the results of multiple linear regression analysis showed that coefficients A and C bear a positive sign (R^2=0.998). It can be concluded from the equation 3 that A showed the less positive effect compare to C then B. The coefficients A, B, AB, AC, BC were found to be significant at P >0 .05.

Selection of Optimized Formulation

An optimization based on desirability criteria was employed to select the optimized formulation whos desirability factor are 0.812. Results of optimized formulation are shown in Table No. 14.

Table 9: Analysis of variance table to predict percentage EE of Amoxicillin microsphere

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob> F	
Model	693.19	6	115.53	3.34	0.3962	not significant
A-GUAR GUM	102.90	1	102.90	2.97	0.3346	
B-SODIUM ALGI	28.61	1	28.61	0.83	0.5303	
C-CHITOSAN	252.49	1	252.49	7.29	0.2258	
AB	37.15	1	37.15	1.07	0.4888	
AC	373.53	1	373.53	10.79	0.1881	
BC	12.84	1	12.84	0.37	0.6518	
Residual	34.62	1	34.62			
Cor Total	727.81	7				

Table 10: Analysis of variance table to predict percentage CDR of Amoxicillin microsphere

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob> F	
Model	473.64	6	78.94	0.69	0.7245	not significant
A-GUAR GUM	40.78	1	40.78	0.36	0.6564	
B-SODIUM ALGI	3.64	1	3.64	0.032	0.8872	
C-CHITOSAN	152.42	1	152.42	1.34	0.4534	
AB	1.40	1	1.40	0.012	0.9296	
AC	153.39	1	153.39	1.35	0.4524	
BC	28.16	1	28.16	0.25	0.7059	
Residual	113.63	1	113.63			
Cor Total	587.26	7				

Table 11: Analysis of variance table to predict percentage Mucoadhesion of Amoxicillin microsphere

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	662.75	6	110.46	883.67	0.0257	significant
A-GUAR GUM	142.16	1	142.16	1137.32	0.0189	
B-SODIUM ALGI	1.90	1	1.90	15.21	0.1598	
C-CHITOSAN	315.53	1	315.53	2524.26	0.0127	
AB	1.13	1	1.13	9.00	0.2048	
AC	406.12	1	406.12	3249.00	0.0112	
BC	1.13	1	1.13	9.00	0.2048	
Residual	0.13	1	0.13			
Cor Total	662.88	7				

Analysis of drug release data

The data obtained for in vitro release where fitted into equations for the zero order, first order, Higuchi and Korsmeyer-Peppas release model. The interpretation of data was based on the value of the resulting regression coefficient. The result showed that the zero

Table 12: Summary of results of regression analysis for responses % EE, % CDR and %Mucoadhesion

Model	R^2	Adjusted R^2	Predicted R^2	SD	% CV
% EE response	0.9524	0.6670	-2.0446	5.88	8.44
%CDR response	0.9961	0.9726	0.9694	2.39	4.78
% Mucoadhesion	0.9998	0.9987	0.9879	0.35	0.65

Table 13: Coefficient Table

Response	Intercept	A	B	C	AB	AC	BC
% EE	27.6172	31.2659	-16.486	48.976	8.61927	-27.3323	-5.06669
p=		0.3346	0.5303	0.2258	0.4888	0.1881	0.6518
% CDR	109.824	-19.6825	-5.8825	-38.0525	1.675	17.515	7.505
p=		0.6564	0.8872	0.4534	0.9296	0.4524	0.7059
% Mucoadhesion	-12.625	36.75	-4.25	54.75	1.5	-28.5	-1.5
p=		0.0189	0.1598	0.0127	0.2048	0.0112	0.2048
Legend		p <.01	.01<= p <.05	.05<= p <.10	p >=.10		

Table 14: Results of optimized formulation

Variables	Predicted response	Observed response	% Predicted error (% PE)	Acceptance criteria for % PE
% EE response	93.46	94.87	1.48%	Less than 5.0 %
%CDR response	66.30	68.52	3.23%	Less than 5.0 %
% Mucoadhesion	54.62	57.41	4.85%	Less than 5.0 %

Table 15: Kinetic study of the optimized formulation

Batch	Zero order		First order		Higuchi model		Korsmeyer- Peppas	
	r^2	k_0	r^2	k_1	r^2	K_H	K_{HP}	n
F-9	0.9596	6.911	0.9179	0.026	0.8599	33.28	0.8336	0.43

order was best fitted to the data and was followed by drug release. By applying model value of n less than 0.45 indicated followed Fickian diffusion [11].

Conclusion

Optimization based on desirability criteria was employed to select the optimized formulation. Formulation F-9 with highest desirability factor 0.812. Optimized formulation (F-9) showed remarkable swelling and mucoadhesion property as evaluated by in vitro method. % EE were exhibit 94.87 ± 1.16. Cumulative % drug release profiles of Amoxicillin from various formulations were performed in HCl buffer (pH 1.2). Result stated that F-9 was exhibited prolonged release profile 68.52 for extended period of 8 h. This sustained release activity of the F-9 might be due to adhesion of polymers to the gastric mucosa for longer periods 57.41% till 8 h. It also favoured by suitable particle size of the optimized formulation. Thus,

Mucoadhesive microspheres of Amoxicillin could be explored further as a promising carrier for treatment of *H.Pylori*.

Conflict of interest

There are no conflicting interests, as the authors have stated.

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Abbreviations

EE= Entrapment Efficiency
DR= Drug Release
DoE= Design of Expert
GG= Guar Gum
SA= Sodium Alginate

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