Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 12s (2025)
https://www.jneonatalsurg.com

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Formulations, Characterization and Evaluation of Clarithromycin loaded Mucoadhesive Microspheres for Peptic Ulcers

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Cite this paper as: Farheen Bano, Mr. Mohd Kalim, Ms Pooja Yadav, (2025) Formulations, Characterization and Evaluation of Clarithromycin loaded Mucoadhesive Microspheres for Peptic Ulcers. *Journal of Neonatal Surgery*, 14 (12s), 800-813.

ABSTRACT

Mucoadhesive formulations orally would achieve a substantial increase in the length of stay of the drug in GI tract. Mucoadhesive microsphere carrier systems are made from the biodegradable polymers in sustained drug delivery. Among all the fabricated formulations, F9 was optimized as final formulation showing first order release kinetics and extended drug release profile over a period of 10h (73.1%) and fitted to our desired target, with acceptable microencapsulation efficiency (78 %) and mucoadhesive property (76%). having good flow properties, and smaller particle size (204±09). the formulation F9 also showed good swelling index (76%). The SEM results indicated that the formulation F9 was spherical and having porous surface,which can influence the rate of release of drug from the microspheres.

Keywords: *Mucoadhesive, Microspheres, Polymers, Ulcers*

1. INTRODUCTION

The stomach and duodenum, which are exposed to gastric acid and pepsin, are the areas of the gastrointestinal tract where peptic ulcers occur [1]. The aggressive (acid, pepsin, bile, and H. pylori) and defensive (gastric mucus and bicarbonate secretion, prostaglandin, nitric oxide, innate resistance of the mucosal cells) factors are likely out of balance [2].

A peptic ulcer is a hole in the esophageal, duodenal, or stomach lining. An ulcer is an erosion or sore that develops when the digestive system's lining is weakened by acidic digestive fluids. Hydrochloric acid and an enzyme called pepsin, which can harm stomach or intestinal cells, are found in the digestive fluids. These may also cause esophageal damage. Between 5% and 10% of persons worldwide are thought to experience peptic ulcers at some point in their lives. Peptic ulcers that affect the stomach are referred to as gastric ulcers, those that impact the duodenum as duodenal ulcers, and those that affect the oesophagus as esophageal ulcers [3-5].

Peptic ulcers can develop when the stomach cells' acidic digesting juices erode the lining of these organs. Less frequently, peptic ulcers can form in the oesophagus, the tube that links the mouth and stomach, directly above the stomach [6]. Recent studies have revealed that bacteria (Helicobacter pylori) are also responsible for them in addition to stomach secretions. The oesophagus, stomach, and duodenum are the areas of the gastrointestinal system that are frequently impacted by ulcers. After a surgical anastomosis (connection) to the stomach, the jejunum may occasionally be impacted [7].

Drugs that kill the bacterium, lower stomach acid, and shield the stomach and duodenal lining are used to treat H. pylori-caused peptic ulcers. Proton pump inhibitors (PPIs) and histamine receptor blockers (H2 blockers) are medications that lower stomach acid [8]. Both acid-reducing medications aid in the repair of peptic ulcers and provide pain relief after a few weeks. H2 blockers and PPIs function differently: By stopping the system that pumps acid into the stomach, PPIs reduce the generation of acid. H2 blockers function by preventing histamine from stimulating the production of acid. One of the primary effects of proton pump inhibitors (abbreviated "PPI") is a significant and sustained decrease in the generation of stomach acid [9].

Dyspepsia, Peptic Ulcer Disease (PUD), Gastro-oesophageal Reflux Disease (GERD), Laryngopharyngeal Reflux Disease, Barrett's Oesophagus [10], Preventing Stress Gastritis, Gastronomes, and other conditions that result in excessive acid secretion, such as Zollinger-Ellison syndrome, are among the numerous conditions that these medications are used to treat. Proton pump inhibitors work by permanently inhibiting the stomach parietal cell's hydrogen/potassium adenosine triphosphatase enzyme system, often known as the H+/K+ ATPase or, more frequently, the gastric proton pump. Since the proton pump is the last stage of gastric acid production and is directly in charge of releasing H+ ions into the stomach lumen, it is a prime candidate to be inhibited [11].

Certain polymers can be used to target a medicine to a specific area of the body for prolonged periods of time because they

become sticky when hydrated. The term "mucoadhesion" was created to describe the polymers' adherence to the mucosal layer's surface [12]. When two materials, at least one of which is biological, are held together by interfacial forces, this is known as bioadhesion. The attachment may occur between a synthetic substance and a biological substrate, as in the example of a polymer bonded to the mucin layer of mucosal tissue, or it may occur between a polymer and a biological membrane [13].

When the mucosal layer lines several bodily parts, such as the gastrointestinal system, urogenital tract, airways, ears, nose, and eye, this is referred to as mucoadhesion. The mucoadhesive drug delivery system may be made for buccal, oral, vaginal, rectal, nasal, and ophthalmic routes of administration since these are possible locations for the bioadhesive system to adhere. Mucoadhesive polymers are swellable networks of water-soluble and water-insoluble polymers that are joined by cross-linking agents. These polymers have the ideal fluidity to allow for the mutual adsorption and interpenetration of the polymer and mucus, as well as the ideal polarity to ensure that they allow for adequate wetting by the mucus [14-16].

The aim of present work was to prepare mucoadhesive microspheres containing Clarithromycin, an anti- *H. pylori* agent, used for treatment of peptic ulcers. Mucoadhesive microspheres were prepared by “Calcium induced ionic gelation” method. Sodium alginate was used as encapsulating agent and Carbopol974P & HPMCK4M were used as bioadhesive polymer.The evaluation parameters included encapsulation efficiency, in vitro mucoadhesion, swelling study, in vitro release study. Our aim to formulate the mucoadhesive drug delivery that can be used for improving the contact time of the drug delivery system with the gastric mucosa.These kinds of drug delivery system canincrease the effective surface area**.** Alsoitis known that the microparticulate carriers can be tailored as mucoadhesive device. These formulations are useful to provide a greater surface area.Thus the mucoadhesive microspheres will provide greater area more contact time as well as control the drug release. Mucoadhesive microspheres provide good contact of drugs with mucus. Thus the drugs can penetrate the microenvironment created by the bacteria. Secondly, microspheres provide more contact area, thus a bigger surface area in the stomach can be targeted. The most important thingis that the controlled release of drug can be achieved to make the therapy convenient and improved. Hence this drug delivery system can enhance the efficiency of anti-*H. pylori* drug

2. METHODOLOGY:

Collection of drug sample & organoleptic studies: The drug was obtained as a gift sample from Plathico pharmaceuticals limited. The organoleptic studies (texture, colour, appearance etc.) and melting point was studied using melting point apparatus [17].

UV-Scans of drug for λ max. : 100mg of Clarithromycin was dissolved in 100ml of 0.1N HCl in a 100 ml volumetric flask and marked as stock solution-I (1000 µg /ml). 5 ml of stock solution-I was further diluted with 0.1N HCl solution. solution in a 100 ml volumetric and marked as stock solution-II (50 µg/ml). The final dilution (5.0 µg/ml) was made in 10 ml volumetric flask by taking 1 ml of stock solution-II and diluting it with 0.1 N HCl solution. The final dilution was scanned in UV-Vis spectrophotometer SHIMADZU against 0.1 N HCl solution as blank [18].

Calibration curve preparation: 100mg of Clarithromyc in was weighed accurately and dissolved in solvent. The volume of solution was made up to 100ml. The solution was marked as stock solution .From stock solution dilution having concentration5µg/ml, 15µg/ml, 20µg/ml, 25µg/ml, 30µg/ml, 35µg/ml, 40µg/ml, 45µg/ml, 50µg/ml, were prepared. Above prepared solution were observed in double beam UV- Spectrophotometer (shimadzu, model No.1700) to measure the absorbance, in increasing order of concentration [19].

Solubility studies of drug: About 10mg of Clarithromyc in was added to 5 ml of various polar and non polar solvents (Methanol, Ethanol, Chloroform, Dichloromethane, Acetone, Distilled Water,) and sonicated for 10 minutes. Then the absorbance was taken at 282nm.

Solution stability of drug in 0.1(N) HCl: The solution stability of drug was assessed in 0.1 (N) HCl for 12 hours at 37 ± 5 ^{o}C to predict their stability in gastric pH environment [20].

FTIR analysis: The IR absorption spectra of pure drug, drug with different excipients and final formulation were taken in the range of 4000-400cm-1using KBr disc method and characteristics peaks of drug.

Microscopy study of the drug: Microscopy of the drug was performed by Direct method, where small quantity of the powder was spread onto the slide uniformly and viewed it under the light microscope. And Smear method, where small quantity of powder was placed on to the slide and wet it with 1 or 2 drops of distilled water, the suspension was spread uniformly by using another slide at 450 angle. After that it was observed under the light microscope [21].

Test for Impurity (BP): 500mg of drug was dissolved in methylenechloride and diluted 25ml with Methylene chloride. The absorbance of the solution was measured at 280 nm [22].

Partition Coeffiecent: The Partition coefficient of Clarithromycin was determined in solvent system: n- Octanol / distilled water and n-Octanol / 0.1N HCl.Accurately weighed quantity of drug (20mg) taken in one stoppered glass vial containing

5.0 ml of n-Octanol. After dissolving the drug in n-Octanol, 5ml distilled water was added to vial and in another vial Octanol / 0.1 N HCl was taken. Then the glass vial was kept to equilibrate by shaking in vertex mechanical shaker for 6 hrs and after shaking, the vial were transferred into separating funnel, kept over night at37±2ºC for equilibrium. The contents and both phases were separated. After appropriate dilutions, the aqueous phase was analyzed for Clarithromycin against reagent blank solution using Shimadzu-1700 E U.V. spectrophotometer. The drug concentration in n-Octanol phase was determined by subtracting the amount in aqueous phase from the total quantity of drug added to the vials [23].

Microsphere formations: Microspheres containing Clarithromycin were prepared employing sodium alginatein combination with HPMCK4M and carbopol974P .The homogeneous polymer (s) solution was prepared in distilled water stirred magnetically with gentle heat.The drug and mineral oil (light liquid paraffin) were added to the polymer solution and mixed thoroughly by stirring magnetically to form a viscous dispersion which was then extruded through a syringe with a needle of size no. 23 into 5% Calcium chloride solution, product thus separated was washed with n-Hexane to remove the traces of paraffin oil. The microspheres were dried for 24 h. Rewash if the oil still found in beads & dry [24].

Table 1:Composition of Clarithromycin Microspheres.

Formulation Code	Sodium Alginate (%)	HPMC*K4M (%)	carbopol 974P (%)	Drug(%)
F1	1	2	1	1
F2	2	2	1	1
F3	3	2	1	1
F4	1	2	-	1
F5	2	2	-	1
F6	3	2	-	1
F7	1	-	1	1
F8	2	-	1	1
F9	3	-	1	1

Microsphere characterization:

Angle of repose: A static heap of powder, when only gravity acts upon it, will tend to forma conical mount. One limitation exists; the angle to the horizontal can not exceed a certain value and this is known as the angle of repose (θ). 20 gm of beads were allowed to flow freely through a funnel having orifice of diameter of 0.95cm, from a height of 10cm from the base. As the heap was formed a circular line was drawn around the heap of granules and diameter was measured with scale. Height of the heap was measured with the help of scale. Angle of repose (θ) was calculated from the equation given below [25].

$\tan \theta = h/r$

Bulk density: Accurately weighed 10gm beads were placed in side a 100ml graduated cylinder .The cylinder was then dropped three times on a bench top from a height of about 1 inch , every 2 seconds so that a constant volume of the beads was obtained. Bulk density was calculated from the formula given below: [25]

Bulk density=Mass of the beads/bulk volume

Tapped density: Accurately weighed 10 gm beads were put inside a 100 ml graduated cylinder. The cylinder was then mechanically tapped for 1250 times using tapped density test apparatus (Veego,Vtap/Matic-II) and V1250volume was calculated using radius of measuring cylinder and height of pellets after 1250 taps.The tapped density was calculated from following formula [25]:

Tapped density(D)=Mass of the beads/V1250

Carr's index and Hausner's ratio: Flow ability of microspheres is evaluated by comparing the bulk density and tapped

density of a microspheres and the rate at which it packed down.The following formulae were utilized for obtaining Carr's index and Hausner's ratio [25]:

Carr'sindex(%)=[(Tapped density–Bulk density)/Tapped density] X 100

Hausner'sratio=Tapped density/Bulk density

Invitro drug release study: Five milli litres of aliquot was withdrawn at predetermined time intervals. The medium was replenished with 5ml of fresh 0.1N HCl.after each withdraw to maintain the volume in the vessel. Samples were filtered through 0.45 µ filter milli pore filtration assembly. The samples were determined at 280 nm using dissolution medium as blank [26].

Kinetic modeling of drug releases: The dissolution profiles of all batches were fitted to zero order,first order,and Higuchi's model to ascertain the kinetic modeling of drug release. The regression coefficient value (r^2) and K values were calculated for the linear curve obtained by regression analysis. Another kinetic model named as Korsmeyer model is widely used when the release mechanism is not clearly observed or when more than one type of release phenomenon could be involved. Korsmeyer and Peppas equation.

$$M_t/M_\infty = K_t^n$$

Where,Mt/M∞=the fractional drug release in time 't'

K=constant in corporative of structural and geometric characteristic of controlled release device.

n = exponent (diffusion release exponent) indicative of release mechanism. The value of n could be used to characterize different release mechanism like: n = 0.5 means Fickian diffusion,

n=0.5 < n < 1 means Non fickian diffusion or anomalous behavior, and n = 1 represents case II diffusion or perfect zero order release [26].

Evaluation of microspheres: prepared microspheres evaluated for their microencapsulation efficiency, particle size, mucoadhesiveness & swelling index. Their surface was examined through SEM (Scanning Electron Microscopy).

Microencapsulation Efficiency: The encapsulation efficiency (EE) was calculated by following formula:

EE (%) = (C/T) x 100

Where C is the calculated drug content and T is the theoretical drug content.

Mucoadhesion studies: Fixed weight of microspheres sample (50mg) was added over an intestinal segment mounted on a tilted slide with an angle of 45.the effluent (0.1N HCl) was run over the segment with a rate of 4 to 5 ml per min. the effluent was collected in a whattman filter paper & weight of detached particle was determined .% of bioadhesion was determined by following formula [27].

% Mucoadhesion = (weight of added sample–weight of detached particle) /weight ofsample ×100

Swelling Index: Swelling of microspheres was determined by soacking 50 mg of microspheres in 0.1 N HCl. swelling index was calculated by using following formula:

Sweling Index=Wt-W_o/ Wo X 100

Where Wt = weight of microcapsules observed after 4 hand W0=the initial weight of microcapsules [28].

3. RESULTS & DISCUSSIONS

Identification of drug was done by using IRspectroscopy, UVspectroscopy and melting point determination. Other official tests referred in British pharmacopoeia 2005 were performed to determine the quality of drug.

The drug was white powder, without any odour , bitter in taste .Microscopy of drug powder confirmed spherical structured particles. The drug showed good flow properties and did not stick to the walls of container.

From the IR spectra of pure drug major functional groups present in the chemical structure of clarithromycin were determined from the peaks present In the IR spectra.The peaks at wave no .1729.22 cm^{-1}(Lactonecarbonyl),1690.50cm^{-1}(Ketonecarbonyl),3450.15cm^{-1}(Hydrogen bonding between OH Groups), and 1375.25cm^{-1}(CH_2).Characteristic peaks ,all these groups were present in chemical structure of Clarithromycin thus ensuring the obtained sample was Clarithromycin.

The U.Vscan of drug was performed to observe the wave length maxima of the drug in 0.1 N HCl buffer. The observed λ max. of Clarithromycin was found 282 nm and reported λ max was 280nm.The melting point of drug was found to be

219ºC.which is within limits of [217o]C to 220 ºC. Solubility analysis of drug was performed in various organic solvents and distilled water. The drug was found to be freely soluble in Acetone and Methylene Chloride, Soluble in Chloroform, Dichloromethane, while it was slightly soluble in Methanol and liquid paraffin. The drug was found to be insoluble in distilled water.

The partition coefficient of Clarithromycin was found 2.17 when analysed with 0.1 N HCl. and that suggest a good partitioning behavior at biological membrane. The standard curves were prepared for Clarithromycin in 0.1N HCl by double beam UV spectrophotometer. It was observed that Clarithromycin follows Beer-Lambert's law and correlation coefficients were found to be near to one for the media used.

Test for Impurity (BP): The absorbance of the solution was measured at 280 nm. Absorbance of the above solution: 0.033nm.

While calculating the Partition coefficient, The log(P) Value for Clarithromycin was found 2.17 for0.1 N HCl.

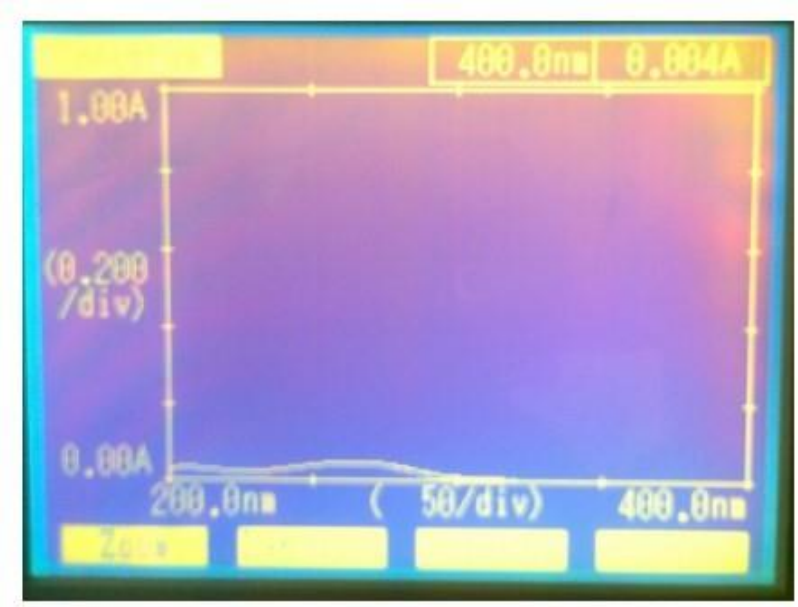


Figure 1:UVScan of Clarithromycin in 0.1N HCl Solution.

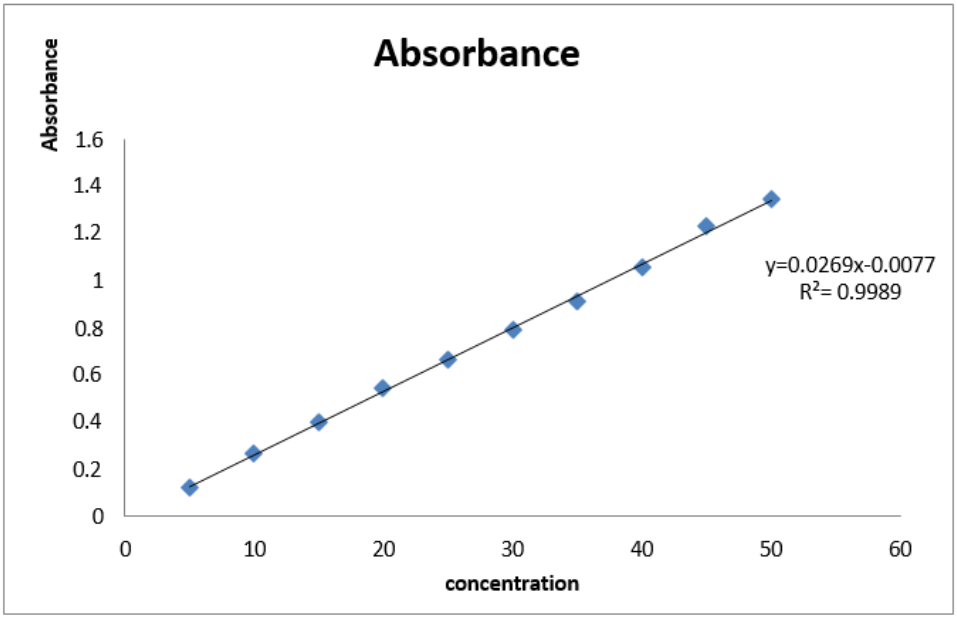
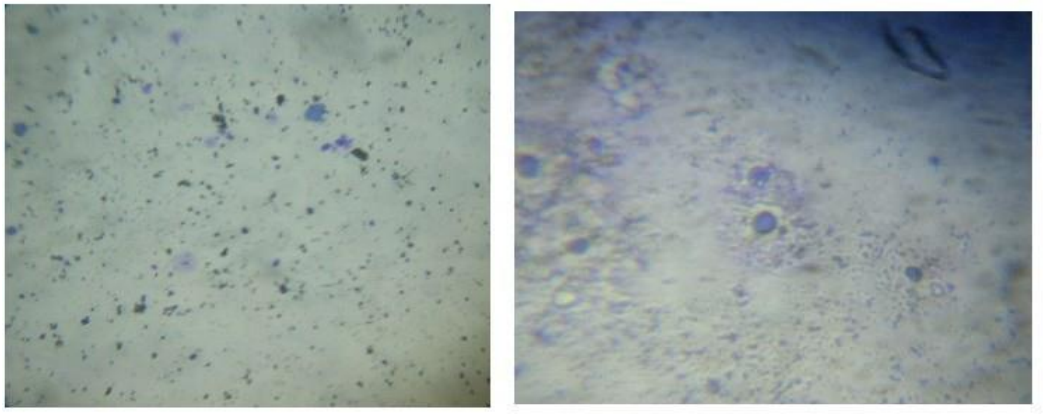


Figure 2:CalibrationcurveofClarithromycinin0.1NHCl.



a. Dry method **b. Smear method**

Figure3: Microscopic image Powder Of Clarithromycin

Table2:Solubility Profile of Clarithromycin.

S.No.	**Solvent**	**Solubility**
1.	Methanol	Soluble
2.	Ethenol	Partially soluble
3.	Chloroform	Soluble
4.	Acetone	Soluble
5.	Dichloromethane	Soluble
6.	Liquid paraffin	Partially soluble
7.	Water	Insoluble
8.	Acetonitrile	Soluble

Table3: Solution stability of Clarithromycin in 0.1 (N) HCl.

Time(hours)	Absorbance	Concentration(mcg/ml)	%Drug remaining
0	1.375	24.9712	99.884
1	1.371	24.8944	99.577
2	1.375	24.9712	99.884
3	1.369	24.8560	99.424
4	1.378	25.0287	100.115
5	1.376	24.9904	99.961
6	1.374	24.9520	99.80
7	1.376	24.9904	99.961
8	1.381	25.0863	100.345

9	1.376	24.9904	99.961
10	1.377	25.0096	100.038
11	1.368	24.8368	99.347
12	1.374	24.9520	99.808

Drug–Excipients compatibility study by FTIR Analysis

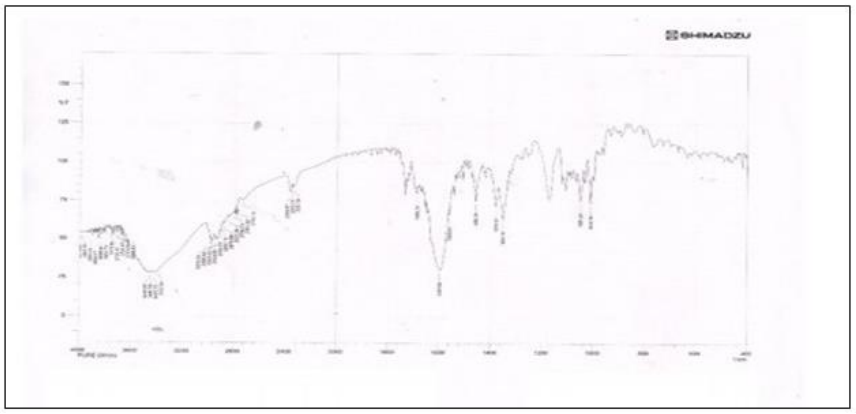


Figure4: IRSpectrum of Clarithromycin (sample)

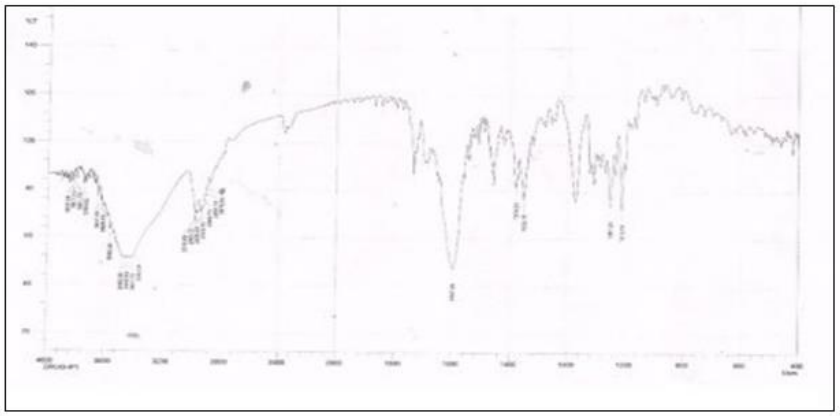


Figure5:IRSpectrum of physical mixture of Drug and Carbopol

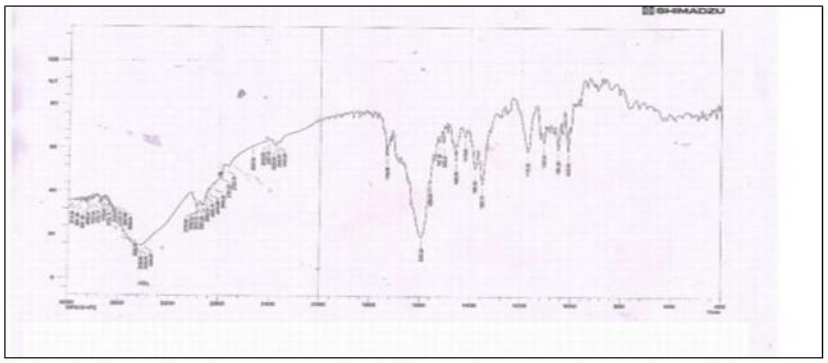


Figure6:IRSpectrum of physical mixture of Drug and HPMC

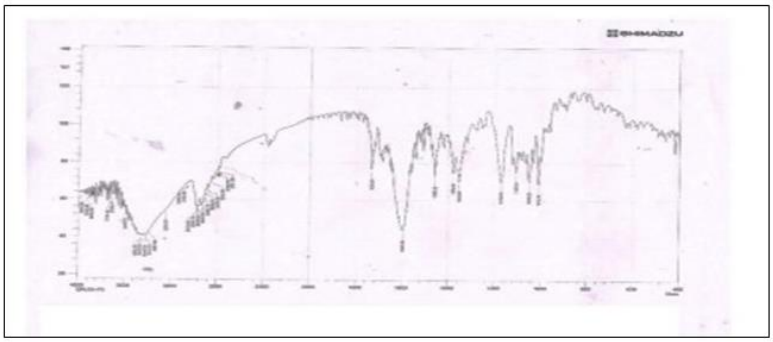


Figure7:IRSpectrum of physical mixture of Drug and Sodium alginate.

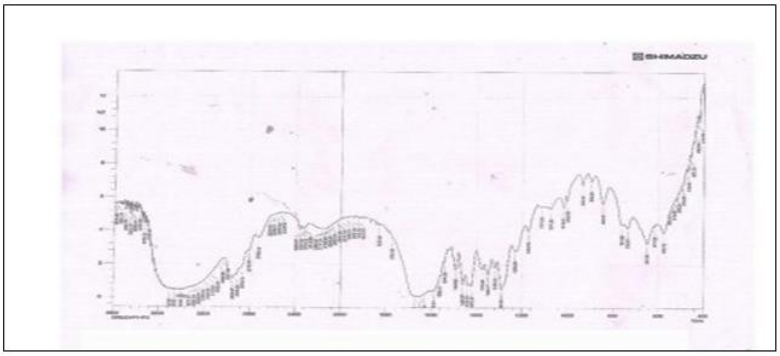


Figure8:IRspectrum of physical mixture of Drug, Carbopol & HPMC.

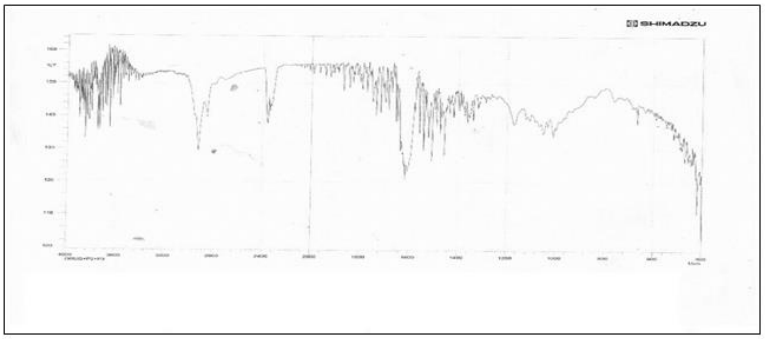


Figure9:IRspectrum of physical mixture of Drug, HPMC & Sodium alginate.

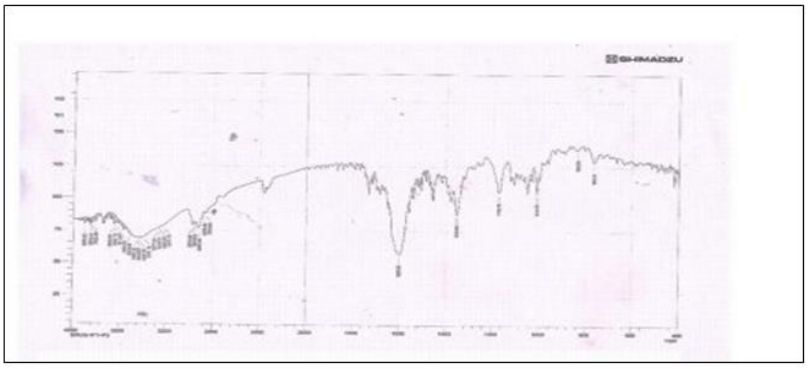


Figure10:IRspectrumofphysicalmixtureofDrug,Carbopol&Sodiumalginate.

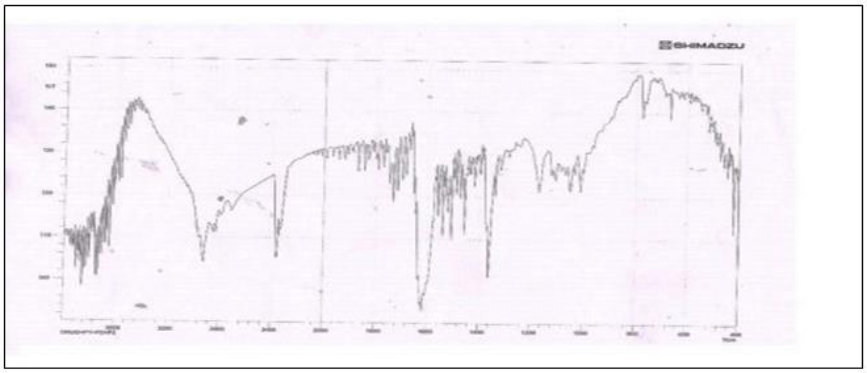


Figure11:IRspectrum of physical mixture of drug, carbopol, HPMC & Sodium Alginate.

Table4:Characteristic Functional group in Clarithromycin.

S.No.	**Waveno.(cm-1)**	**Functionalgroup**
1.	1729.22	Lactonecarbonyl
2.	1690.50	Ketone carbonyl
3.	3450.15	Hydrogen bondingofOH
4.	1375.25	CH_2

Table5:Drug Polymer interaction Profile.

S.No.	**Physical mixture of drug & polymer**	**Result**
1.	Clarithromycin + carbopol	No significant difference found between functional peaks
2.	Clarithromycin + HPMC	No significant difference found between functional peaks.
3.	Clarithromycin + Sodium Alginate	No significant difference found between functional peaks.
4.	Clarithromycin + Carbopol +HPMC	No significant difference found between functional peaks.
5.	Clarithromycin + HPMC + Sodium Alginate	No significant difference found between functional peaks.
6.	Clarithromycin + Carbopol + Sodium Alginate	No significant difference found between functional peaks.
7.	Clarithromycin + Carbopol + HPMC + Sodium Alginate	No significant difference found between functional peaks.

Different excipients (polymer/emulsifying agent) have been used for the formulation of microspheres which imparts mucoadhesion and which are able to work as gastroretentive drug delivery system .Among these combinations of excipients the first combinations of last two formulation showed imcompatability issues and no satisfaction of desired level so no further batch was formulated while other combinations of excipients showed adequate quality .so they were selected for further

study and optimization

Table6:Characterization of formulations

F.Code	Bulk density (g/cm3)	Tapped density (g/cm3)	Carr's Index	Hausner's ratio	Mean θ	Inference
F1	0.4950	0.5052	2.01	1.02	19	Fairpassable
F2	0.4975	0.5104	2.52	1.02	23	poor
F3	0.5102	0.5281	3.38	1.03	22	poor
F4	0.5154	0.5289	2.55	1.02	17	good
F5	0.5944	0.6268	5.16	1.05	15	good
F6	0.5446	0.5836	6.68	1.07	18	Fairpassable
F7	0.6128	0.6511	5.88	1.06	15	good
F8	0.6632	0.6787	2.28	1.02	16	good
F9	0.6612	0.6794	2.67	1.02	15	good

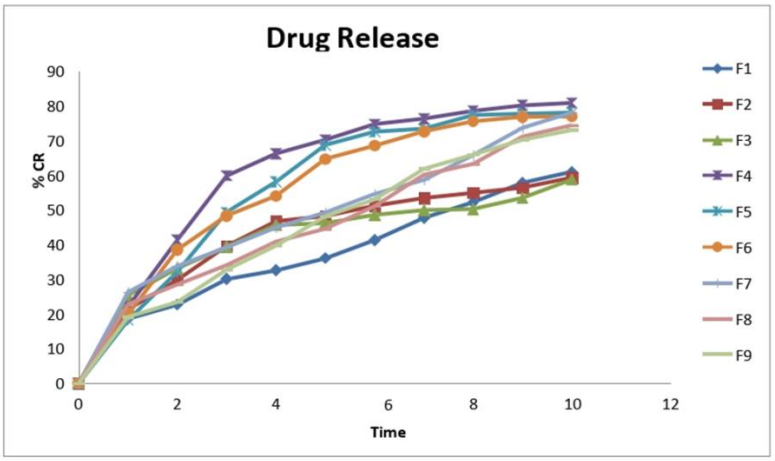


Figure12:Cumulative Percentage Drug Release of all formulation.

The anomalous behavior and non-fickian diffusion generally occur when there lease of drug may be due to relaxation of polymeric chain. Release from initially dry, hydrophilic, glassy polymers that swellin contact with water and become rubber like components and shows anomalous diffusion as a result of rearrangement of macromolecular chain. The interpretation of data is based on the value of resulting regression coefficient (R^2).

Table 7: Mechanism of Release Kinetics.

Formulation	Best fitted model	R2	Exponent Value(n)
F1	First order	0.9824	0.5338
F2	Peppas korsmeyer	0.9662	0.4382

F3	Peppas korsmeyer	0.9740	0.3378
F4	Higuchi matrix	0.9363	0.5318
F5	Peppas korsmeyer	0.9385	0.6366
F6	First order	0.9576	0.5685
F7	Peppas korsmeyer	0.9757	0.4701
F8	Hixon-crowell	0.9835	0.5369
F9	First order	0.9947	0.6343

Table8: Evaluation studies of all Formulations.

F. Code	Encapsulation Efficiency	Particle size in µm (Mean ± SD)	Mucoadhesion(%)	% Swelling
F1	80	318±11	56	50
F2	84	287±06	48	65
F3	64	257±78	68	70
F4	91.2	197±65	70	69
F5	91.4	192±54	74	75
F6	96	322±74	60	80
F7	81.1	379±35	58	65
F8	86	439±23	64	82
F9	78	204±09	76	76

Surface morphology study: The final optimized formulation F9 was subjected for surface morphology study using Scanning electron microscopy.

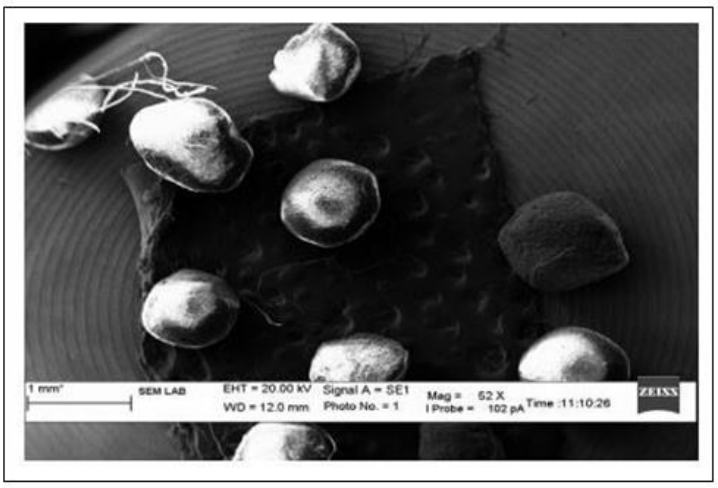


Figure13:SEM Image of Clarithromycin microspheres (F9)

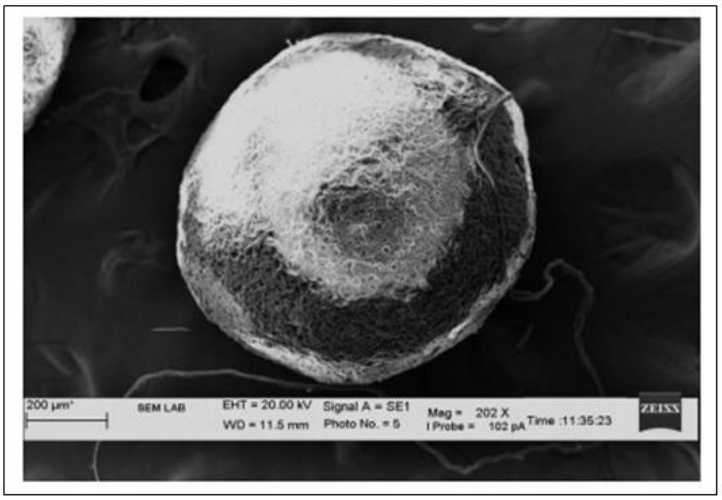


Figure14:SEM Image of Clarithromycin microsphere (F9).

4. CONCLUSION:

Recently, dosage forms that can precisely control the release rates and target drugs to a specific body site have made an enormous impact in the formulation and development of novel drug delivery systems. Microspheres form an important part of such novel drug delivery system. They have varied applications and are prepared using assorted polymers. It would, therefore be advantageous to have means for providing an intimate contact of the drug delivery system with the absorbing membrane. This can be achieved by coupling Bioadhesion characteristics to microspheres and developing bioadhesive microspheres. Bioadhesive microspheres have advantages such as efficient absorption and enhanced bioavailability of drugs owing to high surface to volume ratio a much more intimate contact with the mucus layer and specific targeting of drugs to the absorption site. To overcome the relativity short GI time and improve localization for oral controlled or sustained release drug delivery systems. The polymers which adhere to the mucin epithelial surface are effective and lead to significant improvement in oral drug delivery based on this three broad categories

Controlled release Clarithromycin microspheres for eradication of H.Pylori were successfully prepared employing ionotropic gelation technique. Carbopol and HPMC can be effectively blended with sodium alginate to form microspheres without using organic solvents. Microspheres prepared are spherical in shape and having a smooth surface. The microspheres were found to be effective in sustaining the drug release for10hrs.Drug release was diffusion controlled and followed first order kinetics. Stability studies reviewed that there was no significant change in drug content and dissolution profile of microspheres .The process of drug release from the polymer-drug matrix involves solvent penetration into the dry matrix, gelation of the polymer, dissolution of the drug, and diffusion of drug through resultant layer.

Microspheres of Clarithromycin consisting of sodium alginate andmucoadhesive polymers,Carbopol974P,HPMC in different ratio were prepared by the orifice-ionicgelation process. The percentage microencapsulation efficiency were determined for all the formulations of Clarithromycin microspheres .The microspheres were found to be discrete, spherical, and microspheres having Carbopol shows good flow properties. The prepared batches of microsphere were evaluated for micromeritic study such as angle of repose, Bulk density, Tapped density, Hausner's ratio & Carr's Index. Microspheres also evaluated for their particle size, formulation F5 shows the smallest particle size of 192± 54 µm & F8 shows largest particle size of 439±23 µm**.** Microspheres consisting of sodium alginate and a mucoadhesive polymer exhibited good mucoadhesive properties. The microencapsulation efficiency was in the range of 64 % to 96% being highest for F6 and lowest for F3.

Result of *in vitro* wash off test studies indicate that the formulation F3, F4, F5, and F9 having considerable mucoadhesive property. Clarithromycin release from the microspheres was studied in 0.1 N HCl for 10 hours. Drug release from the microspheres depends on the nature of the polymer and inversely proportional to the amount of polymers added. Observation of all formulation for physical characterization had shown that, all of them comply with the specification of official pharmacopoeias and/or standard references. From the IR-spectrum data of all formulation ,it is clearly evident that there were no interactions of the drug.

IR Spectrum of the pure drug shows the characteristic peaks at 1729.22 cm^{-1}, 1690.50 cm^{-1}, 3450.15 cm^{-1} and 1375.25 cm^{-1}. The IR spectrum of drug and polymer shows that there is no change in the peaks found for the physical mixture of drug and polymer and this confirms the undisturbed structure of the drug in the formulation. This proves the fact that there is no potential in compatabiliy of the drug with the polymer used in the formulation.

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