IJPSR (2020), Volume 11, Issue 10 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 22 October 2019; received in revised form, 20 February 2020; accepted, 10 March 2020; published 01 October 2020

FORMULATION AND *IN-VITRO* EVALUATION OF MESALAMINE MUCOADHESIVE TABLETS FOR COLONIC DRUG DELIVERY

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Keywords:

Mesalamine, Matrix tablet, Sodium alginate, Hydroxypropyl methyl cellulose, Eudragit S100, Colon Specific drug delivery

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ABSTRACT: The objective of the present study is to develop a colon targeted drug delivery system by using sodium alginate as a carrier for Mesalamine. Matrix tablets containing various excipients and sodium alginate were prepared by wet granulation technique using different binder systems. The prepared tablets were evaluated for hardness, weight variation, drug uniformity, friability, and *in-vitro* drug release study. The surface of the device of the best formulation was coated with Eudragit S100 to ensure that the device was more pH-dependent and trigger the drug release only at higher pH. The matrix tablet containing sodium alginate as a carrier and hydroxypropyl methylcellulose as a binder was found to be suitable for targeting mesalamine for local action in the colon as compared to other matrix tablets containing different binders. Matrix tablets containing sodium alginate released 97-99% of mesalamine in the simulated colonic fluid. The stability study for prepared tablets at 40 ºC/75% relative humidity for three months showed no significant change in the *in-vitro* drug release pattern. The results of the *in-vitro* study indicate that a matrix tablet containing sodium alginate as carrier and hydroxypropyl methylcellulose as a binder is most suitable to deliver the drug specifically in the colonic region.

INTRODUCTION: Currently, a novel oral colon-specific drug delivery system (CDDS) has been developing as one of the site-specific drug delivery systems. This delivery system, by means of a combination of one or more controlled release mechanisms, hardly releases the drug in the upper part of the gastrointestinal (GI) tract, but rapidly releases the drug in the colon following oral administration. The necessity and advantage of CDDS have been well recognized and reviewed recently [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.11(10).4982-90

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

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.11(10).4982-90

In view of CDDS specifically delivering a drug to the colon, a lot of benefits would be acquired in terms of improving safety and reducing toxicity when treating local or systemic chronic diseases. First, as for treating localized colonic diseases, *i.e.*, ulcerative colitis, Crohn's disease, and constipation, the optimal drug delivery system, such as CDDS, should selectively deliver the drug to the colon, but not to the upper GI tract [1].

For this reason, the drug concentration was significantly less in the upper GI tract, while increased considerably in the colon, resulting in alleviated GI side effects. Second, the colon is referred to as the optimal absorption site for protein and polypeptide after oral administration, because of the existence of relatively low proteolytic enzyme activities and quite long transit time in the colon [2, 3].

CDDS could provide reliable protection against GI enzymatic degradation by releasing the polypeptide and protein nearly unchanged and fully efficacious in the preferred colon, thereafter resulting in remarkably increased bioavailability for protein and polypeptide. Finally, CDDS would be advantageous when a delay in absorption is desirable from a therapeutical point of view, as for the treatment of diseases that have peak symptoms in the early morning and that exhibit circadian rhythms, such as nocturnal asthma, angina and rheumatoid arthritis [4, 5]. Polysaccharides, the polymer of monosaccharide, retains their integrity because they are resistant to the digestive action of gastrointestinal enzymes.

The matrices of polysaccharides are assumed to remain intact in the physiological environment of the stomach and small intestine, but once they reach in the colon, they are acted upon by the bacterial polysaccharides and results in the degradation of the matrices. A large number of polysaccharides such as amylose, guar gum, pectin, sodium alginate, inulin, cyclodextrins, chondroitin sulphate, dextrans, dextrin, and locust bean gum have been investigated for their use in colon targeted drug delivery systems. The most important fact in the development of polysaccharide derivatives for colon targeted drug delivery is the selection of a suitable biodegradable poly-saccharide. As these polysaccharides are usually soluble in water, they must be made water-insoluble by cross-linking or hydrophobic derivatization. Very important is an optimal proportionality of the hydrophobic and hydrophilic parts, respectively, and the number of free hydroxy groups in the polymeric molecule [6, 7, 8].Mesalamine is used for long-term maintenance therapy to prevent relapses of Crohn's disease and ulcerative colitis. However, when mesalamine is adminis-trated orally, a large amount of the drug is absorbed from the upper gastrointestinal tract and causes systemic side effects. Free mesalamine undergoes rapid and nearly complete systemic absorption from the proximal intestine, depending on concentration and local pH, followed by extensive metabolism [9, 10]. It is thus of tremendous importance to deliver mesalamine locally in order to reduce influences by systemic drug absorption, causing adverse effects. Hence, the selective delivery of mesalamine into the colon is required.

The aim of this study was to explore the feasibility of the colonic microorganism to develop CDDS by using Sodium alginate polysaccharide as a carrier and mesalamine as a model drug.

MATERIALS AND METHODS:

Materials: Mesalamine was gifted from Bengal Chemicals Ltd., Calcutta, sodium alginate from DrReddys Lab, Hyderabad; Hydroxyl propyl methylcellulose (HPMC) (K4M) was gifted from Cadillapharma Ltd., India. Sodium CMC, PVP K-30, Microcrystalline cellulose, Talc, and Magnesium stearate was obtained form National chemicals, Baroda

Methods:

Preparation of Tablets: Sustained release matrix tablets were prepared by wet granulation method. All the ingredients were passed through sieve # 100, weight accurately, mixed and granulated using PVP K-30 in isopropyl alcohol, Sodium CMC (10 % aqueous solution), and HPMC K4M (10% alcoholic solution) as granulating aid [7, 8]. The granules obtained were dried in an oven at 50 ºC for 2 h. After drying, granules passed through sieve # 16 to obtained uniform size granules. After sufficient lubrication, matrix tablets were prepared using Cadmach single punch tablet machine (M/S.

Cadmach Machinery Co. Pvt. Ltd, Ahmedabad) using 10 mm SC (Shallow concave) die and punch set. All the prepared Mesalamine tablets were stored in airtight container at room temperature for further study. Amount of drugs in all formulation was kept constant. The Best tablet formulation was enteric coated with Eudragit S 100 to give pH-dependent release. The surface of the device was coated with Eudragit S100 to ensure that the device was more pH-dependent and trigger the drug release only at higher pH. The composition of various formulations is shown in **Table 1**.

Identification by FT-IR Spectrophotometer: FTIR studies of mesalamine and formulation was carried out to find any possible interactions between the drug and the polymers during formulation. FTIR spectra of drug and drug-polymer in the formulation were obtained in KBr pellets using a Perkin Elmer model spectrum BX-FTIR spectrophotometer in the ranges, 4000-400 cm^{-1} [11, 12].

TABLE 1: COMPOSITION OF DIFFERENT SODIUM ALGINATE MATRIX TABLETS OF MESALAMINE

S. no.	Ingredients	Formulation codes (Quantity of tablet in mg)								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Mesalamine	100	100	100	100	100	100	100	100	100
2	Microcrystalline cellulose	340	310	280	340	310	280	340	310	280
3	Sodium alginate	50	75	100	50	75	100	50	75	100
4	Sodium CMC (10% aq. sol)	5	10	15						
5	Alcoholic PVP K-30				5	10	15			
6	HPMC (10% alcoholic sol.)							5	10	15
7	Magnessium stearate	2	2	2	2	2	2	2	2	2
8	Talc	3	3	3	3	3	3	3	3	3
			500	500	500	500	500	500	500	500

Evaluation of Formulated Tablet:

Tablet Hardness: The strength of the tablet is expressed as tensile strength (Kg/cm^2). The tablet crushing load, which is the force required to break a tablet into halves by compression. It was measured using a tablet hardness tester (Monsanto Tablet Hardness Tester, Mht-20, Campbell electronics)

Weight Variation Test: Weight variation test is done by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weight to the average.

Friability: Friability test is performed to assess the effect of friction and shocks, which may often cause the tablet to chip, cap or break. Roche friabilator (EF2, Eletrolab) was used for the Purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of 6 inches with each revolution.

The pre-weighed sample of tablets was placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted and reweighed. Compressed tablets should not lose more than 1% of their weigh. Thickness was measured by vernier caliper (SV-03, E-Base measuring tools).

Content Uniformity: Twenty tablets of mesalamine were weighed and powdered. Crushed powder of tablets equivalent to 0.15 gm was weighed and dissolved in pH 7.4 Sorensen's Phosphate buffer. The solution was filtered and diluted, and drug content was analyzed spectro-photometrically at about 334.5 nm.

Micro-environment pH: The microenvironment pH (surface pH) of the mesalamine tablets was determined in order to investigate the possibility of any side effects *in-vivo*. As an acidic or alkaline pH may cause irritation to the colon mucosa, it was determined to keep the surface pH as close to neutral as possible. The method adopted by Battenberg *et al.*, [7] was used to determine the surface pH of the tablet. A combined glass electrode was used for this purpose. The tablet was allowed to swell by keeping it in contact with 5 ml of distilled water (pH 6.5 ± 0.05) for 2 h at room temperature. The pH was measured by bringing the electrode in contact with the surface of the tablets and allowing it to equilibrate for 1 min.

Swelling Study: Six mesalamine tablets were individually weighed (W_1) and placed separately in Petri dishes with 5 ml of phosphate buffer of pH 6.8. At the time interval of 1, 2, 4, 6, and 8 h, the tablet was removed from the Petri dish, and excess water was removed carefully using the filter paper. The swollen tablet was then reweighed (W_2), and the percentage hydration was calculated using the following formula [9, 10, 12]:

$$\text{Percentage hydration} = [(W_2-W_1)/ W_1] \times 100$$

***In-vitro* Mucoadhesive Study:** [13, 15] It is measured by using the mucoadhesive force measuring device. The bioadhesive strength of the mucoadhesive polymer under study was determined by measuring the force required to detach the formulation from a mucin disc using the measuring device. Initially, the mucin disc was prepared by compression of the crude porcine disc machine using a flat-faced punch of 8 mm diameter. The mucin disc was fixed to the glass vial using α-cyanoacrylate adhesive.

Then this glass vial was connected to the right arm of the balance in an inverted position. The mucin disc was hydrated with distilled water prior to bioadhesion testing. Each tablet was placed on the lower vial; the lower vial was then elevated till the surface of the tablet came in contact with the mucin disc. Both the tablets & hydrated mucin disc were left in contact for 2 min using a preload of 10 gm. to establish the contact between them & allow the formation of an adhesive bond. The preload time & force were kept constant for all the tested formulation. After completion of the preload time, water was allowed to drip from a glass bottle through an infusion set into a pre-weighed plastic jar placed on the left pan of the balance at a constant rate of 30 drops per minute. The addition of water was stopped when the mucin disc was detached from the tested sample, the filled plastic jar was reweighed & the weight of water required to detach the tested sample from the mucin disc was calculated by difference. The results were the mean of three runs. The mucoadhesive force can be calculated as per the following formula

$$F = 0.00981W/2$$

W = Amount of water.

***In-vitro* Drug Release Study:** The ability of the matrix tablets of Mesalamine to remain intact and to release the active ingredient in the physiological environment of the stomach, small intestine, and colon was assessed by conducting *in-vitro* drug release studies under conditions mimicking mouth to colon [14, 15]. The drug release studies (n = 3) were carried out using USP dissolution rate test apparatus at 100 rpm and 37 ± 0.50 ºC.

900 ml of 0.1 M HCL was used as a dissolution medium in the first two hrs of study as the average gastric emptying time was estimated as 2 h. 5 ml of the dissolution medium was withdrawn after 2 h to determine the drug release. The volume was withdrawn with replaced with fresh media and was accounted for during the calculation of cumulative percentage drug release. The amount of drug release was analyzed by a Double beam UV spectrophotometer (Lambda 2, Perkin– Elmer, USA) at maximum wavelengths of 334.5 nm. The dissolution media was replaced at the end of 2 h. with pH 7.4 Sorensen's Phosphate buffer, 900 ml. and drug release study was continued for another 3 h. (*i.e.*, total 5 h) as the average small intestine transit time is about 3 h. As before, samples were withdrawn at regular time intervals and correspondingly replaced with fresh media. The amount of drug release was analyzed by a Double beam UV spectrophotometer (Lambda 2, Perkin– Elmer, USA) at maximum wavelengths of 334.5 nm [20, 21].

Drug Release Kinetics: To study the release kinetics, data obtained from *in-vitro* drug release studies were plotted in various kinetic models: zero-order (Equation 1) as the cumulative amount of drug released *vs.* time, first-order (Equation 2) as cumulative log percentage of drug remaining *vs.* time, and Higuchi's model (Equation 3) as cumulative percentage of drug released *vs.* square root of time.

$$C + K0t \quad (1)$$

Where K0 is the zero-order rate constant expressed in units of concentration/time, and t is the time in hours. A graph of concentration *vs.* time would yield a straight line with a slope equal to K0 and intercept the origin of the axes [19].

$$LogC + LogCo- kt/2:303 \quad (2)$$

Where C0 is the initial concentration of the drug, k is the first order constant, and t is the time (Bourne 1963).

$$Q + K\,t1/2 \quad (3)$$

Where K is the constant reflecting the design variables of the system, and t is the time in hours. Hence, the drug release rate is proportional to the reciprocal of the square root of time [20].

Mechanism of Drug Release: To evaluate the mechanism of drug release from Matrix tablet, data for the first 60% of drug release were plotted in Korsmeyer *et al.*, equation (Equation 4) as cumulative log percentage of drug released *vs.* log time and the exponent n was calculated through the slope of the straight line.

$$Mt/M8 = K\,tn \quad (4)$$

Where, Mt/M8 is the fractional solute release, t is the release time, K is a constant kinetic characteristic of the drug/polymer system, and n is an exponent that characterizes the mechanism of

release of tracers [21]. For cylindrical matrix tablets, if the exponent n = 0.45, then the drug release mechanism is Fickian diffusion, and if 0.45 < n < 0.89, then it is non-Fickian or anomalous diffusion. An exponent value of 0.89 is indicative of Case-II Transport or typical zero-order release [22].

Stability Study: Best formulation was (F9) exposed to six months of stability study at 40 ºC/75% RH. These samples then again evaluated for drug release study in **Table 8**.

Results and Discussion: Identification by FT-IR spectrophotometer-- FTIR studies of mesalamine and prepared formulation is shown in **Fig. 1** and **2**. It is clear from the FTIR that the characteristic peaks of the drug are also present in the formulation depicting no incompatibility between the drug and polymers in the formulation. Tablets were prepared using wet granulation techniques.

Tablets were obtained of uniform weight due to uniform die fill, with acceptable weight variation as per pharmacopeial specification. The drug content found in the range of 98.36-102.35% (acceptable limit), and the hardness of the tablet was found between 4.0 - 6.03 kg/cm^2. The tablet thickness was found to be around 3.0 mm, friability of tablet was found below 1%, indicating good mechanical resistance. The formulated matrix tablets have content uniformity 95.68 to 104.63 % in **Table 2**.

TABLE 2: EVALUATION PARAMETER OF DIFFERENT SODIUM ALGINATE MATRIX TABLETS OF MESALAMINE

Formulation code	Average weight	Average hardness of tablet (Kg/cm)	Friability of tablet (%)	Average thickness of tablet (mm)	Assay (%Drug content)
F1	501 ± 1.21	6.01 ± 1.34	0.46 ± 0.02	3.1 ± 0.33	100.25 ± 1.21
F2	502 ± 0.34	5.08 ± 0.33	0.42 ± 0.04	3.2 ± 0.32	102.35 ± 1.34
F3	498 ± 1.65	5.02 ± 1.22	0.4 ± 0.03	3.5 ± 0.41	99.65 ± 1.76
F4	496 ± 0.43	5.05 ± 0.42	0.39 ± 0.032	3 ± 0.27	98.36 ± 2.21
F5	492 ± 0.92	6.02 ± 0.11	0.36 ± 0.012	3.2 ± 0.15	98.67 ± 1.83
F6	493 ± 0.85	5.06 ± 0.32	0.39 ± 0.016	3.1 ± 0.12	99.26 ± 0.76
F7	503 ± 0.11	5.03 ± 0.21	0.23 ± 0.022	3.2 ± 0.14	100.36 ± 0.34
F8	502 ± 0.44	5.08 ± 0.15	0.2 ± 0.031	3 ± 0.12	101.36 ± 0.85
F9	490 ± 0.56	6.3 ± 0.21	0.16 ± 0.024	3.1 ± 0.21	99.64 ± 0.45

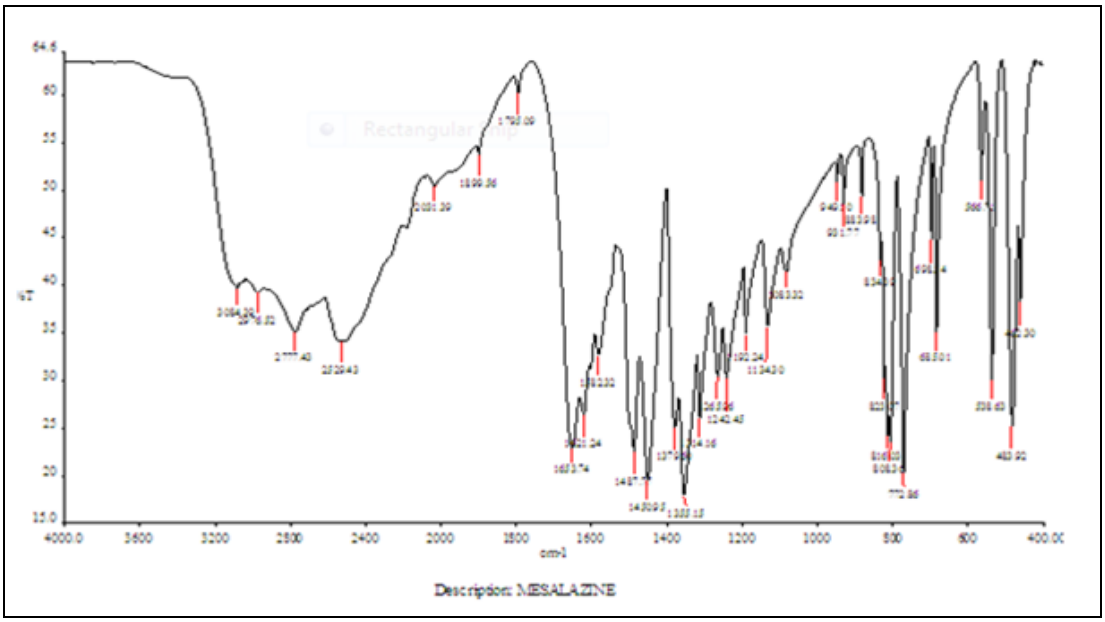

FIG. 1: FTIR SPECTRA OF MESALAZINE

The *in-vitro* release of mesalamine for all the nine batches is shown in **Fig. 1**. The result showed that Sodium CMC and PVP K-30 binder along with Sodium alginate polysaccharides could release the mesalamine in gastric and intestinal fluid. In the case of Sodium CMC, up 60% drug was released in first 5 h, but if the concentration of Sodium alginate was increased (batch F3), the drug release was decreased up to 43%. While in the case of PVP K-30 as a binder, the batch F6 (highest Sodium

alginate con-centration) was released 36%. So, it was decided that Sodium CMC and PVP K-30, along with polysaccharide Sodium alginate, could release the mesalamine in gastric and intestinal fluid. It was concluded drug release from tablets up to 24 h. depend on the amount of Sodium alginate Poly-saccharides.

Sodium alginate is a novel mucoadhesive polymer. It is totally degraded by colonic bacteria but is not digested in the upper GI tract. These poly-saccharides remain intact in the physiological environment of the stomach and the small intestine but are degraded by the bacterial inhabitants of the human colon. So, it was concluded that sodium alginate is used in matrix-forming tablets for colon targeting.

The drug was released only when the dosage form entered in the colon, where colonic bacteria degrade the polysaccharides. So, at a higher level of sodium alginate, the drug was released after 8 h.

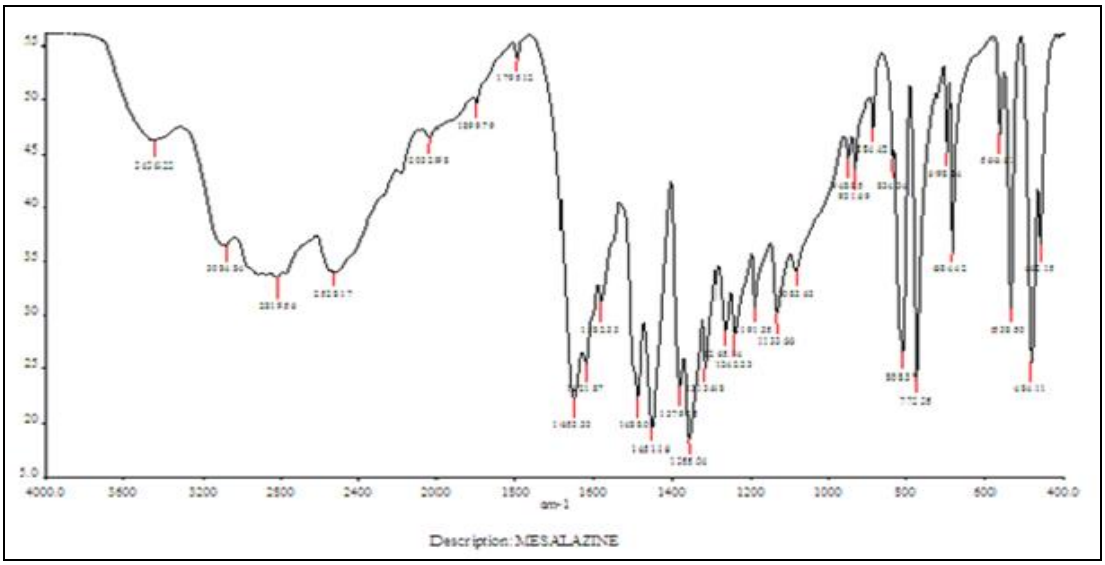

FIG. 2: FTIR SPECTRA OF MESALAMINE FORMULATION

But results showed that HPMC K4M is a good binder for matrix tablet formulations. The *in-vitro* release study of HPMC containing tablets showed that, at the highest sodium alginate concentration (Batch F9), only 12% release of mesalamine occurs. Drug release studies show that F9 shows good release behavior in the colon and restricts release in the stomach and intestine. This study confirms that sodium alginate can act as a good carrier in the form of a matrix tablet for mesalamine to deliver it in colon specifically by using HPMC as a binder.

HPMC is a swellable polymer that shows time dependant release profile when the tablet comes into contact with liquids. HPMC K4M has a viscosity of 3000-5600 cps and was used for matrix formulation. From the *in-vitro* release study, it was concluded that a higher percentage of sodium alginate and HPMC retard the drug release, but drug release from batch F9 was found to be satisfactory because, from this batch, drug release was found to be less than 15% in 5 h. And the total drug was released in 24 h. Which was controlled by enteric coating so, batch F9 was promising batch, and further enteric coating and stability study was performed on F9 batch. The zero-order rate describes the systems where the drug release rate is independent of its concentration. The first order describes the release from systems where the release rate is concentration-dependent. Higuchi's model describes the release of drugs from an insoluble matrix as a square root of a time-dependent process based on Fickian diffusion. The release constant was calculated from the slope of the appropriate plots, and the regression coefficient (r^2) was determined in **Table 3**.

It was found that the *in-vitro* drug release of batch F9 was best explained by Higuchi's equation, as the plots showed the highest linearity (r^2 = 0.9925), followed by zero-order (r^2 = 0.980). This explains why the drug diffuses at a comparatively slower rate as the distance for diffusion increases, which is

referred to as square root kinetics (or Higuchi's kinetics). However, drug release was also found to be very close to zero-order kinetics, indicating that the concentration was nearly independent of drug release.

The dissolution data were also plotted in accordance with the Hixson-Crowell cube root law. The applicability of the formulation to the equation indicated change in surface area and diameter of the tablets with the progressive dissolution of the matrix as a function of time.

TABLE 3: MEASUREMENT OF MUCOADHESIVE FORCE & STRENGTH

S. no.	Mucoadhesive strength (gm)	Mucoadhesive force (dyne)
F1	10.45 ± 1.32	1.12
F2	11.89 ± 1.17	1.16
F3	18.93 ± 2.37	1.85
F4	22.89 ± 4.92	2.24
F5	26.78 ±4.46	2.62
F6	34.27 ± 1.06	3.31
F7	31.69 ± 1.71	3.1
F8	37.43 ± 1.08	3.37
F9	38.46 ± 2.55	3.67

TABLE 4: DRUG RELEASE PROFILES OF MESALAMINE FORMULATION

Release profiles of mesalamine formulation mucoadhesive tablet									
Formulation	Percent mesalamine released at time (h) X^{-} ± S.D.								t50 (h)
	1	2	3	4	6	8	10	12	
F1	15.54 ±1.21	24.67 ±1.76	29.76 ±2.23	47.54 ±2.65	62.54 ±1.65	78.93 ±2.43	86.43 ±1.42	88.54 ±1.23	4.12
F2	14.76 ±1.23	22.65 ±2.21	28.87 ±2.34	45.65 ±1.65	61.19 ±2.98	76.65 ±1.65	82.15 ±2.41	88.6 ±2.54	4.23
F3	12.03 ±1.41	20.53 ±1.98	37.5 ±3.45	41.6 ±2.65	56.2 ±3.42	65.8 ±1.94	76.87 ±1.71	82.5 ±2.51	5.45
F4	15.54 ±2.21	19.56 ±1.43	31.32 ±1.52	37.76 ±1.84	58.76 ±2.61	67.43 ±1.63	78.23 ±2.41	87.87 ±1.51	5.7
F5	13.43 ±2.13	18.65 ±1.43	28.45 ±1.43	32.76 ±3.21	50.76 ±1.94	61.43 ±2.53	75.65 ±1.51	84.76 ±1.21	5.9
F6	12.34 ±0.73	16.65 ±1.65	22.65 ±2.32	28.65 ±2.54	41.54 ±2.76	57.98 ±3.21	71.23 ±2.41	82.23 ±1.43	6.5
F7	8.76 ±1.52	18.61 ±1.65	27.63 ±1.54	37.23 ±1.98	43.42 ±1.87	54.65 ±2.31	70.76 ±1.51	79.58 ±2.41	7.6
F8	6.56 ±2.43	14.54 ±1.43	19.43 ±2.21	28.76 ±2.21	39.51 ±2.76	50.62 ±1.84	69.40 ±2.31	76.23 ±1.21	7.9
F9	4.23 ±2.54	7.87 ±1.54	11.23 ±1.43	13.45 ±2.54	27.95 ±3.52	42.23 ±1.93	58.56 ±2.41	69.74 ±2.23	8.5

TABLE 5: MEASUREMENT OF SWELLING INDEX OF DIFFERENT FORMULATION

Formulation code	Percentage hydration (Swelling index)				
	1 h	2 h	4 h	6 h	8 h
F1	34.3	43.2	51.4	62.3	65.6
F2	36.2	44.3	53.4	63.4	67.6
F3	36.5	44.5	55.3	65.3	68.6
F4	40.8	50.2	59.5	61.4	65.8
F5	38.3	48.6	58.6	60.1	63.9
F6	41.6	49.3	59.4	62.3	66.5
F7	47.9	57.3	65.2	68.3	74.7
F8	47.8	56.2	63.7	67.2	72.7
F9	50.3	55.7	65.7	70.3	78.5

TABLE 6: MEASUREMENT OF SURFACE PH CALCULATION

Surface pH calculation	
Formulation code	Surface pH
F1	7.54
F2	7.43
F3	7.13
F4	6.12
F5	6.23
F6	6.64
F7	6.53
F8	6.54
F9	6.72

TABLE 7: RELEASE KINETICS OF DIFFERENT FORMULATION F1-F9

Formulation	Zero order(r^2)	First Order(r^2)	Higuchi(r^2)	Korsemeyer-peppas(r^2)
F1	0.878	0.858	0.976	0.980
F2	0.898	0.866	0.980	0.984
F3	0.876	0.815	0.991	0.979
F4	0.933	0.902	0.986	0.981
F5	0.977	0.919	0.983	0.990
F6	0.990	0.956	0.965	0.978
F7	0.958	0.839	0.986	0.986
F8	0.992	0.881	0.976	0.996
F9	0.961	0.950	0.929	0.978

TABLE: 8 STABILITY STUDY

Parameters	Initials	1 month (40 ºC/75% RH)	2 month (40 ºC/75% RH)	3 month (40 ºC/75% RH)	4 month (40 ºC/75% RH)	5 month (40 ºC/75% RH)	6 month (40 ºC/75% RH)
Description	Yellowish brown	Same	Same	Same	Same	Same	Same
Av. Weight (mg)	499.4	497.40	496.42	495.4	494.3	493.4	492.3
Hardness (kg/cm^2)	6.3	5.9	5.7	5.65	5.67	5.61	5.59
Dissolution							
0	0	0	0	0	0	0	0
1	4.23	5.12	5.28	5.41	6.71	6.34	6.89
2	7.87	8.52	8.49	7.91	8.27	8.82	9.61
3	11.23	11.73	11.71	11.45	12.73	13.72	14.76
4	13.45	14.92	14.83	13.91	15.62	16.82	17.61
6	27.95	28.81	27.91	27.81	29.81	30.72	32.91
8	42.23	44.72	43.72	44.91	46.71	47.91	48.65
10	58.56	58.62	59.12	60.56	62.34	65.91	68.91
12	69.74	71.27	70.54	12.91	73.82	74.92	75.94

CONCLUSION: The results obtained indicate that sodium alginate could be useful as a matrix system for controlled drug delivery, and various polymers could be used to modulate the drug release from the matrix tablet depending on the need. The matrix tablets were passed in different evaluation tests, content uniformity, and *in-vitro* drug release study. The drug release profile was evaluated in simulated gastric, intestinal fluid, and simulated colonic fluid. Best formulation was F9 on the basis drug release profile in simulated gastric, intestinal and colonic fluid. The matrix tablet containing sodium alginate as a carrier and HPMC as a binder was found to be suitable for targeting mesalamine for local action in the colon as compared to other matrix tablets containing different binders.

The surface of the device was coated with Eudragit S100 to ensure that the device was more pH-dependent and trigger the drug release only at higher pH. The final product is expected to have the advantage of being biodegradable and pH dependant. Matrix tablets containing sodium alginate released 97-99% of mesalamine in the simulated colonic fluid. Drug release kinetics indicated that drug release was best explained by Higuchi's equation, as these plots showed the highest linearity (r^2 = 0.9949), but a close relationship was also noted with zero-order kinetics (r^2 = 0.9850). Korsmeyer's plots indicated an n value of 0.60, which was indicative of an anomalous diffusion mechanism or diffusion coupled with erosion; hence, the drug release was controlled by more than one process. Tablets containing sodium alginate showed no change in physical appearance and dissolution profile upon storage at 40 ºC/75% relative humidity for three months. The results clearly demonstrate that sodium alginate has the potentials for drug targeting to the colon

ACKNOWLEDGEMENT: The authors are grateful to the staff of IPT Salipur for their support and encouragement to carry out this work.

CONFLICTS OF INTEREST: The authors declare that they have no conflicts of interest.

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How to cite this article:
Sahoo PK, Das S, Sahoo AC and Kanungo SK: Formulation and *in-vitro* evaluation of mesalamine mucoadhesive tablets for colonic drug delivery. Int J Pharm Sci & Res 2020; 11(10): 4982-90. doi: 10.13040/IJPSR.0975-8232.11(10).4982-90.