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Wet Granulation Approach for Colon-Specific Drug Delivery: Formulation and Assessment of Ibuprofen Matrix Tablets with a Blend of Natural Gums

Ankur Patel[1], E Nirmala[2], Sudhir Pandya[3*], Touseef Begum[4], Vijaykumar Sidramappa Wakale[5], Sandeep Kumar Mishra[6], Vijay Dhondiram Wagh[7], Arghya Paria[8]

[1]Department of Pharmaceutics, Sardar Patel College of Pharmacy,Vidyanagar-Vadtal Road, Bakrol, 388315
[2]Department of Pharmaceutics, Shri Venkateshwara College of Pharmacy No-13A, Ariyur, Puducherry, Pin: 605102 India
[3*]School of Pharmaceutical Sciences, Faculty of Health Science, JSPM University, Pune-Nagar Road, Pune – 412 207
[4]Department of Pharmaceutical Sciences, Ibn Sina National College for Medical Studies, P. O. Box 31906, Jeddah Kingdom of Saudi Arabia 21418.
[5]Department of Pharmaceutical Chemistry, Samarth Institute of Pharmacy, Belhe, Tal-Junnar, Dist-Pune, Maharashtra PIN- 412410.
[6]RGS College of Pharmacy, Near Itaunja Toll plaza, Village - Karaundi, Itaunja, Bahargaon, Uttar Pradesh 226203.
[7]NGSPMS College of Pharmacy Brahma Valley Campus Nashik 422 213.
[8]Sanaka Educational Trust's Group of Institutions, Malandighi, Durgapur, West Bengal 713212.

[*]**Corresponding Author: Sudhir Pandya[3*]**
[3]School of Pharmaceutical Sciences, Faculty of Health Science, JSPM University, Pune-Nagar Road, Pune – 412 207.

Abstract: Using a combination of natural polysaccharides, such as natural gum produced from two types of okra called Abelmoschus esculentus and Abelmoschus officinalis under research as carriers, an unique colon focused matrix tablet formulation was created. Utilizing Ibuprofen as a model medication, five distinct tablet formulations were created using the wet granulation process. The formulation containing 100 mg of Ibuprofen had matrix tablets with varying amounts of gum mix. FTIR was used to analyse the hardness, weight fluctuation, friability, drug content, thickness, and diameter of the prepared matrix tablets. Additionally, in vitro drug release experiments and swelling index investigations were conducted on matrix tablets. To replicate circumstances from mouth to colon, the release tests were conducted for 2 hours in pH 1.2 Hcl buffer, 3 hours in pH 7.4 phosphate buffer, and 5 hours in simulated colonic fluid. With the use of UV/visible spectroscopy, the medication release from the tablets was tracked. Based on in vitro drug release studies that demonstrated a minimum of 23.56±1.58 percent, 19.89±0.59 percent, 14.28±2.76 percent, 18.81±0.38 percent, and 9.35±1.28 percent of drug release in the first five hours of study, respectively, WGF3, WGF5, and WGF3 were selected as the optimal formulations for additional research. These formulations have demonstrated a maximal release of 53.56±1.15 percent for WGF3 and 50.38±1.08 percent for WGF5 in 5 hours when in the presence of rat caecal medium. As a result, the natural gum mix (AOEG) under study is extremely effective and efficient and has the potential to be a drug delivery vehicle that is specific to the colon. These formulations have demonstrated a maximal release of 53.56±1.15 percent for WGF3 and 50.38±1.08 percent for WGF5 in 5 hours when in the presence of rat caecal medium. As a result, the natural gum mix (AOEG) under study is extremely effective and efficient and has the potential to be a drug delivery vehicle that is specific to the colon.

Keywords: Polysaccharides, colon targeting, Ibuprofen, matrix tablets, microflora, Natural gum.

1. Introduction

Numerous medical conditions can impact the colon, particularly the first segment of the lower intestine, such as infections, Crohn's disease, ulcerative colitis, and constipation. Treatment recommendations include anti-inflammatory drugs, chemotherapy drugs, and/or antibiotics that need to be administered intra-colorectal route. Given that the colon is capable of absorbing some medications, including peptides, proteins, vermifuges, and diagnostic agents, it is also advantageous from a medical standpoint to have dosage forms that can precisely release these medications there (1-5). Before these medications reach the upper section of the colon, they must be transported in sufficient quantities and without release in order to provide the best possible pharmacological effect. Numerous businesses and research organisations have been conducting investigations since the early 1980s to develop dosage forms that can transport certain drugs to this section of the gastrointestinal system. Regretfully, several scientific advancements have resulted in dosage forms that release the medication before it reaches colon (6-10).

When it comes to the rectal route, the medications don't always get to the particular locations where colonic illnesses and absorption occur. The gastrointestinal tract's hurdles must be taken into consideration when formulating dose forms so that the medicine may precisely reach and be absorbed in the colon. The several approaches used to accomplish this aim have made use of this organ's unique properties, such as pH, enzymes, microflora or microbiota, reducing media, and transit time frame. However, these characteristics might differ depending on the disease state, nutrition, and individual differences. The dose forms must pass through the stomach (pH 3.5–3.5), duodenum (pH 6) gut (pH 5.5–6.8), and caecum (pH 6.8–7.3) before they can enter the colon (3, 9, 11, 12). Between 6.4 and 7.0 in the descending and ascending colons, there are pH variations in the colon. The colon has a mean redox potential of -200 mV, making it a reducing medium (13). Considering both inter- and intra-individual differences, these redox potentials can vary from -100 to -400 mV (14). Because the colon has very high pH values, it is essential to construct and synthesize polymers that dissolve at pH more than 7. These include copolymers, like Eudragit®, of methylmethacrylate, ethylacrylate, and methacrylic acid. The colon is additionally distinguished by the presence of anaerobic microflora and the growth of *Bifidobacteria*, *Lactobacillus anaerobicus*, *Clostridium*, and *Bacteroides fecalis* (15-18). Although they might vary numerically, the intestinal flora and the dietary sources that support them stay qualitatively same among individuals. One of the factors that inhibits intestinal microbiota development is oxygen (19), key variables include age, gastrointestinal disorders, medication treatment, and the fermentation of dietary residues can all have an impact on its metabolic activity. The development of certain adverse effects or the inactivation of medications are both possible outcomes of these circumstances. Bacterial colonic microflora may ferment a wide variety of non-absorbable disaccharides, polysaccharides, and oligosaccharides. Furthermore, the small intestine has the ability to ferment non alfa glucan polymers or polysaccharides derived from natural sources, including hemicellulose, cellulose, and pectic materials. Only specific kinds of reducing enzymes or enzymes involved in hydrolysed degradation are the enzymes involved in the metabolism of medicines or other substances (20-23). Such enzymes' existence and abilities have been utilised to precisely cleave particular drug classes that are joined to another molecule or polymer, leading to the development of the idea of prodrugs or conjugated polymers. Nitrogenous double bonds are typically used to bind the medicines together. NADPH and other specific biomolecules, along with the azo-reductase enzyme, cleave the medicines in the anaerobic and reducing media (24). The same concept has also been applied to the production of polymers having nitrogenous double bonds or disulfide bonds in the backbone. The synthesis of polymers with nitrogenous double bonds or disulfide bonds in the backbone has also been done using the same idea (25, 26). When these polymers are used as coverings for dosage forms, the microflora and enzymes must specially breakdown them. Certain investigations carried out on people have shown that transit time in the colon can vary from 0.8 to over 20 hours. Some authors (McNeil & Stevens, 1990) have created dosage forms (Targit®, Time-Clock®, Pulsincap®) in which the drug release is time-dependent, based on the fact that the colon is the final section of the gut (12, 15, 21, 27).

The dangers associated with the variation in parameters among ill individuals apply to all these changes. Premature and non-specific medication delivery in the colon can result from variations in the reducing medium, pH levels, and the transit duration. Moreover, azo - polymers have shown some degree of toxicity (12, 15, 21, 27). Because of all of these factors, current research is using polysaccharides, which are non-toxic and have a colon-specific breakdown. Thus, the goal of the current study was to extract and combine natural polysaccharides or gum to be utilised as a delivery vehicle for Ibuprofen, a medication that is particular to the colon, and then to fabricate matrix tablets for the purpose. The study then attempted to evaluate the matrix tablets as a colon-specific medication delivery method and to define the natural gum blend.

2. Material And Methods

Extraction of natural polysaccharide gum

We bought the fruits of *Abelmoschus esculentus* and *Abelmoschus officinalis*, sometimes referred to as bhindi, from the neighbourhood market (Karnal, India). Ofoefule et al. 2001's method is somewhat modified for the extraction of the natural gums under examination (*Abelmoschus esculentus* and *Abelmoschus officinalis*) (28). The two gums were combined in a 1:1 ratio to create AOEG, a natural gum combination. The samples of the natural gum blend that were being gathered were kept in desiccators in sealed jars. Analytical reagent grade chemicals were utilised for the extraction and characterisation of gum. The polysaccharide known as natural gum is made up of different ratios of galacturonic acid, galactose, rhamnose, and glucose. It has been discovered to be effective in treating urethritis, diabetes, jaundice, and constipation. It is also chilly and stomachic. Peptic ulcers have also been treated using it. The findings of the phytochemical tests indicate the existence of mucilage, fixed oil, and flavonoid glycoside. Seasonal variations in mucilage output ranged from 0.90 to 3.5 percent. The gum can operate as an antioxidant, hepatoprotective agent, flocculant, thickener, or binder. It has been used as a binding agent in tablet dosage forms for pharmaceutical formulation and has demonstrated the capacity to provide tablets with good drug release profiles, friability, and hardness. The mixture of gum and water has been kept in a desiccator until needed. One way to increase bacterial stability is to add 1% w/v sodium metabisulphite. The gum's usual characteristics were pH 6.6, loss on drying percentage -7.81, total ash percentage -7.79, acid insoluble ash percentage - 0.61, and water-soluble ash percentage - 6. 598.

Table 1. Properties of Natural gum blend (AOEG)

Natural gum (% of wet weight)	
Properties	**Purified**
Moisture content	8.44
Protein	8.51
Ash	4.89
Magnesium	0.60
Calcium	2.11
Potassium	0.87
Phosphorus	0.19

Preformulation studies

Preformulation in a broader sense, encompasses all the activities and studies essential to formulate a suitable dosage form for administration to human from an active pharmacological substance (29). It can be defined as an investigation of physical and chemical properties of a drug substance alone or when combined with excipients. The requirements of chemical stability of drug and excipients highlights the importance of preformulation work. The basic information is necessary in order to stabilize the product and/or prevent incompatibilities with pharmaceutical excipients. Preformulation studies including Calibration curve of the drug, Bulk density, tapped density and Biodegradation. The Procedure for various test are given below:

a) pH and viscosity

The pH and viscosity of 1%w/v natural gum solution were determined by using Digital pH meter and Ostwald's viscometer.

b) Bulk Density

After the powder sample was run through sieve number 18, 25g of the sample was precisely weighed and put into a graduated 100 ml cylinder. After levelling the powder, the unsteady volume Vo was recorded. Using the formula, bulk density was computed in g/cm3:

$$Bulk\ density\ =\ M/Vo$$

Where, M = mass of powder taken, Vo = apparent unstirred volume.

c) Tapped density

The powder sample for testing was passed through sieve #18, and a 100 ml graduated cylinder was filled to the weight of the sample, which amounted to 25 g. A tapped density tester was used to mechanically tap the cylinder 500 times at a notional rate of 300 drops per minute. The tapped volume, or Vo, was recorded during this process. Vb was observed as the tapping continued for 750 more times at a higher volume. Vb was regarded as a tapped volume Vf since the difference between the two tapping volumes was less than 2 percent. Using the formula, the tapped density was determined in g/cm3,

$$Tapped\ density\ =\ M/Vf$$

Where, M = weight of sample powder taken, Vf = tapped volume.

d) Compressibility index

A simple test has been developed to evaluate the flowability of a powder by comparing the bulk density and tapped density of a powder and the rate at which it packed down. A useful empirical guide is given by Carr's compressibility index. The compressibility index was computed using the formula after the bulk density and tapped density were determined:

$$\text{Carr's index (\%)} = \frac{Tapped\ density - bulk\ density}{Tapped\ density} \text{ X } 100$$

Table 2. Flow property as depicted by Carr's index.

Carr's index (as %)	Flow Type
5 -15	Excellent
12 -16	Good
18 - 21	Fair to passable
23 - 35	poor
33 - 38	Very poor
➢ 40	Extremely poor

Formulation of matrix tablets

Using a standardised procedure previously published, wet granulation technology was used to make Ibuprofen matrix tablets, with 10% starch paste serving as the binder (30). The lubricant was a combination of magnesium stearate at a 2:1 ratio, and the diluent was lactose. Two naturally occurring biocompatible polymers—natural gum from Abelmoschus officinalis and Abelmoschus esculentus combined—were used as carriers in this investigation. Sample codes for the five matrix tablet formulations, WGF1, WGF2, WGF3, WGF4, and WGF5 that were created with varying concentrations of AOEG. Table 3 displays the contents of the several formulations utilised in the study, each of which contained 100 mg of ibuprofen in each case. Every component was run through sieve number 100. All of the powders—aside from talc and magnesium stearate—were combined with 10% starch paste. After the wet material was run through filter number 16, the wet granules were dried for two hours at 50°C. Following their passage through filter # 18, the dried granules were lubricated with a talc and magnesium stearate combination (2:1). The lubricated granules were compressed using 8mm round, slightly concave punches on a rotating tablet press to a maximum force of compression (4000–5000 kg). The produced tablets were assessed for drug content, percent friability, hardness, thickness, and weight fluctuation.

Table 3. Ibuprofen-Natural Gum Blend (AOEG) formula

Ingredient	Formulation code				
	WGF_1	**WGF_2**	**WGF_3**	**WGF_4**	**WGF_5**
Ibuprofen (mg)	100	100	100	100	100
AEOG (mg)	100	130	160	190	220
Lactose(mg)	120	90	60	30	-

Evaluation of Tablets

Compatibility Studies

To search for any possible chemical interactions between the drug and the polymer, the approach of matching infrared spectra was used. A 400 mg of potassium bromide were combined with the drug, polymer, and physical combination of the two substances (10 mg of each). A hydraulic press operating at 10 tonnes of pressure was used to compress around 100 mg of this mixture into a clear pellet. Using an FTIR spectrophotometer, IR pellets were scanned from 4000 cm-1 to 400 cm-1. The formulation's infrared spectra were compared to those of the pure drug and polymers in order to identify any peak appearances or disappearances.

Content uniformity

The amount of drug per tablet must be monitored batch to batch and tablet to tablet in order to assess a tablet's potential for efficacy (31).The average weight of ten pills was determined by weighing them. After all of the pills

were broken up, 0.1g of Ibuprofen was weighed out to create a sample solution. In a 100 ml volumetric flask, the drug was dissolved in a tiny amount of ethanol, and the volume was adjusted with 0.1N NaOH. This mixture was maintained in a mechanical stirrer to ensure total solubilization. Ultimately, 1 ml of this solution was removed and diluted with 0.1 ml of NaOH in a 100 ml volumetric flask. By measuring absorbance in a UV double beam spectrophotometer at 221 nm, the drug concentration was determined. This mixture was maintained in a mechanical stirrer to ensure total solubilization. Ultimately, one ml of this solution was removed and diluted with 0.1 ml of NaOH in a 100 ml volumetric flask. By measuring absorbance in a UV double beam spectrophotometer at 221 nm, the drug concentration was determined.

Thickness, Hardness and Friability

The uniformity of tablet size was dependent on the thickness of the tablets. The drug release also differs between tablets if the thickness does. A tablet tester was used in the current investigation to assess the thickness of the prepared tablets. Ten pills were averaged, and the standard deviation was computed (32). The hardness of the tablet determines how resistant it is to breakage or shipment during handling, storage, and transportation prior to use. A Monsanto hardness tester was used to determine each formulation's tablet's level of hardness. To endure the mechanical shocks of handling during production, packing, and delivery, tablets need to be strong enough. The strength of a tablet is measured by its friability. The following method was performed to assess the friability using a Roche friabilator. The friabilator was first filled with ten weighted tablets and spun at 25 revolutions per minute for four minutes, or 100 revolutions, dropping the tablets six inches each time. Using the formula, the % friability was determined.:

$$\% \text{ Friability} = \frac{Initial\ weight\ of\ tablets - Final\ weight\ of\ tablets}{Initial\ weight\ of\ tablets} \text{ X } 100$$

Weight variation

An electronic balance was used to weigh 20 tablets as part of the assessment process since variations in weight between the prepared tablets may result in variations in drug content and in vitro behaviour (least count 0.1mg). Every tablet batch's average weight was determined. Because the tablets were more than 100 milligrams in weight, their individual weights were compared to the average weight. According to IP, if no more than two of the individual weights differ by more than 5% from the average weight, the pills pass the test. After that, the standard deviation and average weight were determined and published. Table 4 displays the percentage deviation permitted under the IP weight fluctuation test. An electronic balance was used to weigh 20 tablets as part of the assessment process since variations in weight between the prepared tablets may result in variations in drug content and in vitro behaviour (least count 0.1mg). Every pill batch's average weight was determined. Because the pills were more than 100 milligrams in weight, their individual weights were compared to the average weight. According to IP, if no more than two of the individual weights differ by more than 5% from the average weight, the pills pass the test. After that, the standard deviation and average weight were determined and published.

Table 4. Percentage Deviation permitted.

Average wt. of tablet	% deviation permitted
Less than 80mg	±10
80 to 250mg	±7.5
Greater than 250mg	±5

Swelling index

Every tablet was weighed independently (W1) and placed in a different petri dish containing 10 millilitres of pH 7.4 phosphate buffer. The matrix tablets were carefully taken out of the petri dishes at regular intervals (0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 10, 12, and 24 hours) and any extra water was wiped away with filter paper. The swelled tablets were reweighed (W2), and the following formula was used to determine each tablet's percent swelling index (33):

$$\% \text{ Swelling Index } = \frac{W2 - W1}{W1} \text{ X } 100$$

***In vitro* release studies**

The optimal dissolution testing should closely resemble the in vivo conditions with respect to pH and kinds of enzymes for the in vitro evaluation of colon-specific drug delivery systems. The traditional basket technique of dissolving delivery systems for colons has typically been tested in various buffers over varying times to approximate the pH of the GI tract and the transit duration that the colon-specific delivery system may experience

in vivo (34). USP dissolving apparatus of the basket type was used for the dissolution investigations, which were conducted at 37±1°C and 100 rpm. In vitro drug delivery experiments were performed in 100 ml of simulated colonic fluid for two hours, 900 ml of 1.2 pH (Hcl buffer) for three hours, and 900 ml of 7.4 pH (phosphate buffer) for five hours. Following the completion of the time intervals, 1 millilitre of the sample was obtained, and the quantities were increased to 10 millilitres using the appropriate dissolving solutions. A double beam UV spectrophotometer was used to detect the absorbances at 221 nm in order to determine the quantity of Ibuprofen that was released from the tablets. Testing the efficacy of colon-specific delivery systems induced by colon-specific bacteria has been done utilising guinea pig, rabbit, and rat excrement as an alternative dissolving medium. Rat faeces were employed for dissolving tests because the microbiota of the human and rodent colons is comparable, mostly consisting of *Bifidobacteria*, *Bacteroides*, and *Lactobacillus*.

Preparation of Simulated Colonic Fluid (SCF)

Because rat caecal contents and human intestinal microbiota are comparable, drug release assays were conducted in PBS pH 6.8 in the presence and absence of rat caecal contents to evaluate the natural gum blend's sensitivity to colonic bacteria. In order to create enzymes that specifically act on natural gum in the caecum, four male albino rats weighing 150–200 g and maintained on a normal diet were intubated using Teflon tubing and given 1 ml of a 2 percent w/v dispersion of natural gum in water directly into the stomach. After the tube was taken out, the seven-day course of therapy was continued. Rats were killed by spinal traction thirty minutes prior to the start of drug release trials. The abdomen was opened, and the caecal bag was removed. It was then immediately placed into a pH 6.8 phosphate buffer that had been previously bubbled with CO_2. To achieve a final caecal dilution of 4 percent w/v, the caecal bags were opened, their contents were taken out, weighed separately, pooled, and then suspended in buffer. Since the caecum is anaerobic by nature, CO_2 was used for all of these procedures.

Drug release studies in the presence and absence of rat caecal contents

The drug release experiments were carried out using a USP Dissolve rate test apparatus (1,100 rpm, 37°C) with slight modifications, both with and without rat faeces or faecal matter. The tests used a 150 ml beaker filled with water kept in the flask, which is submerged in the apparatus's water bath, and 100 ml of pH 6.8 phosphate buffer containing 4% rat faeces. The pills were inserted into the device's baskets and submerged in the rat faeces-containing dissolving solution. Continuous CO_2 supply was used to carry out the experiment in the beakers. The experiment was carried out for five hours, removing 1 ml of the sample at various times and replacing it with 1 ml of new phosphate buffer solution that had bubbled with CO_2. After adding phosphate buffer solution to bring the volume to 10 ml, the mixture was filtered. An Ibuprofen content was measured in the filtrate at 221 nm using a Double Beam UV Spectrophotometer.

Analysis of release data

Using PCP Dissolving Software version 3, the mechanism of drug release from Natural gum-based matrix tablets during dissolution experiments in 0.1N Hcl and Phosphate buffer 7.4 was identified to see if it adheres to Zero-order, first-order, Hixson-Crowell, Korsemeyer, and Peppas release models (35).

Statistical Analysis

The release data of natural blend of gum-based matrix tablets, as well as the experimental data in the presence and absence of rat faeces, have been reported as the mean with standard deviation (SD) of several independent determinations. Using the statistical programme GraphPad Prism tm, the unpaired "t" test was used to determine the significance of the differences. For statistical significance, $p < 0.0001$ was used.

3. Results And Discussion

Compatibility Studies

Ibuprofen's compatibility with a natural gum mix was investigated using the FTIR spectral matching method. Figure 1 provides the relevant spectra. Ibuprofen's compatibility with the polymers was established by comparing the spectra, which showed no discernible change in the spectral pattern of the physical mixes of medication and polymer. The major peaks in the samples' IR spectra, which were nearly identical to those of pure drug, showed that there was no interaction between the medication and polymers.

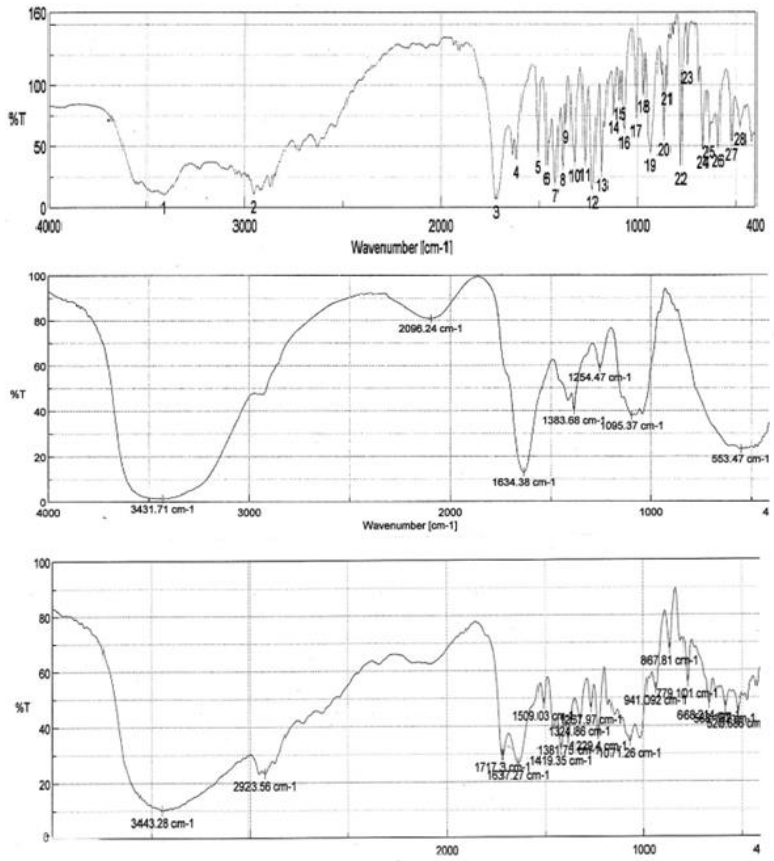

Figure 1. FTIR spectra of Ibuprofen, AOEG and WGF_3

Evaluation of physical Parameters

pH and Viscosity

The pH of the 1% w/v AOEG solution was 6.6. 207.47cp is the viscosity value of AOEG at 1 percent w/v. A polymer's viscosity is a key factor in determining the appropriate release rate. The matrix is more resistant to erosion and dissolving at higher viscosities. Consequently, a polymer gel's viscosity influences how quickly drugs dissolve.

Compressibility Indices and Hausner ratio

Compressibility indices and Hausner ratio results demonstrated the low flow properties of AOEG under examination. Because they had poor flow properties and needed to be incorporated in the matrix tablets in a large amount, ibuprofen tablets were manufactured utilising a wet granulation technique using starch paste as a binder. The results are shown in Table 5.

Table 5. Evaluation of physical parameters

S. No	Ingredient	Bulk density (g/ cm^3)	Tapped density (g/ cm^3)	Compressibility index (%)	Hausner Ratio
1.	AOEG	0.457	0.670	31.79	1.466
3.	Ibuprofen	0.426	0.586	27.30	1.376

Tablet Thickness

Table 6 presents data indicating that the thickness of formulations based on natural gum varies between 4.86±0.02 mm and 5.15± 0.04 mm. Each formulation was confirmed to be consistent due to its uniform thickness and low standard deviation values.

Hardness of Tablet
The developed formulations' hardness ranged from 5..99±1.16 kg/cm2 to 6.61±1.14 kg/cm2. Tables 6 present the results.

Friability
The friability of formulations based on natural gum ranged from 0.12±0.09 to 0.57±0.07 percent, falling below the specified IP standards of less than 1 percent. Table 6 displays the results. Friability values fell as AOEG concentration increased.

Weight Variation
The weights of the formulations ranged from 309.4 ±.04 to 314.86 ± 0.96 for both formulations, according to the data. This suggests that the formulations did not significantly differ in weight. For every formulation, the average weight of 20 pills was determined, and it was discovered to have a variance of less than 5%. Therefore, it complies with the formal IP criteria. Table 6 displays the results.

Content Uniformity
For natural gum-based formulations, the drug concentration ranged from 97.34 ± 0.08 percent to 98.20 ± 1.73 percent for all of the formulations (Table 6). The minimal intra-batch variances demonstrated that the tablet preparation method was appropriate.

Swelling Index
When polymeric matrices tablets come into touch with water, they form a gel coating surrounding the tablet core. The medication release is controlled by this gel layer. Since water permeability forms the gel barrier, swelling kinetics are significant. When compared to other tablets, tablets (WGF3) had much larger swelling indices and a quicker rate of swelling. Table 7 provides the swelling indices. The swelling index's behaviour was investigated in relation to time and was noted that the degree of swelling increased with time.

Table 6. Data for the physical-chemical evaluation of several batches of natural gum-based (AOEG) matrix tablet formulations

S. No	**Parameters**	**Formulations (Codenamed)#**				
		WGF_1	**WGF_2**	**WGF_3**	**WGF_4**	**WGF_5**
1.	Thickness (mm)	5.15± 0.04	4.90±0.03	5.17±0.03	4.86±0.02	4.89±0.04
2.	Weight Variation (mg)	313.5± 2.3	312.2±1.46	312.7±1.19	314.86±0.96	309.4±2.04
3.	Hardness (kg/cm^2)	6.32± 1.26	6.57±1.19	6.61±1.14	6.25±1.22	5.99±1.14
4.	Friability (%)	0.57±0.07	0.54±0.05	0.384±0.11	0.27±0.12	0.12±0.09
5.	Content Uniformity (%)	97.47±1.76	98.20±1.73	97.18±1.76	97.34±2.08	97.78±0.82

 # Result are presented as mean ± SD, n=6

Table 7. Natural gum based (AOEG) matrix tablets' swelling properties

S. No	**Time (h)**	**% Swelling Index**				
		WGF1	**WGF2**	**WGF3**	**WGF4**	**WGF5**
1	0	0	0	0	0	0
2	1	37.28	43.56	78.02	71.83	75.27
3	2	61.38	66.18	92.04	81.17	88.21
4	4	87.20	100.52	138.74	130.40	125.12
5	6	116.51	124.10	158.01	143.14	136.38
6	12	147.21	157.26	182.14	158.44	155.47
7	24	160.56	164.45	199.13	181.24	176.15

In vitro release study

The matrix tablets were subjected to in vitro drug release studies in 0.1N Hcl (2 h), pH 7.4 Sorensen's phosphate buffer (3 h) and 5 h in simulated colonic fluids. From the different formulations, WGF1 have shown 23.56±1.58% of drug release in first 5 hours of study. This might be due to lower gum concentration and higher quantity of diluent in the matrix tablets. The higher proportion of diluent in the swollen hydrophilic matrix tablets might have decreased the gel strength and thereby exhibits higher release. Therefore, WGF1 was not subjected to further studies. The gum becomes hydrated and forms a thick gel layer upon contact with the dissolving fluids, which inhibits the further seepage of fluids towards the core tablets. The dissolving medium's pH does not appear to have an impact on gum hydration. When the concentration of gum increases, the percentage of medication release drops. The gum becomes hydrated and forms a thick gel layer upon contact with the dissolving fluids, which inhibits the further seepage of fluids towards the core tablets. The dissolving medium's pH does not appear to have an impact on gum hydration. When the concentration of gum increases, the percentage of medication release drops.

In vitro release studies in the presence and absence of rat caecal contents

The goal of the colon-targeted drug delivery system is to release the medication in the colon following the enzymatic breakdown by colonic bacteria, in addition to shielding the drug from release in the physiological milieu of the stomach and intestine. Therefore, the in vitro drug release experiments were conducted with and without rat faeces in pH 6.8 phosphate buffer. In the absence of rat caecal matter, the percentage of drug release for WGF3 and WGF5 was found to be 21.18±0.37 percent and 15.65±1.02 percent, respectively. In the presence of rat caecal matter, the drug release percentage for the optimised formulations has been found to be 53.56±1.15 percent and 50.38±1.08 percent, respectively. This indicates susceptibility of natural polysaccharides to colonic bacterial enzymes.

Kinetics of release data

The mechanism of drug release from matrices containing swellable polymers is complex and not completely understood. Some system may be classified as either purely diffusion or swelling or erosion controlled while most systems exhibit a combination of these mechanisms. The release study data of all the batches were fitted to zero order, first order, Hixson-Crowel and Peppas models by using PCP Dissolution software version 3. The release kinetics of all the models is shown in table 12, good fit to Peppas equation indicated combined effect of diffusion and erosion mechanisms for drug release. Peppas used 'n' value in order to characterize different release mechanisms. The interpretation of release mechanisms from polymeric dosage forms is shown in the table 12. According to Peppas model, the mechanism of drug transport for all the formulations is shown in table 13.

Table 8. Interpretation of release mechanisms

Release exponent (n)	Drug transport mechanism
0.5	Fickian diffusion
0.5<n<1.0	Anomalous transport
1.0	Case II transport
Higher than 1.0	Super case II transport

Statistical analysis

Statistical analysis of the release data revealed that there are significant differences ($p<0.001$) between the release data obtained in the presence and absence of rat caecal matter. Statistical analysis indicated insignificance ($p<0.001$) between the release data obtained with Natural gum-based matrix tablets in the absence or presence of colon environment. This revealed that the natural gum-based matrix tablets were having favourable dissolution profiles.

Table 9. In vitro release characteristics of matrix tablets made with AOEG

Serial No.	Time (h)	Formulations (Codenamed)#				
		WGF_1	WGF_2	WGF_3	WGF_4	WGF_5
1	0	0	0	0	0	0
2	1	7.91±1.35	4.72±0.74	4.84±2.19	2.61±0.73	2.21±0.86
3	2	8.19±0.78	8.92±0.87	6.41±1.87	8.54±0.49	2.78±0.39
4	3	18.68±2.61	15.13±0.59	9.76±2.85	15.24±0.32	4.57±0.69
5	4	22.33±2.18	18.82±0.65	11.81±1.87	16.67±0.76	6.48±0.87
6	5	23.56±1.58	19.89±0.59	14.28±2.76	18.81±0.38	9.35±1.28

#Results are presented as mean ± SD, n=3

Table 10. In vitro release profile in the absence of rat caecal matter

S. No	Time (h)	Formulation Code	
		WGF_3	**WGF_5**
1	0	0	0
2	1	7.84±2.38	3.30±0.88
3	2	13.82±1.47	4.41±1.01
4	3	17.18±1.09	7.34±1.11
5	4	20.20±0.43	10.90±0.98
6	5	21.18±0.37	15.65±1.02

Table 11. *In vitro* release profile in presence of rat caecal matter

S. No	Time (h)	Formulation Code	
		WG3	**WG5**
1	0	0	0
2	1	39.28±1.89	35.86±1.02
3	2	41.45±1.95	37.76±1.11
4	3	44.27±1.09	40.17±1.09
5	4	46.76±1.23	45.36±1.21
6	5	53.56±1.15	50.38±1.08

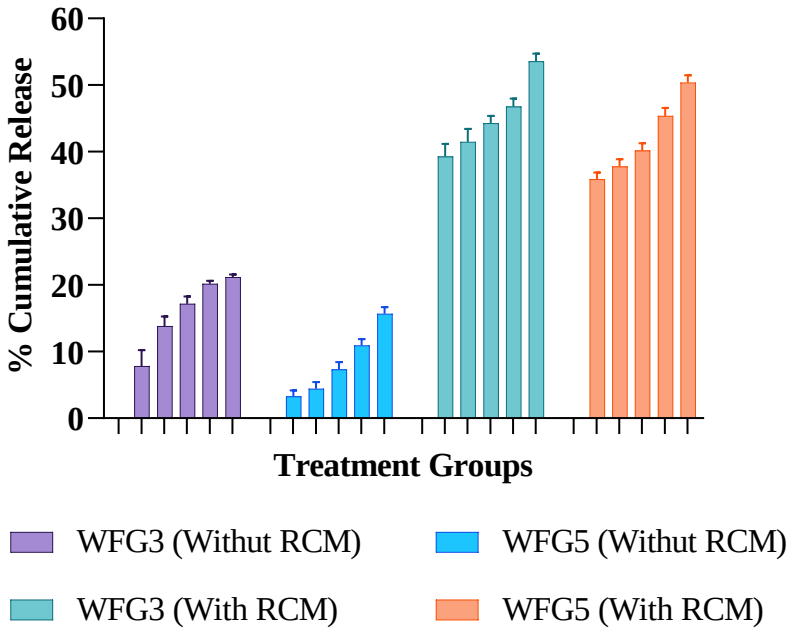

Figure 2. *In vitro* release profile in presence and absence of rat caecal matter

Table 12. Kinetics of Release Data

Formulations	Parameters									
	Zero order		First order		Matrix model		Hix. Crow		Peppas	
	R	k	R	k	R	k	R	k	n	R
WGF1	0.8247	4.1863	0.8317	-0.0456	0.9131	9.2946	0.8299	-0.0125	0.7319	0.9187
WGF2	0.9928	4.14	0.9925	-0.0442	0.9372	9.1039	0.993	-0.0121	1.0577	0.9949
WGF3	0.9708	2.9	0.9651	-0.0289	0.9024	6.3513	0.9673	-0.0074	0.8173	0.9485
WGF4	0.9902	3.7465	0.9919	-0.0391	0.9324	8.2291	0.9916	-0.0106	1.3184	0.9711
WGF5	0.9741	1.6299	0.9705	-0.0142	0.8612	3.4906	0.9717	0.0085	1.2506	0.9693

Table 13. Mechanism of drug transport

Formulation Code	Drug transport mechanism
WGF_1	Anomalous
WGF_2	Super case II transport
WGF_3	Anomalous
WGF_4	Super case II transport
WGF_5	Super case II transport

4. Conclusion

The goal of the current study was to develop Ibuprofen matrix tablets that would target the drug to the colon by utilizing natural polysaccharides as carriers. Matrix tablets were assessed in vitro and ex vivo, as well as for a number of physical characteristics. All assessment test's results were deemed satisfactory. The study focused on assessing the reliability of a drug delivery process aimed at achieving uniform drug loading. Through drug content analysis and weight variation data, the process's reliability was confirmed. Additionally, an FTIR spectra interaction exploration confirmed that there was no any interaction between the drug and the polymers or gum blend used in the fabrication of formulations. Release studies indicated that formulations based on natural gum blend (AOEG) exhibited minimal release in the first 5 hours and higher release in rat caecal medium. The release pattern for all formulations aligned well with the Peppas model. Studies with and without rat caecal matter revealed the natural gum's susceptibility to colonic microflora. Statistical analysis, specifically an Unpaired “t” test, showed highly significant differences in release profiles between formulations in the presence and absence of rat caecal matter. Conclusively, the natural gum blend investigated proved as effective as well as efficient in targeting drug delivery to the colon, suggesting its potential as a colon-specific drug delivery carrier.

5. References

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