Formulation and Assessment of Natural Polysaccharide-Based Matrix Tablets for Colon-Specific Epigallocatechin Gallate Delivery via Wet Granulation Technique

Rajeshwar Vodeti[1], Nirbhay Chalmale[2], Tabrej Mujawar[3*], Gopal Vijaykumar Lohiya[4], Ahamed Vilangalil[5], Swapna. S[6], Sumaila Saifi[7], K. Ramadevi[8],

[1]Department of Pharmaceutics, School of Pharmacy Anurag University Venkatapur, Ghatkesar, Hyderabad-500088 Telangana.

[2]Department of Pharmaceutics, Dayanand College of Pharmacy barshi road Latur, Maharashtra, India Pin- 413512.

[3*]Department of Pharmacology, Gangamai College of Pharmacy, Nagaon Dhule MS India Pin- 424005.

[4]Department of Pharmaceutical Quality Assurance, Dayanand Education Society's, Dayanand College of Pharmacy, Latur-413531, Maharashtra, India.

[5]Department of Pharmaceutical Chemistry, Yenepoya Pharmacy College & Research Centre, Yenepoya (Deemed to be University), Mangalore 570 018, Karnataka, India

[6]Department of Pharmaceutics, School of Pharmacy, Anurag University, Jodimetla, Ghatkesar-500088.

[7]Department of Pharmacognosy and Phytochemistry, MVN University, NH-2, Delhi-Agra Highway, Palwal, Haryana 121105.

[8]Department of Pharmaceutical Chemistry, Anurag University Venkatapur, Ghatkesar, medchal Malkajgiri, India Pin- 500088.

Corresponding Author

Tabrej Mujawar

[3*]tabrejpharma@gmail.com

Abstract

Establishing healthy eating habits among university students is crucial, as the period of university life marks the transition from parental control for many students, allowing them to engage in independent eating habits and establish dietary and lifestyle patterns that will persist into adulthood and old age. This study aims to investigate the healthy lifestyles and eating habits of male university students and to understand the impact of healthy lifestyles on eating habits. It intends to identify the patterns of healthy lifestyles and eating habits among the students and to verify the differences in eating habits based on their healthy lifestyles. Based on this, the research questions were formulated, and an investigation was conducted. The results are as follows. It was observed that there were significant differences in eating habits based on the healthy lifestyles of male university students. Specifically, significant differences were observed in terms of daily meal frequency, overeating frequency, processed food consumption frequency, usual dietary issues, eating habits, preference for seasoning, preferred types of food, and water intake among male university students based on their sleep habits, alcohol consumption, alcohol consumption frequency, portion size, and physical exercise. From the results of this study, it can be inferred that there is a correlation between healthy lifestyles and eating habits of male university students. Furthermore, it was found that sleep habits are associated with several eating behaviors. Therefore, it can be deduced that improving exercise and sleep quality would likely be effective in enhancing eating behaviors.

Keyword: *Colon Targeting, Epigallocatechin Gallate, Natural Polysaccharide, Matrix Tablets, Gut Microflora.*

1. INTRODUCTION

Colon-targeted drug delivery systems are specialized formulations designed to deliver drugs directly to the colon, bypassing the upper gastrointestinal (GI) tract. This targeted approach offers numerous therapeutic and pharmacokinetic advantages, particularly for diseases localized to the colon, such as inflammatory bowel disease (IBD), Crohn's disease, ulcerative colitis, and colorectal cancer. Additionally, colon targeting enables the systemic delivery of drugs that are unstable or degraded in the acidic environment of the stomach or metabolized in the small intestine (Azehaf et al., 2023, Bansal et

al., 2014, Chourasia and Jain, 2004, Gulbake and Jain, 2012, Jain et al., 2007). The colon offers unique physiological and microbiological characteristics favorable for drug delivery. The prolonged residence time in the colon provides a larger window for drug absorption, while the relatively neutral pH and lower enzymatic activity help preserve drug integrity. Furthermore, the presence of a dense microbiota enables the exploitation of enzymatic triggers for the degradation of specialized coatings or polymers, facilitating site-specific drug release (Chadha et al., 2020, Jain and Jain, 2008, Jain and Patil, 2023, Junior et al., 2023, Kotla et al., 2014). Colon-targeted systems are particularly important for reducing systemic side effects and improving therapeutic efficacy in the treatment of localized conditions. These systems also benefit from a lower first-pass metabolism for certain drugs, enhancing their bioavailability. Strategies for colon targeting include the use of pH-sensitive polymers, time-dependent release mechanisms, or polysaccharides that respond to colonic microbial enzymes, offering flexibility in formulation design for various therapeutic needs (Chourasia and Jain, 2004, Junior et al., 2023, Naeem et al., 2020, Omar et al., 2007). Wet granulation is a widely employed technique in pharmaceutical manufacturing due to its numerous advantages in enhancing the physical, mechanical, and chemical properties of drug formulations. This process transforms fine powders into larger granules, improving the flowability and uniformity of the blend, which is crucial for consistent die filling during tablet compression. By binding particles together with a granulating liquid, wet granulation enhances the compressibility of powders, making it suitable for poorly compressible drugs or excipients. Additionally, the process reduces dust generation, ensuring a safer work environment and minimizing the risk of cross-contamination. Wet granulation also ensures better homogeneity, particularly for low-dose active pharmaceutical ingredients (APIs), leading to uniform drug content in the final dosage form. The granules produced are of uniform size, preventing segregation and contributing to consistent drug release profiles. Furthermore, this method can improve the stability of sensitive APIs by incorporating stabilizing excipients and results in stronger tablets with reduced friability, minimizing breakage during handling and transportation. Wet granulation also offers flexibility in formulation by allowing the incorporation of excipients to modify drug release, enhance solubility, or mask unpleasant tastes. These benefits make wet granulation a preferred choice for producing high-quality, robust, and effective pharmaceutical products (Hovgaard and Brondsted, 1996, Van den Mooter and Kinget, 1995, Patel and Amin, 2011, Patel, 2015, Sinha and Kumria, 2001, Van den Mooter, 2006, Friend and Tozer, 1992, Pinto, 2010, Roldo et al., 2007, Sinha et al., 2007, Yang et al., 2002, Omar et al., 2007, Yasmin et al., 2022). The selection of Epigallocatechin gallate (EGCG) as the drug for this study is rooted in its well-documented therapeutic potential and the need for targeted delivery to maximize its efficacy. EGCG, a potent polyphenol derived from green tea, exhibits a wide range of pharmacological activities, including antioxidant, anti-inflammatory, anti-cancer, and anti-microbial effects. Despite its extensive therapeutic benefits, the clinical application of EGCG is limited by its poor bioavailability, rapid degradation in the gastrointestinal tract, and low systemic absorption (Akla et al., 2025, German et al., 2024, Hinton and Johnston, 2024). Colon-specific drug delivery offers a promising strategy to address these limitations by protecting EGCG from premature degradation in the upper gastrointestinal tract and delivering it directly to the colon, where it can exert localized effects or be absorbed into systemic circulation. This approach is particularly beneficial for conditions such as colorectal cancer, inflammatory bowel disease, and microbial infections in the colon (Kumar et al., 2024, Pandey et al., 2024). Furthermore, EGCG's natural origin aligns well with the use of natural polysaccharide-based matrices, enhancing its therapeutic profile while ensuring biocompatibility and safety. The study aims to harness these advantages by formulating EGCG into colon-targeted matrix tablets using a natural polymer blend, thereby optimizing its therapeutic potential and addressing the challenges associated with its delivery (Sun et al., 2024a, Sun et al., 2024b). The rationale for selecting Angelica sinensis polysaccharide (ASP) and okra polysaccharide (Abelmoschus esculentus) as polymers in this study lies in their natural origin, biocompatibility, and multifunctional properties that are highly advantageous for colon-targeted drug delivery. ASP, derived from the medicinal plant Angelica sinensis, is known for its therapeutic benefits, including antioxidant, anti-inflammatory, and immunomodulatory properties, which may complement the therapeutic effects of Epigallocatechin gallate (EGCG) (Sun et al., 2024a, Sun et al., 2024b). ASP forms a strong gel matrix, making it effective in controlling drug release and protecting the active ingredient from enzymatic degradation in the upper gastrointestinal tract. Okra polysaccharide, extracted from Abelmoschus esculentus, is a natural hydrocolloid with excellent swelling, mucoadhesive, and film-forming properties. Its pH sensitivity and biodegradability make it particularly suitable for colon-targeted drug delivery, as it responds to the colonic environment by releasing the drug in a controlled manner. Additionally, OP is a sustainable and cost-effective polymer, further aligning with the study's focus on developing natural and safe drug delivery systems (Omar et al., 2007, Patel and Amin, 2011, Roldo et al., 2007, Yasmin et al., 2022). The combination of both the polysaccharide provides a synergistic approach to enhancing the matrix's mechanical strength, drug release

modulation, and targeted delivery. Together, these polysaccharides enable the formulation of a robust and effective colon-specific drug delivery system for EGCG, addressing its bioavailability challenges and ensuring therapeutic efficacy (Peppercorn and Goldman, 1972, Wilding et al., 1994, Rubinstein et al., 1992). Because of all of these factors, current research is using the combination of 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 EGCG, 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 polysaccharide blend.

2. MATERIAL AND METHODS

Extraction of Natural Polysaccharide Gum

The Angelica sinensis polysaccharide and the fruits of Abelmoschus esculentus (commonly known as bhindi) were procured from the local market in Karnal, India. The extraction of the natural polysaccharide from Abelmoschus esculentus was performed with slight modifications to the method described by Ofoefule et al. (2001) (Ofoefule and Chukwu, 2001). The polysaccharides Angelica sinensis (ASP) and okra (Abelmoschus esculentus) polysaccharide (AEP) were combined in a 1:1 ratio to create ASP-AEP, stored in desiccators to maintain stability. Rich in galacturonic acid, galactose, rhamnose, and glucose, this blend has therapeutic applications, including treating diabetes, jaundice, and peptic ulcers. Phytochemical tests confirmed mucilage, fixed oil, and flavonoid glycosides, with mucilage yield varying seasonally. ASP-AEP also functions as a binder in tablets, offering excellent drug release profiles and stability, enhanced by 1.5% sodium metabisulfite.

Table 1. Properties of Natural Polysaccharide Blend (ASP-AEP)

Natural Polysaccharide Blend (% of wet weight)	
Properties	**Purified**
Moisture content	8.75
Protein	8.91
Ash	5.12
Magnesium	0.73
Calcium	2.33
Potassium	0.87
Phosphorus	0.21

Preformulation Studies

Preformulation broadly refers to the comprehensive set of studies and activities conducted to develop a suitable dosage form for administering an active pharmaceutical ingredient (API) to humans. It involves investigating the physical and chemical properties of the drug, both individually and in combination with excipients, to ensure compatibility and stability (Asian Rockville). Preformulation studies are crucial as they provide the foundational information needed to stabilize the formulation and prevent potential incompatibilities with excipients. These studies emphasize the importance of understanding the chemical stability of both the drug and excipients. Key aspects of preformulation include the development of a calibration curve for the drug, determination of bulk and tapped densities, and evaluation of biodegradation. The procedures for these tests are outlined in detail to ensure accurate characterization and optimization of the formulation. Preformulation thus plays a pivotal role in guiding the successful design and development of pharmaceutical products:

pH and Viscosity

Ostwald's viscometer and a digital pH meter were used to measure the pH and viscosity of a 1% w/v natural gum solution.

Bulk Density and Tapped Density

A graduated 100 ml cylinder was filled with 25g of the powdered material, which had been carefully weighed after passing through sieve number 18. The unstable volume Vo was measured after the powder had been levelled. The formula was used to calculate the bulk density in g/cm3:

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

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

After the testing powder sample was run through sieve #18, a 100 ml graduated cylinder was filled to the sample's weight, which came to 25 g. The cylinder was mechanically tapped 500 times at a theoretical rate of 300 drips per minute using a tapped density tester. Throughout this procedure, the tapped volume, or Vo, was noted. As the tapping went on for 750 more times at a higher volume, Vb was noticed. Since there was less than a 2 percent difference between the two tapping volumes, Vb was considered a tapped volume Vf. The tapped density was calculated in g/cm3 using the formula,

$$Tapped\ density = M / Vf$$

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

Compressibility Index and Hausner Ratio

The flowability of powders was evaluated by determining the bulk density and tapped density, followed by calculating the compressibility index (Carr's Index) and Hausner ratio. Bulk density and tapped density were measured by filling a graduated cylinder with the powder and tapping it to allow for densification. The compressibility index was computed using the formula:

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

Carr's Index provides an empirical guide to flowability, with values categorized as excellent (5-15%), good (12-16%), fair to passable (18-21%), poor (23-35%), very poor (33-38%), and extremely poor (>40%). Additionally, the Hausner ratio, another indicator of flowability, was calculated using the formula:

$$Hausner\ Ratio = \frac{Tapped\ density}{Bulk\ density}$$

A lower Hausner ratio indicates better flow properties, with values ≤1.25 representing good flowability and higher values indicating poor flowability. These parameters were determined for all powder samples, and the results were used to assess their suitability for further formulation processes. The findings, including Carr's Index and Hausner Ratio, provide critical insights into the packing and flow characteristics of the powders.

Preparation of EGCG-Natural Gum Blend (ASP-AEP) Matrix Tablets

*Wet granulation technology, with 10% starch paste acting as the binder, was utilised to create EGCG matrix tablets using a previously published standard procedure (Krishnaiah et al., 2002). The formulations of EGCG matrix tablets were prepared using varying proportions of the natural gum blend (ASP-AEP) and lactose, as outlined in **Table 3**. Each formulation (CTF1 to CTF5) contained a fixed amount of EGCG (100 mg) as the active pharmaceutical ingredient, with the ASP-AEP blend serving as the matrix-forming agent. The amount of ASP-AEP was adjusted across formulations, ranging from 100 mg in CTF1 to 200 mg in CTF5, to study its effect on drug release and tablet properties. Lactose was included as a diluent, with its concentration decreasing progressively from 125 mg in CTF1 to 0 mg in CTF5. All ingredients were accurately weighed and blended thoroughly to achieve homogeneity before being compressed into tablets. This systematic variation in the matrix composition allowed for evaluating the impact of ASP-AEP and lactose on the physicochemical properties and drug release profile of the tablets.*

Table 2. EGCG-Natural Gum Blend (ASP-AEP) Formula

Ingredient	Formulation code				
	CTF_1	CTF_2	CTF_3	CTF_4	CTF_5
EGCG (mg)	100	100	100	100	100
ASP-AEP (mg)	100	120	140	170	200
Lactose (mg)	125	95	65	35	-

Evaluation of Tablets

Compatibility Studies

To investigate potential chemical interactions between the drug and the polymer, Fourier-transform infrared (FTIR) spectroscopy was utilized. The method involved preparing samples by mixing 10 mg each of the drug, polymer, and their physical mixture with 400 mg of potassium bromide (KBr). Approximately 100 mg of this blend was then compressed into a transparent pellet using a hydraulic press at a pressure of 10 tonnes. The prepared IR pellets were analyzed using an FTIR spectrophotometer, scanning in the range of 4000 cm^{-1} to 400 cm^{-1}. The resulting spectra of the formulation were compared with those of the pure drug and polymer to detect any changes, such as the appearance or disappearance of characteristic peaks, which might indicate interactions.

Content Uniformity

To determine whether a tablet has the potential to be effective, the amount of medication in each tablet must be tracked from batch to batch and tablet to tablet (Mishra and Kumari, 2019). The average weight of ten pills was calculated by accurately weighing them together. The pills were then crushed to a fine powder, and 0.1 g of Epigallocatechin gallate (EGCG) was weighed to prepare the sample solution. This amount was transferred to a 100 ml volumetric flask, where it was dissolved in a small quantity of ethanol. The solution was then diluted to the mark with 0.1N NaOH to ensure proper solubilization. The mixture was subjected to mechanical stirring to achieve complete dissolution. Subsequently, 1 ml of this prepared solution was pipetted out and further diluted with 0.1 ml of 0.1N NaOH in another 100 ml volumetric flask. The drug concentration was then determined by measuring the absorbance of the final solution at 273 nm using a UV double-beam spectrophotometer.

Thickness, Hardness and Friability

The thickness of the tablets affected how uniformly they were sized. If the thickness varies between tablets, so does the medication release. The thickness of the manufactured tablets was evaluated in the current study using a tablet tester. The standard deviation was calculated after ten tablets were averaged (Lieberman et al., 2020). The hardness of a tablet is a critical parameter that reflects its ability to resist breakage during handling, storage, and transportation. A Monsanto hardness tester was employed to measure the hardness of tablets from each formulation. Tablets must possess adequate mechanical strength to withstand shocks encountered during manufacturing, packaging, and shipping. The friability of a tablet, which indicates its physical strength, was evaluated using a Roche friabilator. For this assessment, ten pre-weighed tablets were placed in the friabilator, which was operated at 25 revolutions per minute for four minutes, completing a total of 100 revolutions. During each revolution, the tablets were subjected to a six-inch fall, simulating mechanical stress. After the process, the tablets were reweighed, and the percentage friability was calculated using the appropriate formula:

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

Weight Variation

An electronic balance with a least count of 0.1 mg was used to weigh 20 tablets from each batch to assess weight uniformity. Variations in tablet weight can lead to inconsistencies in drug content and in vitro behavior. The average weight of the tablets in each batch was calculated, and the individual tablet weights were compared to this average. Since the tablets weighed more than 100 mg, the test was evaluated based on the Indian Pharmacopoeia (IP) standards. According to the IP guidelines, the batch passes the test if no more than two individual weights deviate by more than 5% from the average weight. Following this, the average weight and standard deviation for each batch were calculated and reported. The allowable percentage deviations under the IP weight fluctuation test are presented in Table 4. This procedure ensured compliance with uniformity requirements, verifying the consistency of tablet production.

Table 3. Percentage Deviation Permitted.

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

Swelling Index

Each tablet was individually weighed (W_1) and placed in separate petri dishes containing 10 milliliters of pH 7.4 phosphate buffer. At predetermined time intervals (0.5, 1, 1.5, 2, 3, 4, 5, 6, 7, 8, 10, 12, and 24 hours), the matrix tablets were carefully removed from the petri dishes, and excess water on their surface was gently blotted using filter paper. The tablets were then reweighed (W_2) to measure their swollen state. The percentage swelling index for each tablet was calculated using the following formula (Rao and Patil, 2007):

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

In Vitro Release Studies

The in vitro release studies were designed to mimic in vivo conditions, particularly the pH environment and enzyme composition, to evaluate colon-specific drug delivery systems effectively. The traditional basket method was employed to test delivery systems under conditions that simulate the pH progression and transit duration in the gastrointestinal (GI) tract. A USP basket-type dissolution

apparatus was used, maintaining a temperature of 37 ± 1°C and a rotation speed of 100 rpm (Prasad et al., 1998). The release studies were conducted sequentially in various simulated fluids:

- ***Simulated gastric fluid:*** *900 ml of HCl buffer at pH 1.2 for 3 hours.*
- ***Simulated intestinal fluid:*** *900 ml of phosphate buffer at pH 7.4 for 5 hours.*
- ***Simulated colonic fluid (SCF):*** *100 ml of fluid for 2 hours.*

At specific time intervals, 1 ml of the sample was withdrawn and diluted to 10 ml using the respective dissolving solution. The absorbance was measured at 273 nm using a double-beam UV spectrophotometer to quantify the release of epigallocatechin gallate (EGCG). To further assess the efficacy of colon-specific delivery systems, alternative dissolution media containing bacteria derived from guinea pig, rabbit, and rat excrement were tested. Rat faeces were selected due to the similarity in microbiota composition between human and rodent colons, particularly in terms of Bifidobacteria, Bacteroides, and Lactobacillus populations.

Preparation of Simulated Colonic Fluid (SCF)

To evaluate the sensitivity of the natural gum blend to colonic bacteria, simulated colonic fluid was prepared using rat caecal contents. Since the intestinal microbiota of rats is similar to humans, male albino rats (150–200 g) were used. These rats were fed a normal diet and orally administered 1 ml of a 2% w/v dispersion of natural gum in water via Teflon tubing daily for seven days. Rats were sacrificed by spinal traction 30 minutes before the start of the drug release studies. Their abdominal cavities were opened, and the caecal bags were excised, weighed, and transferred into pH 6.8 phosphate buffer that had been pre-saturated with CO_2. The caecal contents were pooled and diluted with phosphate buffer to a final concentration of 4% w/v. throughout the preparation, CO_2 was supplied to maintain the anaerobic conditions required for caecal microbiota activity.

Drug Release Studies in the Presence and Absence of Rat Caecal Contents

Drug release studies were performed using a USP dissolution test apparatus with slight modifications, both in the presence and absence of rat caecal contents. The dissolution medium consisted of 100 ml of pH 6.8 phosphate buffer containing 4% w/v rat faeces. The tablets were placed in the apparatus basket and submerged in the rat faeces-containing buffer solution maintained at 37°C. A continuous supply of CO_2 ensured anaerobic conditions during the experiment. The study was conducted for 5 hours, with 1 ml samples withdrawn at regular intervals and replaced with fresh CO_2-bubbled phosphate buffer. The withdrawn samples were filtered, diluted to 10 ml with phosphate buffer, and analyzed for EGCG content at 273 nm using a double-beam UV spectrophotometer. The results provided insights into the behavior of the colon-specific drug delivery system in both the presence and absence of colonic microbiota.

Kinetic Modelling: Analysis of Drug Release Data

Using PCP Dissolving Software version 3, the drug release mechanism from natural gum-based matrix tablets was analyzed during dissolution in 0.1N HCl and phosphate buffer pH 7.4. The release data were fitted to various kinetic models, including Zero-order, First-order, Hixson-Crowell, Higuchi, and Korsmeyer-Peppas. These models provided insights into release mechanisms such as diffusion, erosion, and swelling. The Korsmeyer-Peppas model identified transport mechanisms through the n value. The analysis optimized matrix composition for targeted delivery, confirming diverse release behaviors tailored to therapeutic needs (Vandamme et al., 2002).

Statistical Analysis

The release data for natural gum-based matrix tablets, including experimental results in the presence and absence of rat faeces, were expressed as the mean ± standard deviation (SD) from multiple independent experiments. To analyze the significance of differences between these experimental conditions, an unpaired t-test was performed using the statistical software GraphPad Prism™. A p-value threshold of $p < 0.0001$ was considered statistically significant, indicating a high level of confidence in the observed differences between the groups.

3. RESULTS AND DISCUSSION

Compatibility Studies

The compatibility of Epigallocatechin gallate (EGCG) with the ASP-AEP polymer blend was evaluated using Fourier-transform infrared (FTIR) spectroscopy. The FTIR spectra of pure EGCG, ASP-AEP, and their physical mixture were compared to identify any potential chemical interactions. Key characteristic

peaks of EGCG, such as those corresponding to hydroxyl and aromatic functional groups, were observed in the spectrum of the physical mixture without significant shifts or disappearance. Similarly, the characteristic peaks of ASP-AEP were retained in the physical mixture, indicating the absence of new bond formation or chemical interactions. These findings suggest that the components are compatible, with no evidence of incompatibility in the physical mixture. The preservation of functional group peaks supports the hypothesis that EGCG and ASP-AEP coexist without undergoing chemical modification, making the blend suitable for formulation development. The FTIR data is presented in Figure 1, demonstrating consistent spectral patterns across samples.

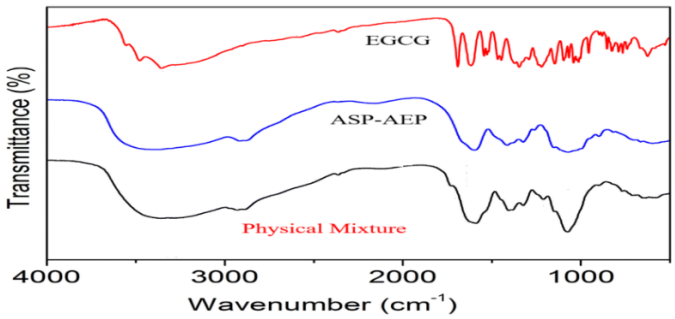

Figure 1. FTIR Spectra of EGCG, ASP-AEP and Physical Mixture

Evaluation of Physical Parameters

pH and Viscosity

The pH of a 1% w/v ASP-AEP solution was measured at 6.8, and its viscosity was determined to be 211.71 cp. The viscosity of a polymer is a critical parameter in controlling drug release rates. Higher viscosity values indicate increased resistance of the polymer matrix to erosion and dissolution, which can slow down the drug release process. In the case of ASP-AEP, its viscosity suggests that the matrix can form a robust gel barrier, effectively regulating drug dissolution and prolonging the release. This property is particularly advantageous in sustained-release formulations, where controlled drug delivery is required. Therefore, the high viscosity of ASP-AEP at 1% w/v highlights its potential utility in achieving desirable release profiles in matrix-based drug delivery systems.

Compressibility Indices and Hausner Ratio

The physical parameters of ASP-AEP and EGCG were evaluated to determine their flow and compressibility characteristics. The bulk and tapped densities of ASP-AEP were 0.514 g/cm³ and 0.701 g/cm³, respectively, indicating a higher compaction tendency upon tapping compared to EGCG, which exhibited values of 0.501 g/cm³ and 0.612 g/cm³. The compressibility index, which reflects the material's flow behavior, was 26.68% for ASP-AEP, signifying poor flow properties. In contrast, EGCG displayed a lower compressibility index of 18.14%, suggesting relatively better, though still fair, flowability. Similarly, the Hausner ratio for ASP-AEP was 1.36, further supporting its poor flow characteristics, while EGCG had a Hausner ratio of 1.22, indicating moderate flow properties. These findings highlight that ASP-AEP has inferior flowability compared to EGCG, which may impact its handling and processing during formulation. Enhancing the flow properties of ASP-AEP may require granulation techniques or the inclusion of suitable excipients.

Table 4. Evaluation of Physical Parameters

S. No	Ingredient	Bulk density (g/ cm^3)	Tapped density (g/ cm^3)	Compressibility index (%)	Hausner Ratio
1.	ASP-AEP	0.514	0.701	26.68	1.36
3.	EGCG	0.501	0.612	18.14	1.22

Thickness, Hardness and Friability of Tablet

The thickness of the matrix tablets across different formulations varied slightly, ranging from 4.11 ± 0.04 mm (CTF2) to 5.28 ± 0.05 mm (CTF3). This consistency in thickness suggests uniformity in compression during manufacturing. Hardness values, indicating the mechanical strength of the tablets, ranged from 6.10 ± 1.03 kg/cm² (CTF5) to 6.72 ± 1.07 kg/cm² (CTF3). These values suggest adequate tablet strength to withstand handling and transportation stresses. The friability, which measures tablet

resistance to breakage, ranged from 0.24 ± 0.001% (CTF5) to 0.68 ± 0.003% (CTF1), well within acceptable limits (<1%). This indicates that all formulations exhibit sufficient mechanical integrity. Notably, CTF5 showed the lowest friability, indicating superior physical robustness compared to the other formulations.

Weight Variation and Content Uniformity

The weight variation of the tablets ranged from 312.5 ± 5.11 mg (CTF5) to 325.97 ± 4.56 mg (CTF4), all within acceptable pharmacopoeial limits, ensuring uniformity in tablet mass. Content uniformity, a critical parameter for dose accuracy, ranged from 96.29 ± 1.95% (CTF3) to 97.31 ± 1.90% (CTF2). These results confirm that the drug distribution across the batches was consistent and met regulatory requirements. Together, the results for weight variation and content uniformity validate the precision of the manufacturing process and ensure reliable drug delivery across all tablet formulations.

Swelling Index

The swelling properties of matrix tablets made with the natural gum blend (ASP-AEP) were assessed over a 24-hour period, as indicated by the percentage swelling index for each formulation. Initially, all formulations showed negligible swelling at 0 hours. At 1 hour, the swelling indices ranged from 39.47% (CTF1) to 80.68% (CTF3), indicating rapid hydration and water uptake, particularly in CTF3, CTF4, and CTF5. By 6 hours, the swelling indices increased significantly, with CTF3 exhibiting the highest index of 160.32%, suggesting superior water absorption capacity due to its formulation composition. At 12 and 24 hours, swelling indices continued to rise, with CTF3 reaching the maximum index of 201.24% at 24 hours. In comparison, CTF1 and CTF2 showed lower swelling indices, indicating relatively slower hydration. The differences in swelling behavior among the formulations may be attributed to variations in the polymer concentration and matrix structure. The higher swelling index observed in CTF3 suggests a stronger gel formation, which could prolong drug release by creating a more robust barrier. Formulations with lower swelling indices, such as CTF1 and CTF2, may erode or dissolve more quickly, leading to faster drug release. The swelling properties of these matrix tablets play a critical role in modulating drug release. Formulations like CTF3, with higher swelling indices, are better suited for sustained-release applications, while those with lower swelling indices may be more appropriate for immediate or shorter-term drug delivery. The results highlight the versatility of ASP-AEP in tailoring drug release profiles through controlled swelling behaviour.

Table 5. Results For the Physicochemical Evaluation of Several Batches Matrix Tablet Formulations Prepared By Natural Polysaccharide Blend (ASP-AEP) (# Result Are Presented As Mean ± SD, N=6)

S. No	Parameters	Formulations (Codenamed)#				
		CTF_1	CTF_2	CTF_3	CTF_4	CTF_5
1.	Thickness (mm)	5.26± 0.06	4.11±0.04	5.28±0.05	4.97±0.03	4.90±0.06
2.	Weight Variation (mg)	324.6± 5.26	323.4±5.11	323.8±4.99	325.97±4.56	312.5±5.11
3.	Hardness (kg/cm^2)	6.43± 1.07	6.68±1.10	6.72±1.07	6.36±1.05	6.10±1.03
4.	Friability (%)	0.68±0.003	0.65±0.001	0.49±0.007	0.38±0.002	0.24±0.001
5.	Content Uniformity (%)	96.58±1.98	97.31±1.90	96.29±1.95	96.45±2.01	96.89±1.21

Table 6. Swelling Properties of the Natural Gum Based (ASP-AEP) Matrix Tablets

S. No	Time (h)	% Swelling Index				
		CTF_1	CTF_2	CTF_3	CTF_4	CTF_5
1	0	0	0	0	0	0
2	1	39.47	45.90	80.68	73.92	77.54
3	2	63.71	68.80	94.17	83.59	90.68
4	4	89.58	102.66	140.55	132.77	127.45
5	6	118.88	126.44	160.32	145.46	138.91

6	12	149.37	159.56	184.66	160.71	157.69
7	24	162.46	166.90	201.24	183.44	178.34

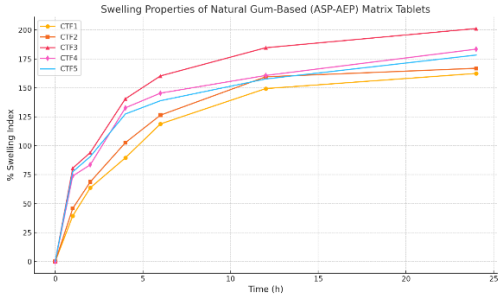

Figure 2. Swelling Properties of the Natural Gum Based (ASP-AEP) Matrix Tablets

In Vitro Release Study

The in vitro drug release profiles of matrix tablets formulated with ASP-AEP were evaluated over a period of 5 hours to study their release characteristics under simulated conditions. At 1 hour, the percentage drug release was minimal across all formulations, with values ranging from 3.10 ± 0.97% (CTF5) to 8.80 ± 0.99% (CTF1). This indicates an initial lag phase or controlled release mechanism. Over time, the drug release increased gradually, with significant differences observed between the formulations. At 2 hours, CTF2 showed the highest release (9.81 ± 0.99%), while CTF5 maintained the lowest release (3.67 ± 0.51%), reflecting its potential for sustained release. By 4 hours, CTF1 exhibited the highest drug release (23.24 ± 1.04%), while CTF5 continued to release the drug at a slower rate (7.37 ± 0.98%). At the end of 5 hours, CTF1 again demonstrated the maximum cumulative release (24.45 ± 1.03%), followed by CTF2 (20.78 ± 0.98%) and CTF3 (15.17 ± 0.94%). The varying drug release rates among formulations can be attributed to differences in polymer concentration and matrix structure, which influence the hydration, swelling, and erosion behavior of the tablets. CTF1, with the highest release rates, suggests a less compact matrix structure, facilitating faster drug diffusion. Conversely, CTF5, with the slowest release, indicates a denser matrix or higher polymer content, enhancing sustained-release capabilities. The release profiles demonstrate the versatility of ASP-AEP in modulating drug release. Formulations like CTF5 are ideal for sustained-release applications due to their slower and controlled release rates, while CTF1 is more suited for immediate or faster release requirements. These findings highlight the role of matrix composition in designing tailored drug delivery systems.

Table 7. In Vitro Release Characteristics of Matrix Tablets Made With ASP-AEP

Serial No.	Time (h)	Formulations (Codenamed)#				
		CTF_1	CTF_2	CTF_3	CTF_4	CTF_5
1	0	0	0	0	0	0
2	1	8.80±0.99	5.61±0.98	5.73±0.23	3.50±0.84	3.10±0.97
3	2	9.08±0.99	9.81±0.99	7.30±1.09	9.43±0.55	3.67±0.51
4	3	19.57±1.01	16.02±0.98	10.65±0.79	16.13±0.46	5.46±0.77
5	4	23.24±1.04	19.71±0.88	12.70±103	17.56±0.88	7.37±0.98
6	5	24.45±1.03	20.78±0.98	15.17±0.94	19.70±0.49	10.24±1.39

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

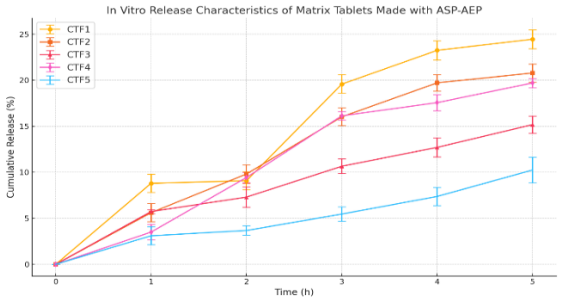

Figure 3. In Vitro Release Profile

In Vitro Release Studies in the Absence of Rat Caecal Contents

The drug release profiles of formulations CTF3 and CTF5 were studied in vitro in the absence of rat caecal matter over 5 hours to assess the impact of physiological conditions on release behavior. At 1 hour, both formulations showed minimal drug release, with CTF3 releasing 8.92 ± 0.89% and CTF5 releasing 4.41 ± 0.79%. The slower release from CTF5 highlights its potential as a sustained-release formulation. By 2 hours, the release increased to 14.98 ± 0.98% for CTF3 and 5.52 ± 0.90% for CTF5, with CTF3 consistently demonstrating a higher release rate. At 5 hours, CTF3 exhibited a cumulative release of 22.91 ± 0.88%, while CTF5 released 16.78 ± 0.99%. These results indicate that CTF3 has a relatively faster release profile compared to CTF5, which maintains a slower and more controlled release throughout the study duration. The difference in release profiles can be attributed to the formulation's matrix structure and polymer composition. CTF3, with higher release rates, suggests a less dense matrix, allowing for quicker drug diffusion. In contrast, the slower release from CTF5 may result from a denser matrix or higher polymer content, contributing to its sustained-release characteristics. In the absence of rat caecal matter, both formulations demonstrate their ability to modulate drug release. CTF3 is more suitable for scenarios requiring faster drug availability, while CTF5 shows promise for prolonged release applications. These findings underline the flexibility of ASP-AEP-based formulations in achieving varied release profiles.

Table 8. In Vitro Release Profile in the Absence of Rat Caecal Matter

S. No	Time (h)	Formulation Code	
		CTF_3	CTF_5
1	0	0	0
2	1	8.92±0.89	4.41±0.79
3	2	14.98±0.98	5.52±0.90
4	3	18.99±0.92	8.55±0.89
5	4	21.78±0.68	11.89±0.97
6	5	22.91±0.88	16.78±0.99

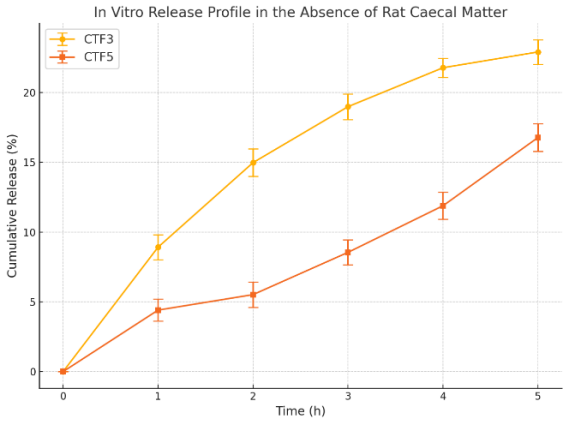

Figure 4. In Vitro Release Profile in Absence of Rat Caecal Matter

In Vitro Release Studies in the Presence of Rat Caecal Contents

The in vitro release profiles of formulations CT3 and CT5 were evaluated in the presence of rat caecal matter to simulate colonic conditions and assess the impact of colonic microbiota on drug release behavior. At 1 hour, both formulations demonstrated a substantial drug release, with CT3 releasing 40.39 ± 1.22% and CT5 releasing 36.97 ± 1.01%. This rapid release can be attributed to the enzymatic degradation of the polymer matrix by the microbiota. By 2 hours, the drug release increased marginally to 42.56 ± 1.31% for CT3 and 38.87 ± 1.06% for CT5, maintaining a consistent difference in release rates between the two formulations. At 5 hours, CT3 exhibited a cumulative drug release of 54.67 ± 1.12%, while CT5 showed a slightly lower release of 51.49 ± 1.11%. The gradual increase in release over time suggests a sustained enzymatic activity contributing to matrix erosion and drug liberation. The presence of rat caecal matter significantly accelerated the drug release for both formulations compared to release in its absence. This highlights the role of colonic microbiota in breaking down the polymer matrix, facilitating drug release. CT3 consistently released more drug than CT5, likely due to differences in matrix composition, with CT5 exhibiting a more controlled release behavior. The results confirm that the ASP-AEP-based formulations are sensitive to colonic conditions, making them suitable

for colon-targeted drug delivery. CT3 demonstrated a faster release profile, while CT5 provided a slightly slower and more sustained release, aligning with its potential as a controlled-release formulation under colonic conditions. These findings emphasize the suitability of these formulations for site-specific drug delivery in the colon.

Table 9. In Vitro Release Profile in Presence of Rat Caecal Matter

S. No	Time (h)	Formulation Code	
		CT3	CT5
1	0	0	0
2	1	40.39±1.22	36.97±1.01
3	2	42.56±1.31	38.87±1.06
4	3	45.38±1.10	41.28±1.03
5	4	47.87±1.13	46.47±1.00
6	5	54.67±1.12	51.49±1.11

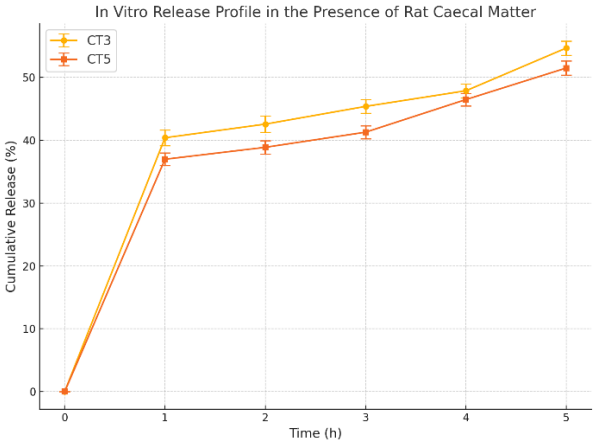

Figure 5. In Vitro Release Profile in Presence of Rat Caecal Matter

Kinetics of Release Data

The release kinetics of the ASP-AEP-based matrix tablet formulations were evaluated using various models, including Zero Order, First Order, Higuchi, and Korsmeyer-Peppas. Each model provides insights into the drug release mechanism and the influence of the polymer matrix. The Zero Order model, which assumes a constant release rate over time, showed moderate to high correlation coefficients (R^2), with values ranging from 0.9369 (CTF1) to 0.9716 (CTF5). Among the formulations, CTF5 exhibited the lowest k value (1.9545), indicating the slowest release, consistent with its sustained-release characteristics. The First Order model, suitable for drug release proportional to the remaining drug concentration, demonstrated the best fit for most formulations, with R^2 values exceeding 0.9456. The k values ranged from 0.0204 (CTF5) to 0.0621 (CTF1), confirming that CTF5 releases the drug more gradually. The Higuchi model, which describes drug release through diffusion, also showed high R^2 values, particularly for CTF3 (0.9760). The k values ranged from 3.6923 (CTF5) to 10.4459 (CTF1), indicating that formulations with lower polymer content (e.g., CTF1) allow faster diffusion. The Korsmeyer-Peppas model provides insight into the drug release mechanism. The n values ranged from 0.6738 (CTF3) to 0.8435 (CTF4), suggesting anomalous transport (combination of diffusion and erosion). CTF5, with an n value of 0.9603, approached Case II transport, indicative of swelling-controlled release. The R^2 values for the Peppas model were consistently high, reaching up to 0.9925 for CTF3, indicating excellent model fit. The release kinetics indicate that CTF5 is the most suitable formulation for sustained release, as it demonstrates the slowest release rate and swelling-controlled behavior. CTF1 and CTF3, with higher k values and lower n values, are more suited for immediate or faster drug release. The data highlights the versatility of ASP-AEP in achieving tailored drug release profiles based on matrix composition and polymer concentration.

Table 10. Kinetics of Release Data

Formulation	Zero Order (k, R^2)	First Order (k, R^2)	Higuchi (k, R^2)	Peppas (k, n, R^2)
CTF1	5.4705, 0.9369	0.0621, 0.9456	10.4459, 0.9163	7.4710, 0.7696, 0.9493
CTF2	4.6551, 0.9694	0.0518, 0.9787	8.8744, 0.9453	6.1973, 0.7887, 0.9829
CTF3	3.2533, 0.9670	0.0350, 0.9729	6.2548, 0.9760	5.0462, 0.6738, 0.9925
CTF4	4.3544, 0.9555	0.0481, 0.9645	8.2630, 0.9167	5.3852, 0.8435, 0.9651
CTF5	1.9545, 0.9716	0.0204, 0.9697	3.6923, 0.8958	2.0631, 0.9603, 0.9709

Mechanism of Drug Transport

The mechanism of drug transport for ASP-AEP-based matrix tablet formulations was evaluated using the Korsmeyer-Peppas model, providing insights into the release mechanism through the n value. Formulations CTF1, CTF2, CTF3, and CTF4 exhibited n values between 0.45 and 0.89, indicating anomalous transport. This mechanism involves a combination of drug diffusion through the hydrated polymer matrix and erosion of the matrix, suggesting that drug release is influenced by both the swelling behavior of the polymer and its gradual degradation over time. In contrast, CTF5 demonstrated an n value nearing 0.89, which corresponds to nearly Case II transport. This predominantly swelling-controlled release mechanism is characterized by drug liberation regulated by the relaxation of polymer chains as the matrix hydrates. These findings indicate that formulations CTF1 through CTF4 are suitable for sustained and controlled release due to their mixed transport mechanism, while CTF5's nearly Case II transport mechanism aligns with its potential for prolonged drug delivery. This study underscores the versatility of ASP-AEP in modulating drug transport mechanisms based on formulation composition.

Table 11. Mechanism of Drug Transport

Formulation Code	Drug transport mechanism
CTF_1	Anomalous transport
CTF_2	Anomalous transport
CTF_3	Anomalous transport
CTF_4	Anomalous transport
CTF_5	Nearly Case II transport

4. CONCLUSION

This study successfully formulated and evaluated colon-targeted matrix tablets containing Epigallocatechin gallate (EGCG) using a natural polysaccharide blend (ASP-AEP) derived from Angelica sinensis and Abelmoschus esculentus. The wet granulation approach, combined with systematic variations in matrix composition, allowed for the optimization of drug release profiles. FTIR analysis confirmed the compatibility of EGCG with the excipients, while preformulation studies demonstrated favorable flow and compressibility properties of the blends. Swelling studies and drug release kinetics indicated that formulations exhibited either anomalous or nearly Case II transport mechanisms, driven by a combination of swelling, diffusion, and matrix erosion. The presence of rat caecal matter significantly enhanced drug release, confirming the suitability of ASP-AEP for colon-specific delivery. CTF5, with its slower and controlled release profile, emerged as the most promising formulation for prolonged drug delivery. This work underscores the utility of ASP-AEP as a

biocompatible, sustainable polymer matrix capable of overcoming the bioavailability challenges of EGCG. Furthermore, the study highlights the potential of this system in targeting colon-specific diseases, such as colorectal cancer and inflammatory bowel diseases, providing a robust platform for further exploration in natural polymer-based drug delivery technologies.

5. REFERENCES

[1] AKLA, N., VEILLEUX, C. & ANNABI, B. 2025. The Chemopreventive Impact of Diet-Derived Phytochemicals on the Adipose Tissue and Breast Tumor Microenvironment Secretome. Nutr Cancer, 77, 9-25.
[2] ASIAN ROCKVILLE, M. D. United States Pharmacopoeia 24/NF19. 2000.
[3] AZEHAF, H., BENZINE, Y., TAGZIRT, M., SKIBA, M. & KARROUT, Y. 2023. Microbiota-sensitive drug delivery systems based on natural polysaccharides for colon targeting. Drug Discov Today, 28, 103606.
[4] BANSAL, V., MALVIYA, R., MALAVIYA, T. & SHARMA, P. K. 2014. Novel prospective in colon specific drug delivery system. Polim Med, 44, 109-18.
[5] CHADHA, S., KUMAR, A., SRIVASTAVA, S. A., BEHL, T. & RANJAN, R. 2020. Inulin as a Delivery Vehicle for Targeting Colon-Specific Cancer. Curr Drug Deliv, 17, 651-674.
[6] CHOURASIA, M. K. & JAIN, S. K. 2004. Polysaccharides for colon targeted drug delivery. Drug Deliv, 11, 129-48.
[7] FRIEND, D. R. & TOZER, T. N. 1992. Drug glycosides in oral colon-specific drug delivery. Journal of controlled release, 19, 109-120.
[8] GERMAN, I. J. S., BARBALHO, S. M., ANDREO, J. C., ZUTIN, T. L. M., LAURINDO, L. F., RODRIGUES, V. D., ARAÚJO, A. C., GUIGUER, E. L., DIREITO, R., POMINI, K. T. & SHINOHARA, A. L. 2024. Exploring the Impact of Catechins on Bone Metabolism: A Comprehensive Review of Current Research and Future Directions. Metabolites, 14.
[9] GULBAKE, A. & JAIN, S. K. 2012. Chitosan: a potential polymer for colon-specific drug delivery system. Expert Opin Drug Deliv, 9, 713-29.
[10] HINTON, T. & JOHNSTON, G. A. R. 2024. GABA, epigallocatechin gallate, tea, and the gut-brain axis. Neurochem Int, 180, 105860.
[11] HOVGAARD, L. & BRONDSTED, H. 1996. Current applications of polysaccharides in colon targeting. Critical Reviews™ in Therapeutic Drug Carrier Systems, 13.
[12] JAIN, A., GUPTA, Y. & JAIN, S. K. 2007. Perspectives of biodegradable natural polysaccharides for site-specific drug delivery to the colon. J Pharm Pharm Sci, 10, 86-128.
[13] JAIN, S. K. & JAIN, A. 2008. Target-specific drug release to the colon. Expert Opin Drug Deliv, 5, 483-98.
[14] JAIN, S. N. & PATIL, S. B. 2023. Perspectives of colon-specific drug delivery in the management of morning symptoms of rheumatoid arthritis. Inflammopharmacology, 31, 253-264.
[15] JUNIOR, A. G. T., DE ARAÚJO, J. T. C., DUARTE, J. L., SILVESTRE, A. L. P., DI FILIPPO, L. D. & CHORILLI, M. 2023. Polymeric Systems for Colon-specific Mesalazine Delivery in the Intestinal Bowel Diseases Management. Curr Med Chem, 30, 1351-1367.
[16] KOTLA, N. G., GULATI, M., SINGH, S. K. & SHIVAPOOJA, A. 2014. Facts, fallacies and future of dissolution testing of polysaccharide based colon-specific drug delivery. J Control Release, 178, 55-62.
[17] KRISHNAIAH, Y. S. R., REDDY, P. R. B., SATYANARAYANA, V. & KARTHIKEYAN, R. S. 2002. Studies on the development of oral colon targeted drug delivery systems for metronidazole in the treatment of amoebiasis. International journal of pharmaceutics, 236, 43-55.
[18] KUMAR, G., VIRMANI, T., CHHABRA, V., VIRMANI, R., PATHAK, K., AKHTAR, M. S., HUSSAIN ASIM, M., ARSHAD, S., SIDDIQUE, F. & FONTE, P. 2024. Transforming cancer treatment: The potential of nanonutraceuticals. Int J Pharm, 667, 124919.
[19] LIEBERMAN, H., RIEGER, M. & BANKER, G. S. 2020. Pharmaceutical Dosage Forms: Disperse Systems, CRC Press.
[20] MISHRA, M. K. & KUMARI, P. 2019. A review on pharmaceutical process validation. The Pharma Innovation Journal, 6, 960-958.
[21] NAEEM, M., AWAN, U. A., SUBHAN, F., CAO, J., HLAING, S. P., LEE, J., IM, E., JUNG, Y. & YOO, J. W. 2020. Advances in colon-targeted nano-drug delivery systems: challenges and solutions. Arch Pharm Res, 43, 153-169.
[22] OFOEFULE, S. I. & CHUKWU, A. 2001. Application of Abelmoschus esculentus gum as a mini-matrix for furosemide and diclofenac sodium tablets. Indian journal of pharmaceutical sciences, 63, 532-535.
[23] OMAR, S., ALDOSARI, B., REFAI, H. & GOHARY, O. A. 2007. Colon-specific drug delivery for mebeverine hydrochloride. J Drug Target, 15, 691-700.
[24] PANDEY, P., VERMA, M., LAKHANPAL, S., PANDEY, S., KUMAR, M. R., BHAT, M., SHARMA, S., ALAM, M. W. & KHAN, F. 2024. An Updated Review Summarizing the Anticancer Potential of Poly(Lactic-co-Glycolic Acid) (PLGA) Based Curcumin, Epigallocatechin Gallate, and Resveratrol Nanocarriers. Biopolymers, e23637.
[25] PATEL, M. & AMIN, A. 2011. Recent trends in microbially and/or enzymatically driven colon-specific drug delivery systems. Crit Rev Ther Drug Carrier Syst, 28, 489-552.
[26] PATEL, M. M. 2015. Colon: a gateway for chronotherapeutic drug delivery systems. Expert Opin Drug Deliv, 12, 1389-95.

[27] PEPPERCORN, M. A. & GOLDMAN, P. 1972. The role of intestinal bacteria in the metabolism of salicylazosulfapyridine. Journal of Pharmacology and Experimental Therapeutics, 181**,** 555-562.
[28] PINTO, J. F. 2010. Site-specific drug delivery systems within the gastro-intestinal tract: from the mouth to the colon. Int J Pharm, 395**,** 44-52.
[29] PRASAD, Y. V. R., KRISHNAIAH, Y. S. R. & SATYANARAYANA, S. 1998. In vitro evaluation of guar gum as a carrier for colon-specific drug delivery. Journal of controlled release, 51**,** 281-287.
[30] RAO, K. P. & PATIL, C. C. 2007. Formulation and evaluation of colon targeted oral tablets of naproxen. Indian Journal of Pharmaceutical Education and Research, 41**,** 146-149.
[31] ROLDO, M., BARBU, E., BROWN, J. F., LAIGHT, D. W., SMART, J. D. & TSIBOUKLIS, J. 2007. Azo compounds in colon-specific drug delivery. Expert Opin Drug Deliv, 4**,** 547-60.
[32] RUBINSTEIN, A., NAKAR, D. & SINTOV, A. 1992. Chondroitin sulfate: a potential biodegradable carrier for colon-specific drug delivery. International journal of pharmaceutics, 84**,** 141-150.
[33] SINHA, V., SINGH, A., KUMAR, R. V., SINGH, S., KUMRIA, R. & BHINGE, J. 2007. Oral colon-specific drug delivery of protein and peptide drugs. Crit Rev Ther Drug Carrier Syst, 24**,** 63-92.
[34] SINHA, V. R. & KUMRIA, R. 2001. Polysaccharides in colon-specific drug delivery. Int J Pharm, 224**,** 19-38.
[35] SUN, J., JIANG, Y., FU, J., HE, L., GUO, X., YE, H., YIN, C., LI, H. & JIANG, H. 2024a. Beneficial Effects of Epigallocatechin Gallate in Preventing Skin Photoaging: A Review. Molecules, 29.
[36] SUN, W., YANG, Y., WANG, C., LIU, M., WANG, J., QIAO, S., JIANG, P., SUN, C. & JIANG, S. 2024b. Epigallocatechin-3-gallate at the nanoscale: a new strategy for cancer treatment. Pharm Biol, 62**,** 676-690.
[37] VAN DEN MOOTER, G. 2006. Colon drug delivery. Expert Opin Drug Deliv, 3**,** 111-25.
[38] VAN DEN MOOTER, G. & KINGET, R. 1995. Oral colon-specific drug delivery: a review. Drug delivery, 2**,** 81-93.
[39] VANDAMME, T. F., LENOURRY, A., CHARRUEAU, C. & CHAUMEIL, J. C. 2002. The use of polysaccharides to target drugs to the colon. Carbohydrate polymers, 48**,** 219-231.
[40] WILDING, I. R., DAVIS, S. S. & O'HAGAN, D. T. 1994. Targeting of drugs and vaccines to the gut. Pharmacology & therapeutics, 62**,** 97-124.
[41] YANG, L., CHU, J. S. & FIX, J. A. 2002. Colon-specific drug delivery: new approaches and in vitro/in vivo evaluation. Int J Pharm, 235**,** 1-15.
[42] YASMIN, F., NAJEEB, H., SHAIKH, S., HASANAIN, M., NAEEM, U., MOEED, A., KORITALA, T., HASAN, S. & SURANI, S. 2022. Novel drug delivery systems for inflammatory bowel disease. World J Gastroenterol, 28**,** 1922-1933.