J Nanostruct 16(1): 966-977, Winter 2026

RESEARCH PAPER

Synthesis and Characterization of New Nanopolymer for Colon-Specific Controlled Release

Hadeel Salih Mahdi [1]*, ***Saif M. Alshrefi*** [2]

[1] *Department of Science, College of Basic Education, University of Misan, Misan, Iraq*

[2] *Department of Laser Physics, College of Science for Women, University of Babylon, Iraq*

ARTICLE INFO

Article History:
Received 02 September 2025
Accepted 19 December 2025
Published 01 January 2026

Keywords:
Colon specific drug delivery
Controlled release
Nano platform
Nanopolymers
Smart polymers
Stimuli responsive polymers

ABSTRACT

New polymeric nanoparticles were to be developed for biomedical purposes as the purpose of this study. It was thought that the production of materials with novel properties and functions could be accomplished by meticulous design and synthesis, as well as the research of structure-property connections. nano "drug delivery" systems in the context of colon-specific drug delivery. These systems serve as a crucial link amongst the therapeutic needs as well as "drug delivery". Stimuli-responsive polymers show case a non-linear reaction to minor stimuli, leading to notable alterations in their properties and structure. Stimuli-sensitive polymers demonstrate a notable alteration in their physicochemical characteristics when subjected to slight modifications in their environment, including temperature, pH, and light. The significance of "colonic drug delivery" is grown in the management of ailments like Crohn's disease, ulcerative colitis, and colon cancer. The progress in polymer-based systems, possessing enhanced adaptability, versatility, and unexplored potential, presents fresh prospects for the advancement of biomedicine. By integrating the notion of intelligence into therapeutically and diagnostically significant systems, a fresh epoch of intelligent therapeutics can be initiated, enhancing the realm of healthcare. This mechanism has been recognized as a responsive framework for dispensing medications precisely at the designated location and moment, owing to its remarkable responsiveness to stimuli.

How to cite this article
Salih Mahdi H., Alshrefi S. Synthesis and Characterization of New Nanopolymer for Colon-Specific Controlled Release. J Nanostruct, 2026; 16(1):966-977. DOI: 10.22052/JNS.2026.01.086

INTRODUCTION

By integrating the notion of intelligence into therapeutically and diagnostically significant systems, a fresh epoch of intelligent therapeutics can be initiated, enhancing the realm of healthcare. This mechanism has been recognized as a responsive framework for dispensing medications precisely at the designated location and moment, owing to its remarkable responsiveness to stimuli. [9,10].

* *Corresponding Author Email: hadeel.salih@uomisan.edu.iq*

As one moves out of the stomach (pH 1.5-3) to the terminal ileum (pH 7-8) [11], the pH levels in the gastrointestinal tract gradually rise. To make use of this pH gradient, pH-sensitive delivery systems employ polymeric materials that are insoluble in the acidic environment of the upper gastrointestinal tract but dissolve in the higher, nearly neutral pH of the distal gut. Delivery systems that are activated by microflora are considered more desirable and have shown potential [12]. The

human colon is a dynamic and ecologically diverse system that contains over 400 distinct bacterial species [13], which secrete various enzymes. [14].

The main source of nutrition for bacteria is non-starch polysaccharides, which undergo fermentation in the colon as they are not significantly crashed in the stomach and small intestine [15]. Currently, natural polysaccharides are commonly used in the production of solid dosage forms for drug delivery to the colon [16]. However, relying solely on pH-sensitive [11] or microflora-activated systems for colon-specific delivery is considered unreliable due to the fluctuations in pH or water swelling within the gastrointestinal tract.

Chitosan, a natural polysaccharide of high molecular weight, possesses numerous desirable properties such as complete biodegradability, non-toxicity, affordability, and favorable gelation characteristics [17]. It is significant to note that chitosan is not susceptible to human digestive enzymes in the upper gastrointestinal tract [18,19], but can be hydrolyzed by microbial enzymes in the colon through glycosidic reactions [20,21,22]. Different forms of chitosan, such as capsules [23], matrices [24], hydrogels [25], and microspheres [26], are utilized in colon-targeted drug delivery systems, highlighting its potential as a coating material. However, it is crucial to consider that chitosan dissolves in acidic solutions, which may limit its applications in colon-targeted drug delivery.

The biophysical and biochemical properties of the drugs selected for treatment primarily determine the choice of an optimal nano-drug delivery system [27]. However, it is significant to consider the potential toxicity associated with nanoparticles when applying nanomedicine. In latest years, there has been a growing trend of combining nanoparticles with natural products to address these toxicity concerns. The use of a green chemistry approach in the development of drug-loaded nanoparticles is strongly recommended as it reduces the presence of hazardous components in the biosynthetic process. As a result, the use of green nanoparticles for drug delivery has the potential to reduce the negative effects of medications. [28].

The current investigation aims to create a delivery system using nanocopolymer (Chitosan-co-HEMA) that is cross-linked with 1,6-hexandimethacrylate. The emphasis of this work is to analyze and determine the drug delivery prospective of the developed systems in various pH mediums.

MATERIALS AND METHODS

Materials

Various materials are employed in the manufacturing of cements, such as 1,6-hexanedioldiacrylate (HDODA), 5-Amino salicylic acid(5-ASA) sourced from ALDRICH, Chitosan obtained from HIMEDIA, 2-hydroxyethyl methacrylate (HEMA) provided by ALDRICH, 1-hydroxycyclohexyl phenyl ketone (photoinitiator) also acquired from ALDRICH, nitrogen cleansed, refined water, and phosphate buffer saline (PBS) obtained from HIMEDIA.

Instruments

At Shahid Beheshti-Tehran University in Iran , the NMR spectra were acquired using a Bruker Ultra Shield 300 MHZ Switzerland instrument with Dichloromethane as the solvent. For the thermogravimetric analysis (TGA), the sample underwent heating from 40 to 500 oC at a rate of 10 oC/min in an argon atmosphere. In Tehran, Iran, the USpicydownlight, (Bow, USND-1801 18W Driven, American, homogenizer(korea), and the American PerkinSTA6000 Differential warm examination (DSC) estimation device were utilized. The industry warmed ultrasonic cleaner warm, TESCAN Mira3 (Geoslovkia) filtering electron magnifying instrument (SEM) was used in Tehran, Iran. The UV Biochrom 118034 Ultraviolet-Visible Spectrophotometer was used in Britain, and the PH-Meter from OHAUS Organization was used in the USA.

Synthesis for all nanopolymers nanocopolymers (Cs-co-HEMA) hydrogel

The hydrogels monomers (Chitosan (Cs) as well as 2-hydroxyethyl methacrylate (HEMA) are polymerized thru free-radical polymerization within the presence of crosslinking agent HDODA and photo initiator PI184, just (Cs) was dissolved in acetic acid but other monomer didn't need that, at room temperature and at different times as shown in Table 1. The oxygen was removed from the reaction mixtures by degassing with nitrogen for a duration of 30 minutes. Following this, the organic phase was introduced to an aqueous stabilizer mixture while being stirred thru a homogenizer at a speed of 3000 rpm. The

emulsion was then stirred at room temperature for 15 mints before being homogenized at 12700 rpm for another 15 minutes using a TOPS-SR30 homogenizer. The combination was then exposed to UV light below 365 nm for a period of 5-30 minutes. Subsequently, the lens was soaked in a liquid cleanser containing 20% ethanol in order to eliminate any photoinitiator and unreacted monomers. To rinse the ethanol from the lens, the ethanol was removed using a ratio of 0.625 wt % HDODA and 0.05 wt % PI184 in sequence for the total formulas.

Ultraviolet (UV) Measurements

The stacked and discharged sums of the show sedate Phenacetin were calculated at max 297.0 nm employing a UV/Vis Spectrometer and the Biochrom LDT Show.

pH Measurements

Citric acid/tri sodium citrate as well as sodium dihydrogen phosphate/disodium hydrogen phosphate were utilized, separately for plan buffer arrangements with concentrations of 2, 4, 7, and 8 [29].

Preparation of Calibration Curve

In order to minimize wavelength-setting errors, the wavelength is selected to coincide with the region of the spectrum's overseas greatest where as it were one component within the test altogether assimilates. Beneath the presumption that the Lambert-Beer law compliance direct range is built up which the medicate concentration is balanced inside the perfect run for the instrument sort in address, two measurement strategies are utilized.

Each gather of tests is gone before and allowed by the standard in the event that an satisfactory sedate standard is accessible and the calibration chart passes through zero. On the off chance that typically the case, the average is reproduced as well as the tests are lead in bracketing arrange and at the same concentration. beneath the same

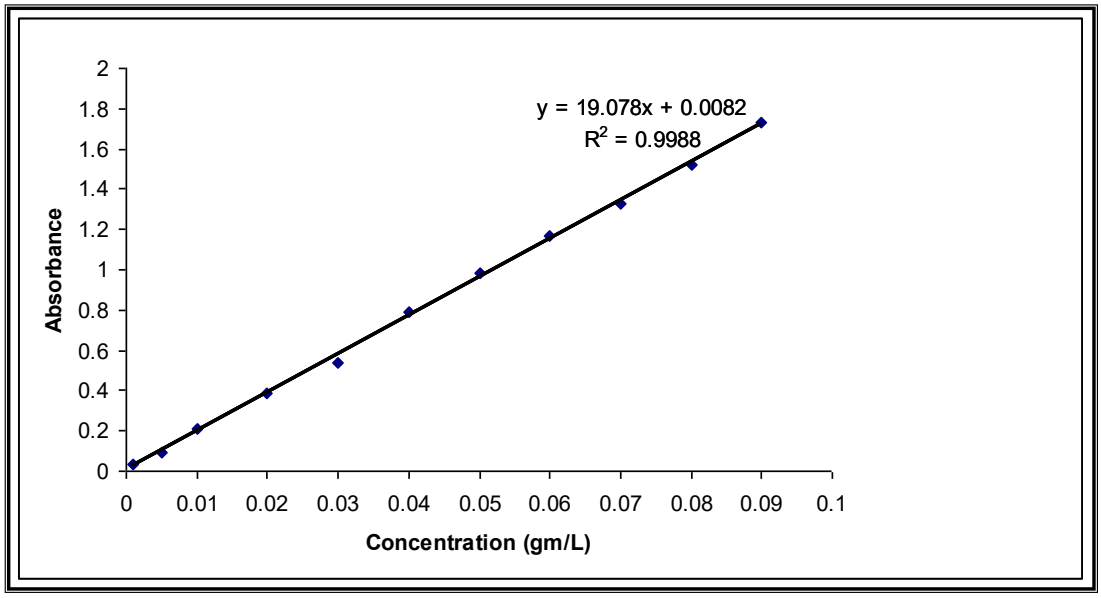

Fig. 1. The working calibration curve for the data of (5-Amino salicylic) (the absorbance in 1 cm cell) at λmax 297.0 nm.

Table 1. Formulations of Nano polymers hydrogel by monomers.

Sample	"Monomer1 / Wight (mg) "	"Monomer2/ Wight (mg) "	Copolymerization	Time irradiation (min)
1	Chitosan 20 mg	HEMA / 400 mg	(Cs-co-HEMA)	4

temperature and dissolvable conditions, utilizing the same coordinated cells.

A linear relationship between the concentration of 5-Amino salicylic acid and the absorbance was determined by conducting regression analysis on a standard curve. The standard curve was constructed using solutions prepared within the concentration range of 0.001 to 0.09 $g.L^{-1}$, with distilled water as the solvent. The absorbance of these solutions was measured at a wavelength of 297.0 nm, with distilled water used as the blank.

Similarly, the calibration curve was established by employing distilled water having a pH value of 7, while the absorbance was determined at a wavelength of 297.0 nm.

Swelling Measurement

In double-distilled water, the dynamic swelling properties of all hydrogels were explored. The balance swelling was calculated employing a gravimeter. The hydrogels (0.1gm) were drenched in 100 ml of dissimilar pH arrangements (pH=2, 4, 7, as well as pH=8) for 10 days at different temperatures (37 and 39 ^{0}C) in arrange to reach the swelling balance. The swollen gels were occasionally evacuated out of the water, softly wiped with channel paper to evacuate any overabundance surface water, and weighed. As a result, the equation grams of water per grams of polymer (g/g) was utilized to calculate the swelling sum [30].

The variables Ws and Wd represent the weights of the dry sample and the swollen gel, respectively, at a specific time. The swelling degree (g/g) can be calculated using the formula A Swelling Degree = (Ws - Wd) / 100Wd.

Loading Drugs to Nanopolymeric Hydrogels

The drug loading process involved the utilization of synthesized hydrogels through the swelling equilibrium technique. These hydrogels were then subjected to swelling in a predetermined concentration of sedate solution for a duration of 24 hours, at pH levels of 2, 4, 7, and 8. Afterward, the hydrogels were dried at room temperature. The concentration of the unabsorbed solution was

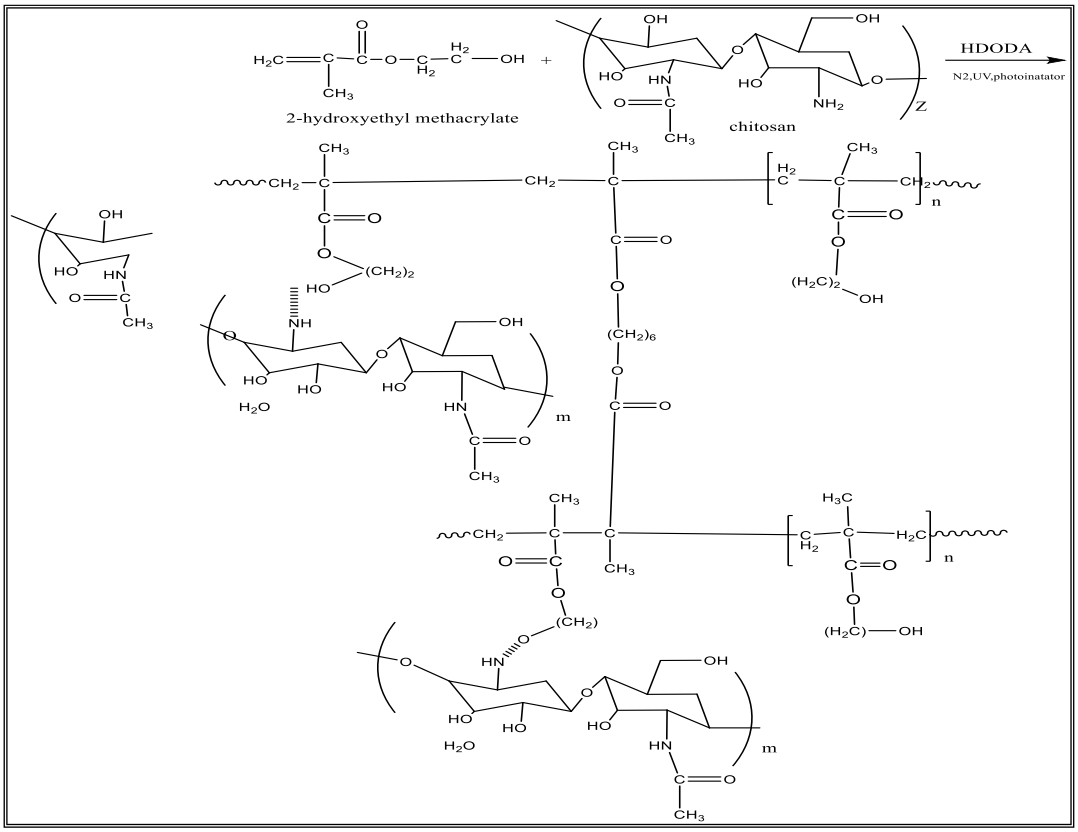

Fig. 2. Synthesis of polymer (Cs-co-HEMA).

measured to ascertain the rate of drug adsorption within the polymer framework [31].

In Vitro Drug (5-Amino salicylic acid(5-ASA)) Release Studies

Calculating the sum of 5-Amino salicylic acid(5-ASA) discharged out of the hydrogel organize requires a stacked hydrogel test. The sum of **5**-Amino salicylic acid(5-ASA) discharged is measured employing a UV spectrophotometer at a greatest 250 nm each day wherever the test was dried as well as weighed (100.300.500 mg) sometime recently being doused in 100ml of different arrangements of pH (2,4,7, and PH = 8) by including 100mg of a Benzocaine medicate for ten days [32].

RESULTS AND DISCUSSION

Characterization and Synthesis of Nanocopolymers
Synthesis and Characterization of (Cs-co-HEMA)

(Cs-co-HEMA) The synthesis of this material involved copolymerizing (Cs) and (HEMA) with the aid of HDODA as a crosslinking agent as well as 1-hydroxycyclohexyl phenyl ketone as a photoinitiator. The mixture was stirred in a dark environment at room temperature whereas nitrogen is purged over it for 30 minutes to remove any dissolved oxygen. After pouring the mixture into polypropylene molds, it was cured under a 365 nm UV light for 4 minutes. Fig. 2 illustrates this reaction.

FTIR Spectrum of (Cs-co-HEMA)

Spectrum of the FTIR of (Cs-co-HEMA) is depicted in Fig. 3. It exhibits various absorption bands at specific wavenumbers. These include an absorption band at 3348 cm^{-1}, which corresponds to the (-OH str. group in the polymer). Additionally, there are absorption bands at 3292 cm^{-1} (N-H str. of Cs), 2943 cm^{-1} and 2887 cm^{-1} (C-H str. of the polymer backbone), 1728 cm^{-1} (C=O str., ester group), 1620 cm^{-1} (N-H-C=O), 1170 cm^{-1} and 1083 cm^{-1} (C-O-C str.), 1033 cm^{-1} (-C-O of C-OH str.), and 1170 cm^{-1} (C-N str.) [33-35].

^{1}HNMR spectrum of (Cs-co-HEMA)

spectrum of the 1HNMR of (HEMA-co-Cs) is depicted in Fig. 4. It shows peaks at different chemical shifts: a singlet at 0.9δ ppm for 3H of CH_3 HEMA and CH_3 HDODA, a multiplet ranging from 1.23 to 1.8 δ ppm for 2H of CH_2 HEMA and CH_2 HDODA, a singlet at 2.1 δ ppm for 3H of $COCH_3$, a singlet at 3.4 δ ppm for 1H of OH HEMA, a singlet at 3.58 δ ppm for 2H of CH_2OH HEMA, a multiplet ranging from 3.9 to 4.0 δ ppm for 2H of $COOCH_2$ HEMA, a multiplet ranging from 4.2 to 4.8 δ ppm for 2H of $COOCH_2$ HDODA, and a singlet at 5.58 δ ppm for 1H of NH Cs. These chemical shifts were

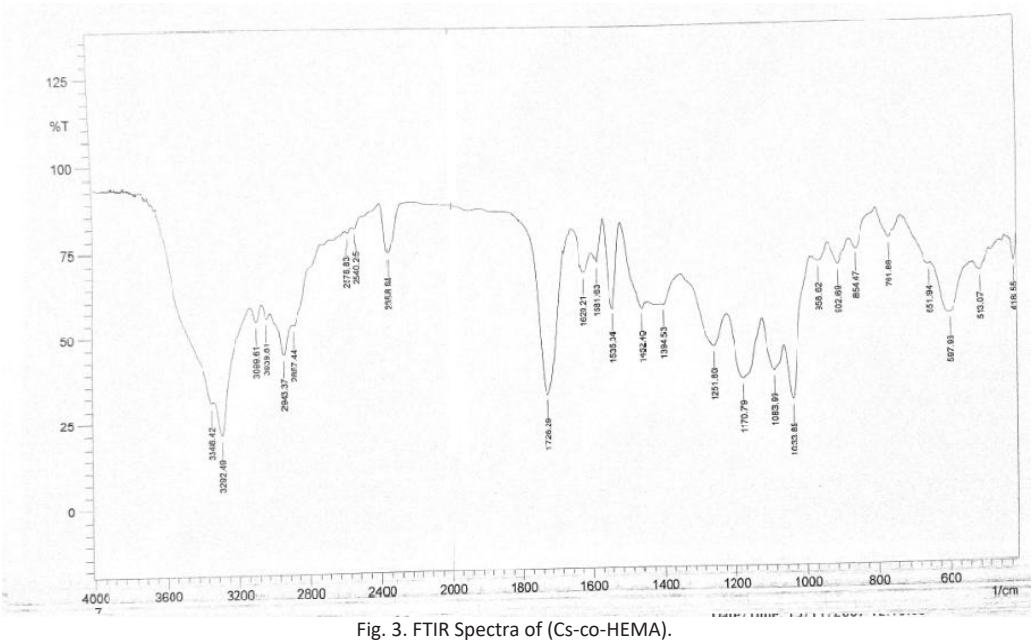

Fig. 3. FTIR Spectra of (Cs-co-HEMA).

reported in the range of 33-35.

Scanning Electron Microscopy (SEM)

To determine the surface topography of the nanopolymer utilized in the study, an SEM analysis was conducted. The scanning electron micrograph (SEM) is utilized to ascertain the shape and surface morphology of the nanopolymer produced. The copolymerization of Cs and HEMA led to the formation of a porous framework, where the pores are considered to be the regions where water can permeate and interact within the hydrophilic groups of the graft copolymers in response to external stimuli. Fig. 5 illustrates the

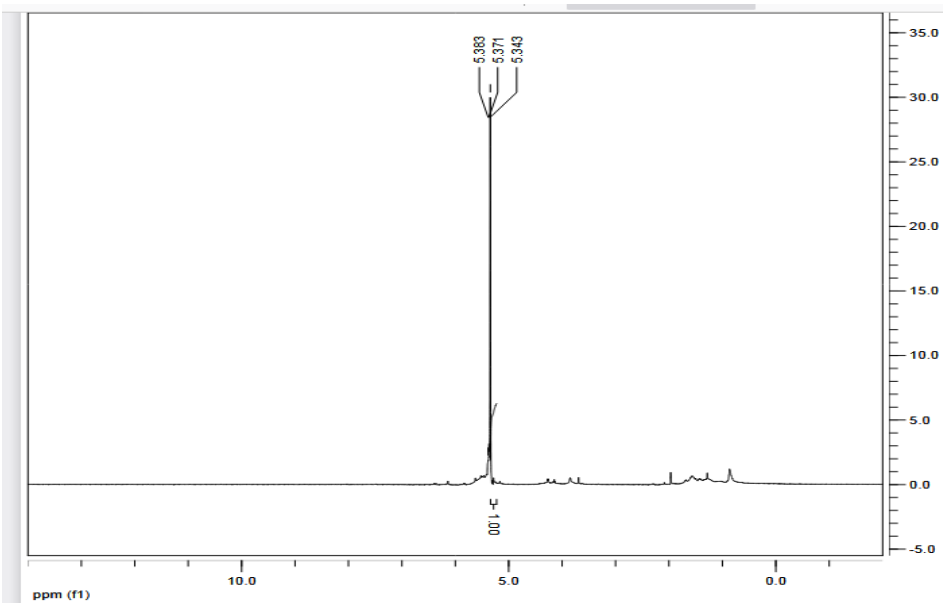

Fig. 4. ^{1}HNMR Spectra of nanopolymer (Cs-co-HEMA).

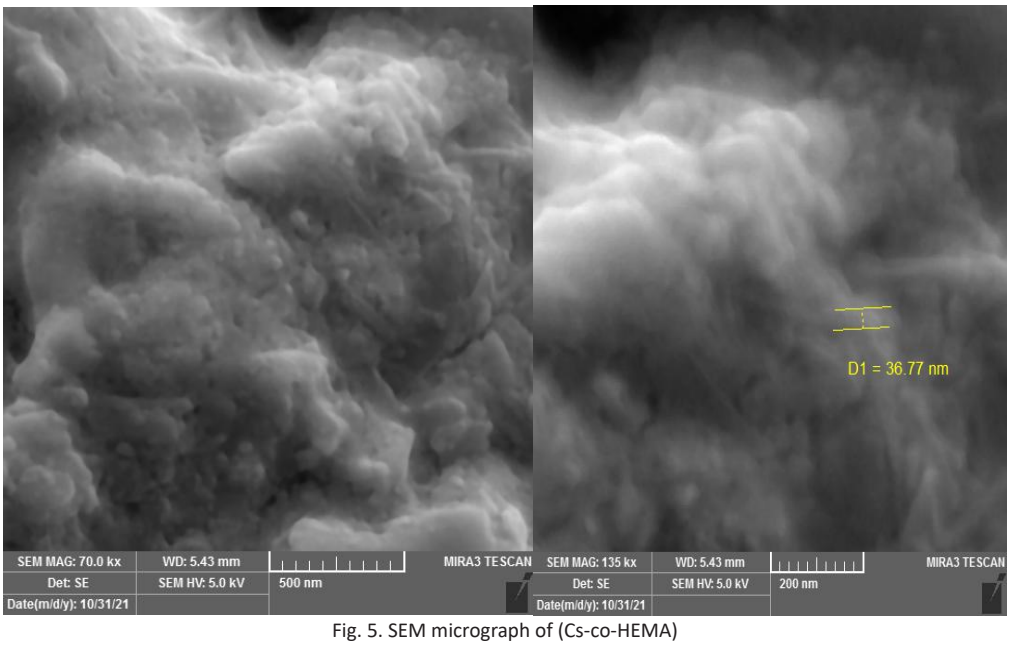

Fig. 5. SEM micrograph of (Cs-co-HEMA)

morphology and dimensions of the nanopolymer at two different magnifications, namely 200 nm and 500 nm.

X– Ray Diffraction Analysis (XRD)

X-ray Diffraction (XRD) is the most commonly used analytical technique for determining the phase composition, grain size, and crystal structure of materials. According to the distribution of the pigments, the composition of the material can be qualitatively analyzed by comparing the powder diffraction. XRD analysis of the catalysts was carried out at room temperature within the Bragg angle range10°≤ 2Θ≤ 90° at a scan speed of 2°.min^{-1} by an X-ray diffract meter, using Cu K α- radiation.

$$2d_{(hkl)}\sin\theta = m\lambda \quad (1)$$

Where:

λ: is wavelength of the X-ray, θ: is the Bragg diffraction angle of the XRD peak in degree (scattering angle), m: is integer representing the order of the diffraction peak and d_{hkl}: is inter-plane distance of (i.e atoms or ions or molecules).

Fig. 6 show the XRD spectra of the (Cs-co-HEMA). The crystal structure of the compounds were identified to be crystalline. The diffraction peaks were identified between 10°-75° in 2θ. The patterns show that all the nanocopolymer has peaks appear, which could be related to 2θ=29.7728, 31.800, 32.2032, 34.014640.2146, 45.6535, 56.9997, 66.5896, and75.6692. In addition to these peaks in the compounds, there is a broad peak appeared for these compounds. Most these diffraction peaks can be perfectly indexed to the monoclinic system crystalline and nano structure of (Cs-co-HEMA, not only in peak position, but also in their relative intensity of the characteristic peaks. The structure of these (Cs-co-HEMA showed crystalline, the crystallite size (D) calculated by using Eq. 2:

$$D = \frac{0.94\,\lambda}{\beta\cos\theta} \quad (2)$$

It was calculated from the full width at half maximum (FWHM) (β) of the preferred orientation diffraction peak by using the Debye-Sherrer's equation. Shown in Table 2. This result in good agreement with.

Degree of swelling of (Cs-co-HEMA) as function of Cs:HEMA composition ratio

Fig. 7 illustrates the time-dependent swelling behavior of hydrogel PHEMA at various pH levels. The incorporation of chitosan into the hydrogel

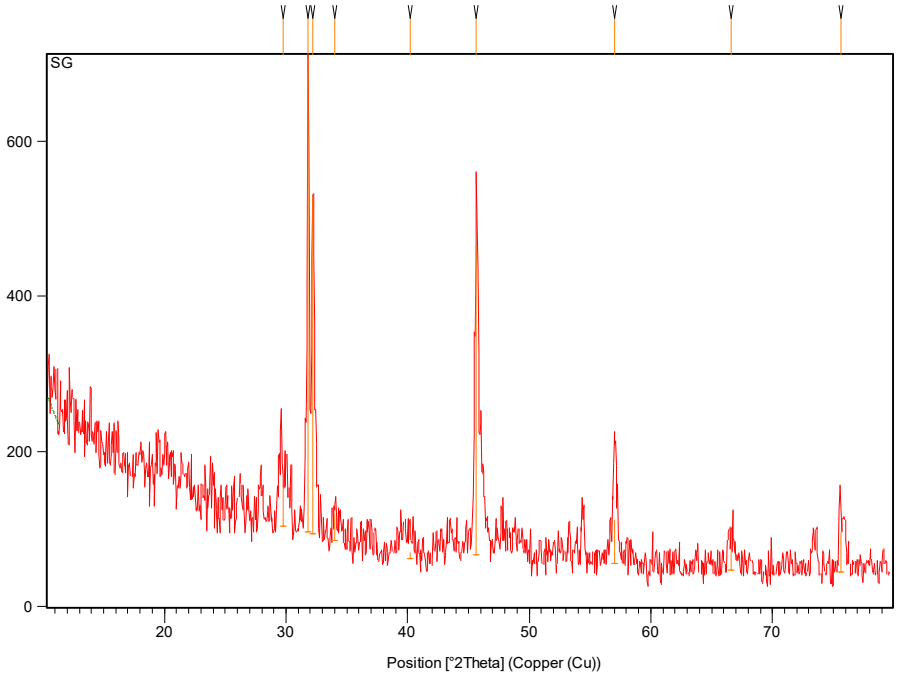

Fig. 6. X– Ray Diffraction for (Cs-co-HEMA).

leads to an increase in water content. This may be credited for the attendance of hydroxyl (-OH) and amino (-NH) groups in chitosan, which may crystalize hydrogen bonds thru water molecules. As an outcome, the Swelling Ratio of the hydrogel reaches 356, indicating a significant enhancement in its ability to engross water. This demonstrates the effectiveness of using hydrophilic monomers to improve the water uptake aptitude of hydrogels [36].

Method of analysis drug (5-Amino salicylic acid) (5-ASA)

Accuracy and precision to the technique of analysis is too vital in drug connected works. Therefore, initially UV-visible method to the analysis of (5-Amino salicylic acid) was developed, to analyze these components in drug loading and release medium.

5-Amino salicylic acid (5-ASA) is available in a crystalline form. To create a stock solution, It is possible to dissolve the compound (5-ASA) in an organic solvent that has been purged with an inert gas. Despite its insolubility in ethanol, (5-ASA) may be dissolved in organic solvents like (DMSO) and dimethyl formamide (DMF). The solubility of (5-ASA) in (DMSO) is approximately 4 mg/ml, while in (DMF) it is around 1.6 mg/ml. Upon dissolution in either of these solvents, (5-ASA) gives rise to a yellow-colored solution [37].

The active ingredient in medications used for extended upkeep therapy to stop the recurrence of Crohn's disease as well as ulcerative colitis is 5-Amino salicylic acid (5-ASA). However, when

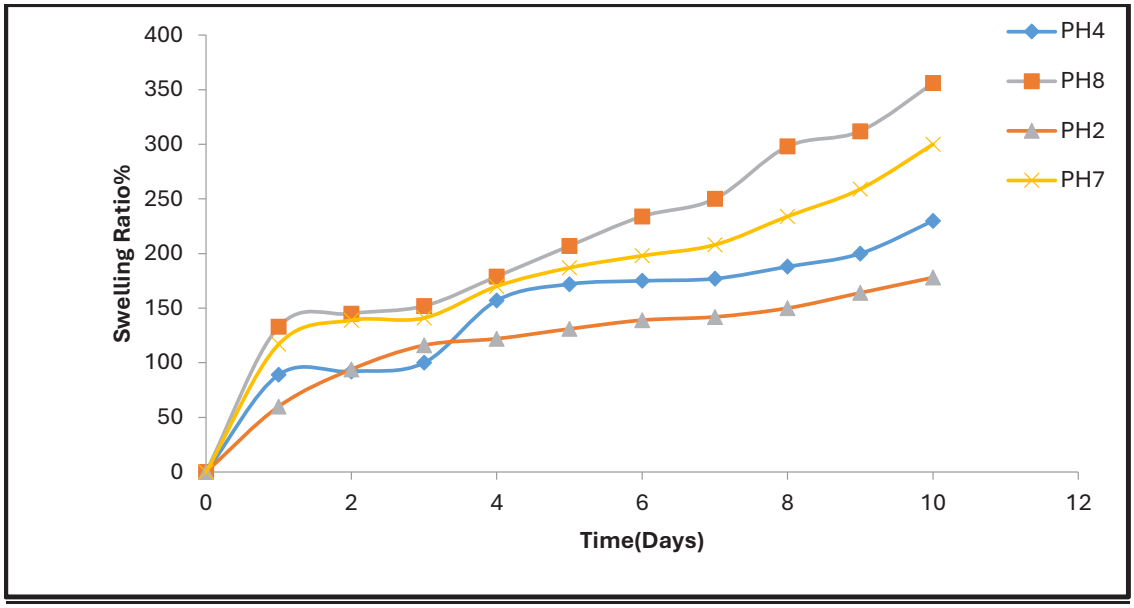

Fig. 7. Swelling ratio (Rs) for (Cs-co-HEMA) at time within different pH range.

Table 2. X-ray diffraction parameters for (Cs-co-HEMA).

Pos. [°2Th.]	Height [cts]	FWHM [°2Th.]	d-spacing [Å]	Rel. Int. [%]	Tip width [°2Th.]	D(nm)
29.7728	51.06	3.0867	2.99840	8.35	3.7040	0.47372
31.8000	611.63	0.1465	2.81173	100.00	0.1758	9.9834
32.2032	435.57	0.2223	2.77744	71.21	0.2667	6.58
34.0146	34.28	0.2316	2.63356	5.60	0.2780	6.315
40.2146	8.54	1.5168	2.24068	1.40	1.8201	0.9640
45.6535	399.26	0.4222	1.98558	65.28	0.5066	3.4639
56.9997	56.67	2.1676	1.61435	9.27	2.6011	0.6745
66.5896	24.08	1.2299	1.40323	3.94	1.4759	1.1888
75.6692	51.55	1.4130	1.25582	8.43	1.6956	1.0348

taken orally, the drug is significantly absorbed out of the upper gastrointestinal tract (GIT), resulting in systemic side effects. Consequently, it is preferable to aim for the drug to be delivered directly to the colon. Various methods have been developed to accomplish this objective, including the use of biodegradable polymer coatings, pH-sensitive polymer coatings, time-dependent formulations, and the creation of biodegradable matrices.

The effect of pH on the release of drug (5-ASA)

The 5-ASA release rates from Cs/HEMA hydrogels were measured at various pH levels (2, 4, 7, and 8) as shown in Fig. 9. It is worth noting that the highest release rate of 5-ASA was observed at pH 8, which can be attributed to the hydrogels' greater swelling ratio. This can be explained by the presence of a high concentration of H^+ ions, which promotes the ionization of NH_2 and increases the overall ion number concentration within the gel matrix. As a result, the hydrogels have an enhanced ability to interact with water molecules through increased solvation. Conversely, at a low pH of 2, the amino groups of Chitosan undergo protonation, leading to repulsion between the polymer chains and subsequent drug release.

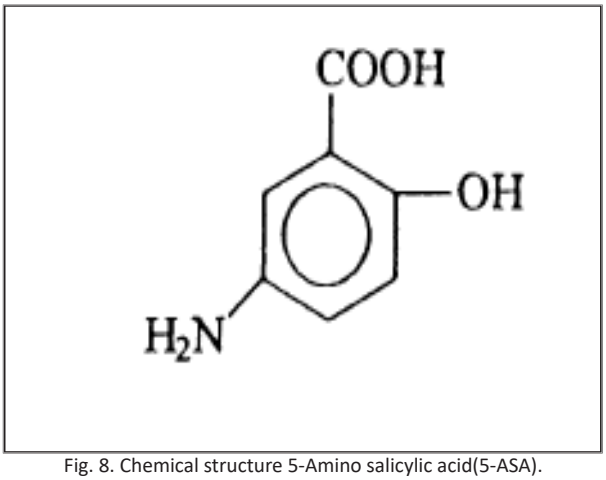

Fig. 8. Chemical structure 5-Amino salicylic acid(5-ASA).

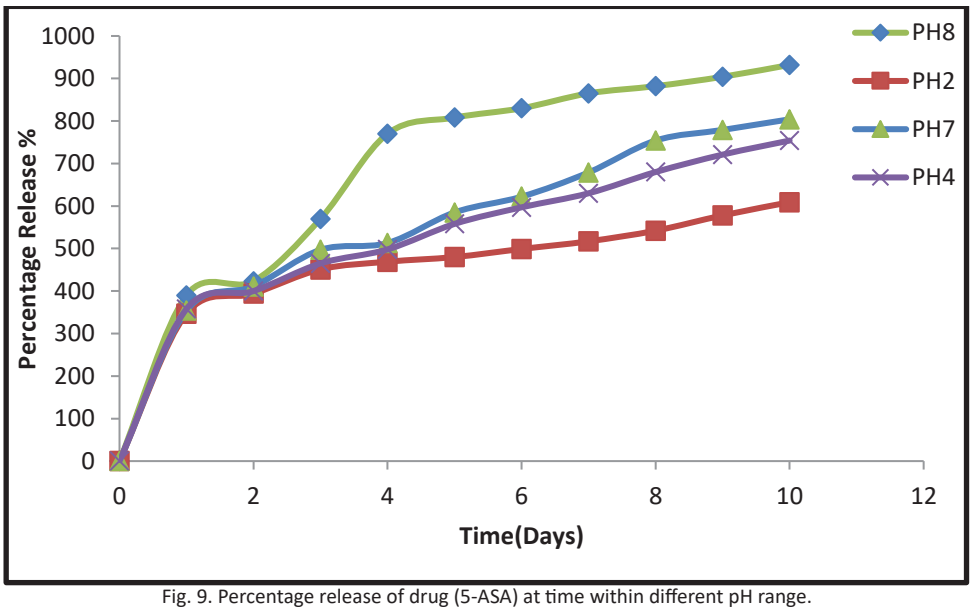

Fig. 9. Percentage release of drug (5-ASA) at time within different pH range.

The decrease in the pH 2-induced release of (5-ASA) can be ascribed to the diminished swelling ratio of the hydrogels. This decline is a consequence of the deprotonation of the amino groups, leading to a reduction in repulsion between the polymer chains and ultimately causing the hydrogels to shrink. [39].

The effect of temperature on the release of drug (5-ASA)

The impact of temperature on the level at which (5-ASA) is released has also been investigated in this study. According to Fig. 10, It has been noted that the rate of release is greater at 39 °C in contrast to 37 °C. This variation can be ascribed to the connection or separation of hydrogen bonding among the amino groups found in the Chitosan chains. The rise in temperature enables the polymer chains to unwind, resulting in the separation of secondary interactions such as intramolecular hydrogen bonding. Consequently, this permits a larger amount of water to penetrate the gel network. [39]. Hence, with the growth in temperature, the swelling ratio of all hydrogels increased, which could have a significant impact on the release rate of (5-ASA) by expanding the diffusion pathways within the superabsorbent. These two factors are believed to work together to increase the release rate of (5-ASA) as the temperature rises.

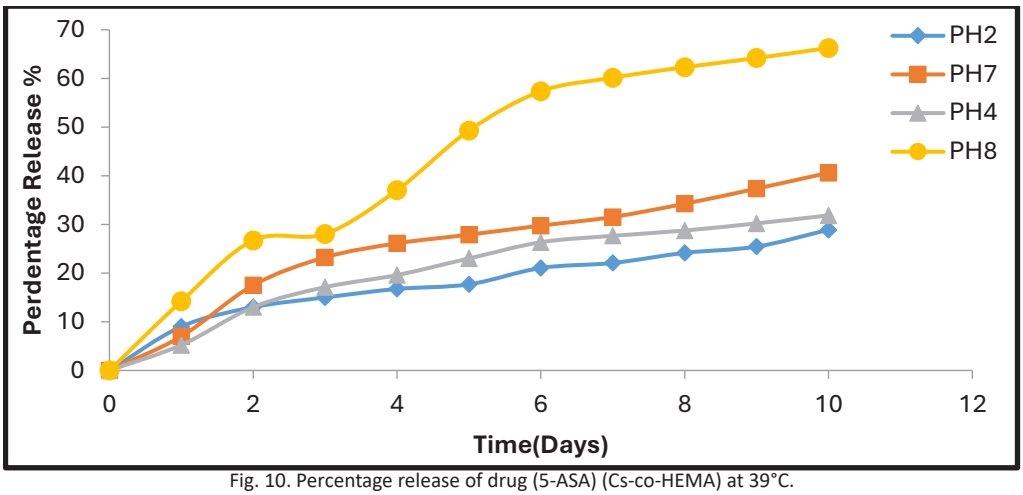

Fig. 10. Percentage release of drug (5-ASA) (Cs-co-HEMA) at 39°C.

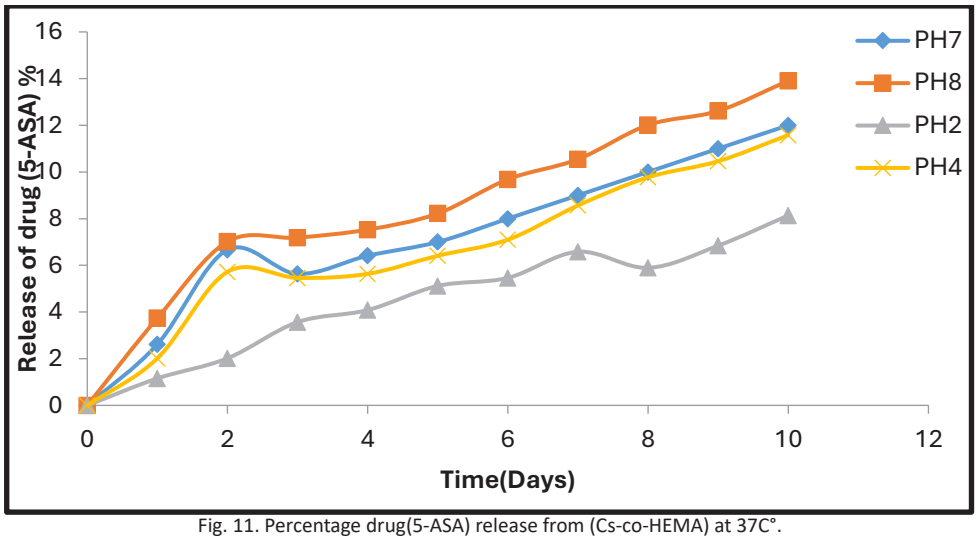

Fig. 11. Percentage drug(5-ASA) release from (Cs-co-HEMA) at 37C°.

The effect of amount of loading on release of drug (5-ASA)

The porous Cs/HEMA hydrogel was loaded with different amounts of (5-ASA) and its release profile is examined at various pH levels (2, 4, 7, and 8). The findings, depicted in Fig. 11, demonstrate that the loading capacity rises as the concentration of (5-ASA) in the loading medium increases. Moreover, the released profiles reveal that the quantity of (5-ASA) released also increases with higher loading of the active agent. The speed at which the solvent front enters the hydrogel surface rises as the loading increases. This phenomenon can be attributed to the existence of empty spaces within the matrix, which restricts the transportation of (5-ASA) molecules. The release of drugs through microspheres is affected by multiple factors including particle size, polymer crystallinity, surface properties, molecular weight, polymer composition, swelling ratio, degradation rate, drug binding affinity, and hydrogel rate [40].

CONCLUSION

The selection of the cross-linking agent, along with its hydrophilicity and the crosslinking density, plays a crucial role in determining the pH-sensitive swelling behavior and stability of Chitosan modified hydrogel membranes. The expansion of a Cs/HEMA hydrogel may be effectively elucidated thru the Donnan swelling equilibrium, that is controlled thru the osmotic pressure gradient amongst the interior as well as exterior of the hydrogel. This gradient arises from the presence of electrostatic charges and the concentration of counterions accumulated within the hydrogel. The swelling as well as shrinking of the hydrogel in solutions thru varying pH levels have provided evidence for this particular type of swelling phenomenon. The behavior of hydrogels is characterized by their responsiveness to changes in pH levels. Specifically, these materials tend to exhibit maximum swelling at low pH levels, while swelling is minimized at high pH levels as follows:

pH=8 > pH=7 > pH=4 > pH=2

In a pH range of 2-4, Chitosan's unreacted amino groups undergo ionization in an acidic environment. This results in the bonding of ammonium ions to the hydrogels through ionic bonds, causing an increase in the weight of the hydrogels in an acidic buffer. Conversely, at a high pH of 8, Chitosan's amino group exists as -NH2, leading to a lower equilibrium water content compared to lower pH levels. This behavior, sensitive to pH, is a distinctive characteristic of ionic hydrogels. It was noted that the hydrogel structures had a greater release rate at pH=8 in comparison to other pH levels. Additionally, the maximum swelling ratio for the four samples with high swelling ratios was observed at 39 °C instead of 37 °C. All hydrogels exhibit a swelling behavior that is responsive to temperature, which is attributed to the connotation and separation of hydrogen bonding facilitated through the amino groups of Chitosan within the hydrogels. Consequently, the swelling ratio of all hydrogels is observed to escalate as the temperature rises.

In relation to the impact of temperature on the release of (5-ASA) for these four samples with a high release rate drug, it has been observed that the release rate is higher at 39 °C compared to 37 °C. It was observed that an elevated Chitosan concentration led to a greater release rate when considering the impact of Chitosan concentration on drug release.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

REFERENCES

1. Chourasia MK, Jain SK. Polysaccharides for Colon Targeted Drug Delivery. Drug Deliv. 2004;11(2):129-148.
2. Jain SK, Jain A. Target-specific drug release to the colon. Expert Opinion on Drug Delivery. 2008;5(5):483-498.
3. Luo J-Y, Zhong Y, Cao J-C, Cui H-F. Efficacy of oral colon-specific delivery capsule of low-molecular-weight heparin on ulcerative colitis. Biomedicine and Pharmacotherapy. 2011;65(2):111-117.
4. Rubinstein A. Approaches and Opportunities in Colon-Specific Drug Delivery. Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):101-149.
5. Dhaneshwar SS, Gairola N, Kandpal M, Vadnerkar G, Bhatt L. Colon-specific, mutual azo prodrug of 5-aminosalicylic acid with l-tryptophan: Synthesis, kinetic studies and evaluation of its mitigating effect in trinitrobenzenesulfonic acid-induced colitis in rats. Bioorganic and Medicinal Chemistry. 2007;15(14):4903-4909.
6. Yin H, Lee ES, Kim D, Lee KH, Oh KT, Bae YH. Physicochemical characteristics of pH-sensitive poly(l-Histidine)-b-poly(ethylene glycol)/poly(l-Lactide)-b-poly(ethylene glycol) mixed micelles. Journal of Controlled Release. 2008;126(2):130-138.
7. Vaghani SS, Patel MM, Satish CS. Synthesis and characterization of pH-sensitive hydrogel composed of carboxymethyl chitosan for colon targeted delivery of ornidazole. Carbohydr Res. 2012;347(1):76-82.
8. Fude C, Lei Y, Jie J, Hongze P, Wenhui L, Dongmei C. Preparation and In Vitro Evaluation of pH, Time-Based and

Enzyme-Degradable Pellets for Colonic Drug Delivery. Drug Development and Industrial Pharmacy. 2007;33(9):999-1007.
9. Dev RK, Bali V, Pathak K. Novel microbially triggered colon specific delivery system of 5-Fluorouracil: Statistical optimization, in vitro, in vivo, cytotoxic and stability assessment. Int J Pharm. 2011;411(1-2):142-151.
10. Yang L. Biorelevant dissolution testing of colon-specific delivery systems activated by colonic microflora. Journal of Controlled Release. 2008;125(2):77-86.
11. Gupta VK, Beckert TE, Price JC. A novel pH- and time-based multi-unit potential colonic drug delivery system. I. Development. Int J Pharm. 2001;213(1-2):83-91.
12. Li-Fang F, Wei H, Yong-Zhen C, Bai X, Qing D, Feng W, et al. Studies of chitosan/Kollicoat SR 30D film-coated tablets for colonic drug delivery. Int J Pharm. 2009;375(1-2):8-15.
13. Cummings JH, Macfarlane GT. The control and consequences of bacterial fermentation in the human colon. J Appl Bacteriol. 1991;70(6):443-459.
14. Guarner F, Malagelada J-R. Gut flora in health and disease. The Lancet. 2003;361(9356):512-519.
15. Englyst HN, Cummings JH. Digestion of the polysaccharides of some cereal foods in the human small intestine. The American Journal of Clinical Nutrition. 1985;42(5):778-787.
16. Nath B, Nath LK. Studies on Stercuia Gum Formulations in the Form of Osmotic Core Tablet for Colon-Specific Drug Delivery of Azathioprine. PDA J Pharm Sci Technol. 2013;67(2):172-184.
17. Singla AK, Chawla M. Chitosan: some pharmaceutical and biological aspects - an update. Journal of Pharmacy and Pharmacology. 2001;53(8):1047-1067.
18. Bhattarai N, Gunn J, Zhang M. Chitosan-based hydrogels for controlled, localized drug delivery. Adv Drug Del Rev. 2010;62(1):83-99.
19. Park JH, Saravanakumar G, Kim K, Kwon IC. Targeted delivery of low molecular drugs using chitosan and its derivatives. Adv Drug Del Rev. 2010;62(1):28-41.
20. Advances of nano-targeted drug delivery systems in traditional Chinese medicine anticancer therapy. Journal of Chinese Pharmaceutical Sciences. 2024;33(4):285.
21. McConnell EL, Murdan S, Basit AW. An Investigation into the Digestion of Chitosan (Noncrosslinked and Crosslinked) by Human Colonic Bacteria. J Pharm Sci. 2008;97(9):3820-3829.
22. Muzzarelli RAA. Biomedical Exploitation of Chitin and Chitosan via Mechano-Chemical Disassembly, Electrospinning, Dissolution in Imidazolium Ionic Liquids, and Supercritical Drying. Mar Drugs. 2011;9(9):1510-1533.
23. Tozaki H, Odoriba T, Okada N, Fujita T, Terabe A, Suzuki T, et al. Chitosan capsules for colon-specific drug delivery: enhanced localization of 5-aminosalicylic acid in the large intestine accelerates healing of TNBS-induced colitis in rats. Journal of Controlled Release. 2002;82(1):51-61.
24. Di Colo G, Falchi S, Zambito Y. In vitro evaluation of a system for pH-controlled peroral delivery of metformin. Journal of Controlled Release. 2002;80(1-3):119-128.
25. Zhang H, Alsarra IA, Neau SH. An in vitro evaluation of a chitosan-containing multiparticulate system for macromolecule delivery to the colon. Int J Pharm. 2002;239(1-2):197-205.
26. Lorenzo-Lamosa ML, Remuñán-López C, Vila-Jato JL, Alonso MJ. Design of microencapsulated chitosan microspheres for colonic drug delivery. Journal of Controlled Release. 1998;52(1-2):109-118.
27. Xu B, Watkins R, Wu L, Zhang C, Davis R. Natural product-based nanomedicine: recent advances and issues. International Journal of Nanomedicine. 2015:6055.
28. Lam P-L, Wong W-Y, Bian Z, Chui C-H, Gambari R. Recent Advances in Green Nanoparticulate Systems for Drug Delivery: Efficient Delivery and Safety Concern. Nanomedicine. 2017;12(4):357-385.
29. Phillips I. Medical microbiology. Volume two: the practice of medical microbiology: Edited by R. CRUICKSHANK, J. P. DUGUID, B. P. MARMION AND R. H. A. SWAIN. 12th ed., 1975. Edinburgh, London and New York: Churchill Livingstone. Pp x and 587. Hard cover, 11; soft cover, 7{middle dot}50. J Med Microbiol. 1976;9(3):366-367.
30. Tran N-P-D, Yang M-C. Synthesis and characterization of soft contact lens based on the combination of silicone nanoparticles with hydrophobic and hydrophilic monomers. Journal of Polymer Research. 2019;26(6).
31. Abou Taleb MF, Abdel-Aal SE, El-Kelesh NA, Hegazy E-SA. Adsorption and controlled release of Chlortetracycline HCl by using multifunctional polymeric hydrogels. Eur Polym J. 2007;43(2):468-477.
32. Czarnecka E, Nowaczyk J. Synthesis and Characterization Superabsorbent Polymers Made of Starch, Acrylic Acid, Acrylamide, Poly(Vinyl Alcohol), 2-Hydroxyethyl Methacrylate, 2-Acrylamido-2-methylpropane Sulfonic Acid. Int J Mol Sci. 2021;22(9):4325.
33. Named Organic Reactions, 2nd ed By Thomas Laue and Andreas Plagens (Volkswagen AG, Wolfsburg, Germany). John Wiley and Sons, Ltd: Chichester, U.K. 2005. x + 310 pp. $55.00. ISBN 0-470-01041-X. Journal of the American Chemical Society. 2005;127(33):11878-11878.
34. Erratum. Relict Species: Springer Berlin Heidelberg; 2009. p. 450-450.
35. Guthrie RD. Introduction to Spectroscopy (Pavia, Donald; Lampman, Gary M.; Kriz, George S., Jr.). J Chem Educ. 1979;56(10):A323.
36. Sannino A, Esposito A, Nicolais L, Del Nobile MA, Giovane A, Balestrieri C, et al. Cellulose-based hydrogels as body water retainers. J Mater Sci Mater Med. 2000;11(4):247-253.
37. Wahl C, Liptay S, Adler G, Schmid RM. Sulfasalazine: a potent and specific inhibitor of nuclear factor kappa B. J Clin Invest. 1998;101(5):1163-1174.
38. Guan YL, Shao L, Liu J, De Yao K. pH effect on correlation between water state and swelling kinetics of the crosslinked chitosan/polyether semi-IPN hydrogel. J Appl Polym Sci. 1996;62(8):1253-1258.
39. Rohindra DR, Nand AV, Khurma JR. Swelling properties of chitosan hydrogels. The South Pacific Journal of Natural and Applied Sciences. 2004;22(1):32.
40. Synthesis and Characterization of PH Sensitive Poly(Vinyl Acetate- Co-Methacrylic Acid) Microspheres for Control Release of Acebutolol Hydrochloride. Micro- and Nanostructured Polymer Systems: Apple Academic Press; 2016. p. 119-136.