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DEVELOPMENT OF NATURAL POLYMER BASE POLYMERIC FORMULATIONS FOR COLON TARGETING

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ABSTRACT

Colon-targeted drug delivery has gained significant attention for improving localized therapy and minimizing systemic adverse effects. In the present work, sodium alginate-based polymeric films were formulated as a pH-responsive delivery system for aspirin using a solvent casting technique followed by calcium ion-induced crosslinking. The prepared films were systematically evaluated for their physicochemical, mechanical, and drug release characteristics.

The formulations demonstrated satisfactory uniformity, flexibility, and drug loading efficiency. Swelling studies revealed a pronounced pH-dependent behaviour, indicating limited hydration in acidic medium and enhanced swelling at higher pH conditions. Drug release analysis confirmed a delayed and controlled release pattern, with minimal release in simulated gastric fluid and increased release in colonic conditions, suggesting effective protection of the drug in the upper gastrointestinal tract.

Further characterization using spectroscopic, thermal, and morphological techniques confirmed the structural integrity of aspirin and its uniform incorporation within the polymer matrix. The study highlights the suitability of sodium alginate as a natural, biocompatible polymer for designing colon-specific drug delivery systems with controlled release properties.

Keywords:

Colon targeting, Sodium alginate film, Aspirin delivery, pH-responsive system, Controlled drug release, Natural polymer, Drug–polymer compatibility

INTRODUCTION

Colon-specific drug delivery systems have emerged as an important approach for directing therapeutic agents precisely to the large intestine, thereby enhancing treatment outcomes while limiting unwanted systemic exposure. This strategy is particularly useful for conditions

affecting the colon, including inflammatory bowel diseases, colorectal malignancies, and localized infections. However, traditional oral delivery methods often face limitations such as unintended drug release and degradation in the stomach and small intestine, which reduces the amount of drug reaching the target site.[1]

To address these challenges, multiple formulation approaches have been investigated, with natural polymers emerging as highly promising candidates. Polymers such as sodium alginate, pectin, chitosan, guar gum, and dextran are extensively utilized because of their excellent biocompatibility, biodegradability, low toxicity, and cost-effectiveness. These materials remain relatively stable in the acidic conditions of the stomach and resist digestion in the upper gastrointestinal tract, but are readily broken down by the microbial flora present in the colon. This unique property makes them suitable for achieving targeted and controlled drug release at the colonic site.[2]

Among the various natural polymers, sodium alginate has attracted considerable interest as a carrier for colon-targeted drug delivery owing to its ability to form gels in the presence of divalent ions such as calcium. The ionotropic gelation method is widely utilized to fabricate alginate-based beads and microspheres capable of efficiently entrapping drugs and providing controlled release profiles. Nevertheless, formulations based solely on alginate often need to be with other polymers or modified chemically to improve their mechanical stability and achieve better control over drug release characteristics.[4] In recent years, increasing emphasis has been placed on developing eco-friendly and sustainable drug delivery systems utilizing polymers derived from plant sources. These strategies reduce reliance on hazardous chemicals and support greener manufacturing practices. Moreover, formulations based on natural polymers can be tailored to respond to physiological stimuli such as variations in pH, enzymatic action, and gastrointestinal transit time, thereby improving the precision and effectiveness of drug release in the colon.[5]

Recent progress in polymeric nanoparticle-based delivery systems has created new possibilities for effective colon targeting. These systems contribute to improved drug stability, enable sustained and controlled release, and enhance overall bioavailability. Additionally, they can be strategically designed to provide accurate site-specific delivery, leading to improved therapeutic efficacy in the treatment of colonic diseases.[6]

Accordingly, the present work is directed toward the design and development of polymeric formulations based on natural polymers for targeted delivery to the colon, with the objective

of achieving controlled and site-specific drug release. The study involves careful selection of appropriate natural polymeric materials, optimization of formulation parameters, and comprehensive evaluation of physicochemical as well as biological properties to improve overall therapeutic performance.

BACKGROUND

Colon-targeted drug delivery is designed to deliver drugs specifically to the colon, improving therapeutic efficacy and minimizing systemic side effects, especially in conditions like inflammatory bowel disease and colorectal cancer. Conventional oral systems often fail due to premature drug release in the upper gastrointestinal tract.[7-8] Natural polymers such as alginate, pectin, and chitosan are widely explored for colon targeting because of their biocompatibility, biodegradability, and susceptibility to degradation by colonic microflora, enabling site-specific drug release.[2,18] Polymeric films prepared from these natural polymers offer advantages like controlled drug release, uniform drug distribution, and enhanced stability, which can be further optimized through crosslinking and formulation modifications.[4,11] Additionally, the use of plant-based polymers supports green and sustainable pharmaceutical development.[12] Therefore, natural polymer-based polymeric films represent a promising approach for effective colon-targeted drug delivery.[7,12]

MECHANISM OF ACTION

Sodium alginate-based polymeric films act as colon-targeted delivery systems by protecting the incorporated active pharmaceutical ingredient (API), aspirin, during transit through the upper gastrointestinal tract and enabling its controlled release in the colon. Sodium alginate, an anionic polysaccharide, forms a gel matrix in the presence of divalent cations such as calcium ions, creating a crosslinked network that is resistant to acidic gastric conditions. This prevents premature drug release in the stomach and small intestine.[4,14] Upon reaching the colon, the alginate matrix undergoes swelling and partial degradation due to the higher pH and the presence of colonic microflora, leading to a gradual and site-specific release of aspirin.[2,8]

Once released, aspirin (acetylsalicylic acid) exerts its anti-inflammatory effect primarily through the irreversible inhibition of cyclooxygenase enzymes (COX-1 and COX-2). This inhibition reduces the synthesis of prostaglandins, which are key mediators of inflammation, pain, and swelling in colonic tissues. By decreasing prostaglandin production, aspirin helps alleviate inflammation associated with conditions such as inflammatory bowel disease and colorectal inflammation.[15]

Additionally, the controlled release of aspirin from the alginate film minimizes direct exposure of the drug to the gastric mucosa, thereby reducing gastrointestinal irritation and systemic side effects commonly associated with conventional oral administration. The sustained release profile also maintains therapeutic drug concentrations at the target site over an extended period, enhancing local efficacy.[16]Therefore, sodium alginate-based films provide a dual advantage of targeted delivery and controlled drug release, improving the therapeutic performance of aspirin in the treatment of colonic inflammation.[13]

MATERIALS AND METHODS

Materials

Sodium alginate was used as a natural polymer owing to its biocompatibility, biodegradability, and pH-sensitive gel-forming ability.[14] Aspirin (acetylsalicylic acid) was selected as the model anti-inflammatory drug due to its therapeutic relevance in inflammatory conditions. Calcium chloride ($CaCl_2$) was used as an ionic crosslinking agent. Glycerol was employed as a plasticizer to improve flexibility of the polymeric film.[21] All other reagents, including hydrochloric acid, potassium dihydrogen phosphate, and sodium hydroxide, were of analytical grade and used for preparation of buffer solutions (pH 1.2, 6.8, and 7.4). Distilled water was used throughout the study.

Method of Preparation of Polymeric Film

1. PREPARATION OF SODIUM ALGINATE SOLUTION

Sodium alginate (2–4% w/v) was accurately weighed and dispersed in distilled water under continuous magnetic stirring until a homogeneous viscous solution was obtained. The solution was allowed to stand for 4–6 hours to ensure complete hydration and removal of air bubbles.[14]

2. INCORPORATION OF ASPIRIN

Aspirin was dissolved in a small volume of ethanol and added slowly to the polymeric solution under continuous stirring to obtain a uniform drug-polymer mixture. Glycerol (1–2% w/v) was incorporated as a plasticizer to enhance film flexibility and prevent brittleness.[21]

3. CASTING OF POLYMERIC FILM (SOLVENT CASTING METHOD)

The prepared solution was poured into levelled glass Petri dishes and allowed to dry on heating mantle at 10-20 degree Celsius for 30 minutes to form a uniform film. Solvent casting is a

widely used technique for preparing polymeric films with uniform thickness and drug distribution.[17]

Fig no.1 (Casting and drying of film)

4. CROSSLINKING OF FILM

The dried films were immersed in calcium chloride solution (2–5% w/v) for 15–30 minutes to achieve ionic crosslinking. The calcium ions interact with the carboxyl groups of sodium alginate forming a three-dimensional "egg-box" structure, which enhances mechanical strength and modulates drug release.[14,18] The films were then rinsed with distilled water to remove excess $CaCl_2$.

5. DRYING AND STORAGE

The crosslinked films were dried at room temperature until constant weight was achieved and stored in a desiccator to prevent moisture uptake.[17]

Fig no.2 (Dried film)

Evaluation of Polymeric Film

6. PHYSICAL APPEARANCE

The prepared films were visually inspected to assess their color, transparency, surface uniformity, and flexibility. This preliminary evaluation ensured the films were free from visible defects such as air bubbles, cracks, or surface irregularities.[21]

7. THICKNESS AND WEIGHT UNIFORMITY

The thickness of the films was measured at multiple locations using a micrometer screw gauge, and the mean value was calculated to ensure uniformity. For weight variation, individual film

samples were weighed using a calibrated analytical balance to confirm consistency in mass distribution.[17]

8. FOLDING ENDURANCE

Mechanical strength of the films was evaluated by repeatedly folding a film sample at the same location until it showed signs of breaking. The total number of folds required to cause breakage was recorded as the folding endurance.[21]

9. DRUG CONTENT UNIFORMITY

A defined portion of the film was dissolved in phosphate buffer (pH 7.4) and filtered to obtain a clear solution. The drug concentration was then quantified using UV-visible spectrophotometry at 276 nm to determine uniform distribution of aspirin within the film.[19]

10. SWELLING STUDY

The swelling behaviour of the films was studied by immersing them in buffer media of varying pH values (1.2, 6.8, and 7.4). At predetermined time intervals, the films were removed, blotted to remove excess liquid, and weighed. The swelling index was calculated to evaluate the pH-dependent swelling characteristics, which play a key role in colon-targeted drug delivery.[4]

11. IN VITRO DRUG RELEASE STUDY (USP APPARATUS I – BASKET TYPE)

The in vitro drug release study of the prepared sodium alginate-based polymeric films containing aspirin was carried out using a USP dissolution apparatus I (basket type) to simulate gastrointestinal transit conditions.

Fig no.3 (In Vitro drug release study of film)

Accurately weighed film samples (equivalent to a known amount of aspirin) were placed inside the dissolution basket. The study was performed using a rotational speed of 50–100 rpm and maintained at 37 ± 0.5°C to mimic physiological conditions (Aulton & Taylor, 2018).

A sequential pH method was employed to simulate the passage of the formulation through different regions of the gastrointestinal tract:

0–2 hours: 900 mL of 0.1 N HCl (pH 1.2) to simulate gastric fluid

2–5 hours: Phosphate buffer pH 6.8 to simulate intestinal fluid

At predetermined time intervals (e.g., 0,10,30,60,120,180,240 minutes) 5 mL samples were withdrawn and replaced with an equal volume of fresh dissolution medium maintained at the same temperature to maintain sink conditions (USP, 2020).[20]

DRUG PROFILE

Aspirin (acetylsalicylic acid) is a widely used non-steroidal anti-inflammatory drug (NSAID) that exhibits analgesic, antipyretic, and anti-inflammatory properties. It exerts its therapeutic effect primarily through the irreversible inhibition of cyclooxygenase (COX-1 and COX-2) enzymes, leading to a reduction in prostaglandin synthesis, which plays a central role in inflammation.[15] Due to this mechanism, aspirin has been investigated for its potential role in managing inflammatory conditions of the gastrointestinal tract, including colonic inflammation.

Chemical and Physical Properties of Aspirin (Acetylsalicylic Acid):

1. Chemical Identity

Aspirin, chemically termed acetylsalicylic acid, is an aromatic ester derived from salicylic acid. Its structure contains both an ester functional group and a carboxylic acid group, which contribute to its reactivity and pharmacological behaviour.

Table no.3 Chemical properties of aspirin

Parameter	**Description**
Chemical name	Acetylsalicylic acid
Molecular formula	$C_9H_8O_4$

Molecular weight	180.16g/mol
Chemical class	Salicylate ester (NSAIDs)
Functional groups	Ester and carboxylic acid

Physical Properties

Table no. 4 Physical properties of aspirin

Property	**Description**
Appearance	White, crystalline powder
Odour	Slight acetic acid odour
Taste	Slightly bitter
Melting point	135-136 degree Celsius
Solubility	Slightly soluble in water, freely soluble in ethanol
pKa	3.5 Weak acid
Partition coefficient	Moderate lipophilicity

For colon-targeted drug delivery, aspirin presents certain advantages, including its well-established pharmacological profile and effectiveness in reducing inflammatory mediators. In the context of colonic diseases such as inflammatory bowel disease (IBD), localized delivery of aspirin can help minimize systemic side effects while maximizing therapeutic concentration at the site of inflammation.[22] Colon targeting is particularly beneficial as it protects aspirin from premature degradation and absorption in the upper gastrointestinal tract, thereby enhancing site-specific action.

However, conventional oral administration of aspirin is associated with gastric irritation and mucosal damage due to local prostaglandin inhibition in the stomach lining. This limitation highlights the importance of developing colon-targeted delivery systems that can bypass the stomach and small intestine, reducing gastrointestinal side effects.[16] Polymeric systems,

particularly those based on natural polymers such as sodium alginate, offer a promising approach by providing pH-sensitive and controlled drug release, ensuring that aspirin is predominantly released in the colonic region.

Furthermore, aspirin has demonstrated potential chemopreventive effects in colorectal inflammation and related disorders by modulating inflammatory pathways and inhibiting platelet aggregation, which is linked to disease progression.[21] These properties make it a suitable candidate for incorporation into colon-targeted drug delivery systems aimed at treating localized inflammation.

RESULTS

The sodium alginate-based polymeric films loaded with aspirin were successfully prepared using the solvent casting method followed by ionic crosslinking. The prepared films were smooth, uniform, and free from visible imperfections such as cracks or air bubbles, indicating appropriate formulation and processing conditions.[17]

Physical Characterization

All formulations exhibited acceptable physical characteristics, including good transparency and flexibility. The films were easy to handle and peel, which may be attributed to the incorporation of glycerol as a plasticizer.[24] Thickness measurements showed minimal variation across different regions, suggesting uniform casting of the polymeric solution. Similarly, weight variation among samples remained within acceptable limits, confirming consistency in film preparation.[17]

Mechanical Properties

The folding endurance results indicated that the films possessed adequate mechanical strength and flexibility. The presence of glycerol improved the elasticity of the films, reducing brittleness and enhancing their ability to withstand repeated folding.

Drug Content Uniformity

The drug content analysis demonstrated uniform distribution of aspirin within the polymeric films. The percentage drug content was found to be within the acceptable pharmacopeial limits (95–105%), indicating efficient drug incorporation and minimal loss during formulation.[19]

Swelling Behaviour

Swelling studies revealed that the films exhibited pH-dependent swelling behavior. Limited swelling was observed in acidic medium (pH 1.2), while a gradual increase was noted at pH 6.8. Maximum swelling occurred at pH 7.4, which corresponds to colonic conditions. This behaviour is characteristic of sodium alginate due to ionization of carboxyl groups at higher pH, facilitating polymer relaxation and water uptake.[4,14]

In Vitro Drug Release Study

The in vitro drug release profile demonstrated a controlled and site-specific release of aspirin. Negligible drug release was observed in simulated gastric fluid (pH 1.2), indicating protection of the drug in acidic conditions. A moderate increase in drug release was observed in intestinal pH (6.8), whereas a significant and sustained release was achieved in colonic pH (7.4). This confirms the effectiveness of sodium alginate-based films in achieving colon-targeted drug delivery.[17,21]

Stability Studies

Stability studies showed that the optimized formulation remained stable under specified storage conditions, with no significant changes in physical properties, drug content, or release profile. This indicates good stability of the sodium alginate-based polymeric film formulation.[20]

UV–Visible Spectroscopy

UV–visible spectroscopic analysis of aspirin in phosphate buffer (pH 6.8) showed a characteristic absorption peak (λ max) at approximately 226 nm, confirming the identity of the drug. The calibration curve demonstrated good linearity within the selected concentration range, indicating the suitability of the method for quantitative analysis. Drug content analysis of the polymeric film showed no significant shift in λ max, suggesting that there was no chemical interaction between aspirin and sodium alginate during formulation.[19]

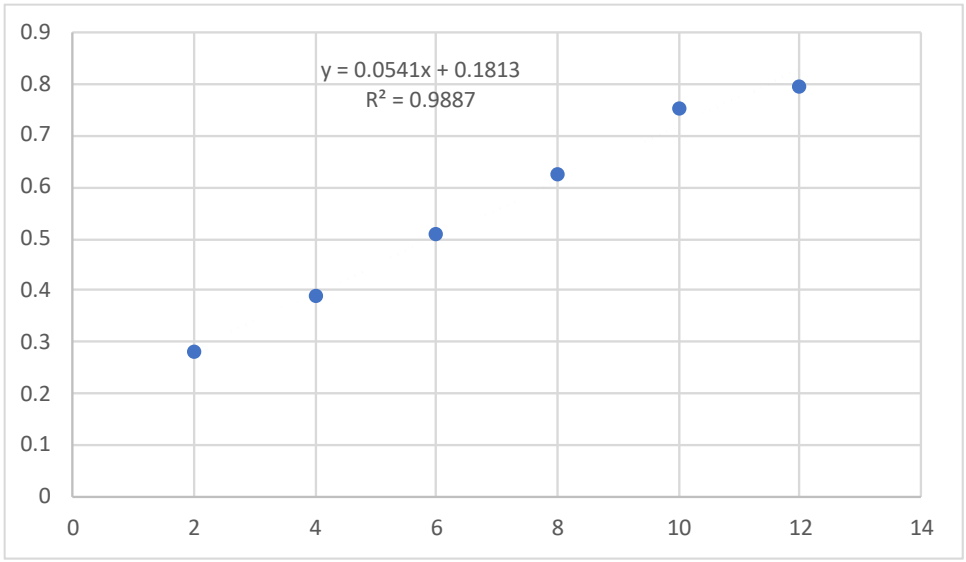

Fig no.4 (Linearity graph of aspirin)

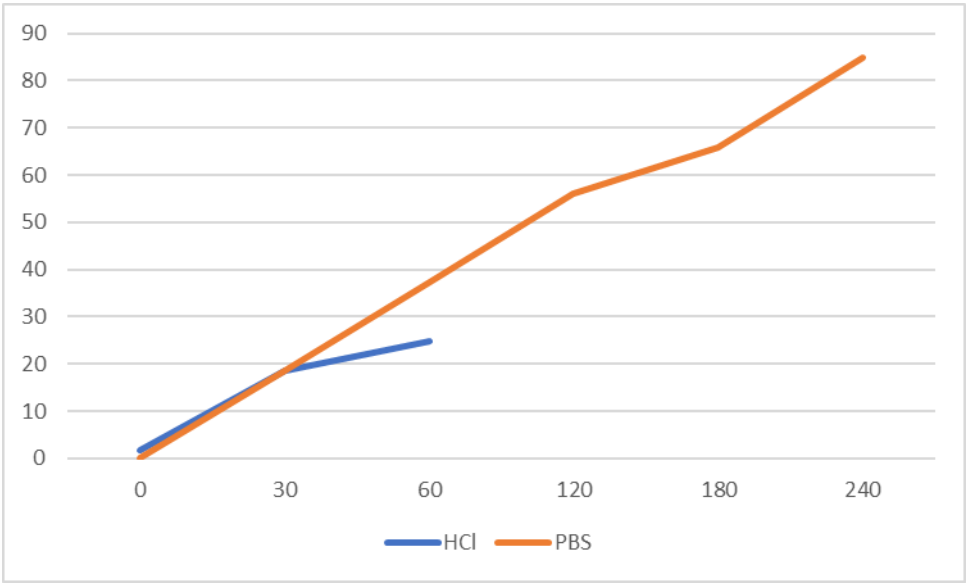

Fig no.5 (Calibration plot for aspirin)

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectrum of aspirin showed characteristic peaks at ~3491 cm^{-1} (O–H stretching), 1760 cm^{-1} (ester C=O stretching), and 1600 cm^{-1} (aromatic C=C stretching). Peaks at 1310 cm^{-1} and 1000–1200 cm^{-1} confirmed C–O and C–O–C stretching vibrations, while bands in the 700–900 cm^{-1} region indicated aromatic C–H bending. These findings confirm the structural integrity and purity of aspirin.

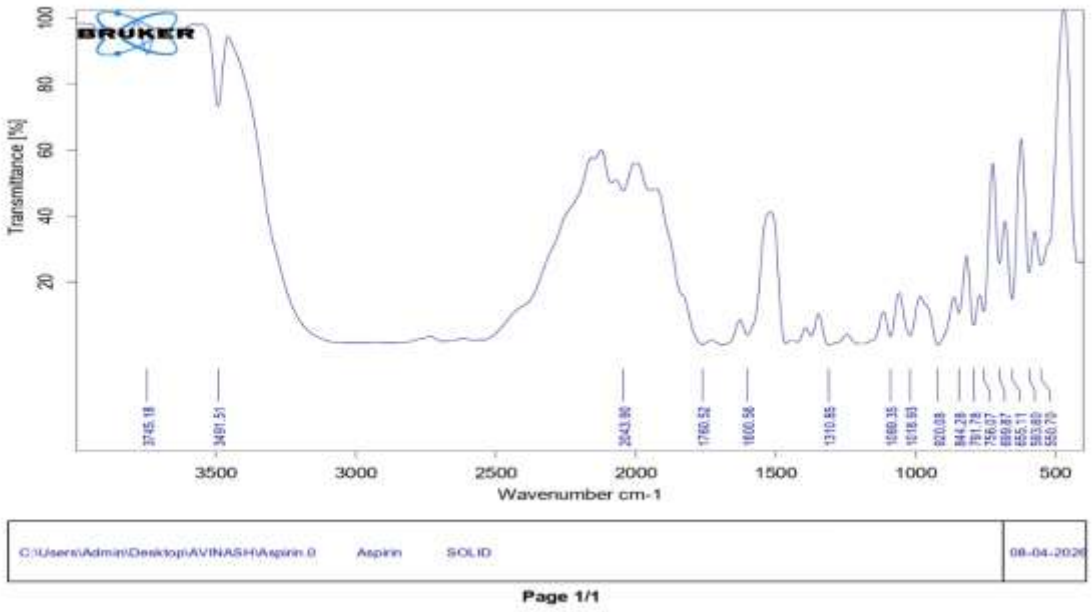

Fig no. 6 (FTIR graph of aspirin)

FTIR analysis of sodium alginate showed a broad peak at ~3418 cm^{-1} (O–H stretching), 2931 cm^{-1} (C–H stretching), and characteristic carboxylate peaks at 1609 cm^{-1} and 1416 cm^{-1}. Peaks in the range of 1000–1100 cm^{-1} confirmed C–O–C stretching of the polysaccharide backbone, while bands at 800–950 cm^{-1} indicated mannuronic and guluronic residues. These results confirm the typical structure of sodium alginate.

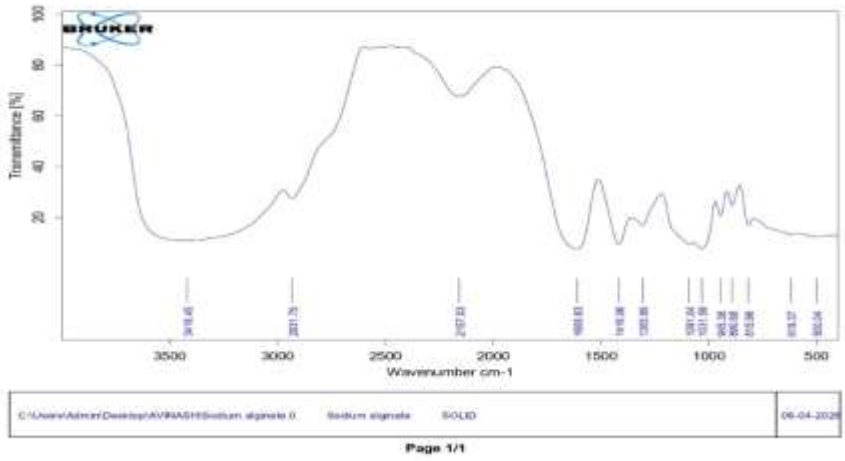

Fig no.7 (FTIR of sodium alginate)

FTIR spectrum of the polymeric film showed a broad O–H peak at ~3404 cm^{-1}, C–H stretching at 2929 cm^{-1}, and a characteristic carbonyl peak at 1637 cm^{-1}. Peaks at 1456 cm^{-1} and 1392 cm^{-1} confirmed carboxylate groups of alginate, while 1255 cm^{-1} indicated ester C–O stretching of aspirin. The band at 1041 cm^{-1} corresponded to polysaccharide backbone vibrations. Slight

shifts and broadening of peaks suggest hydrogen bonding between drug and polymer, confirming compatibility and successful incorporation.

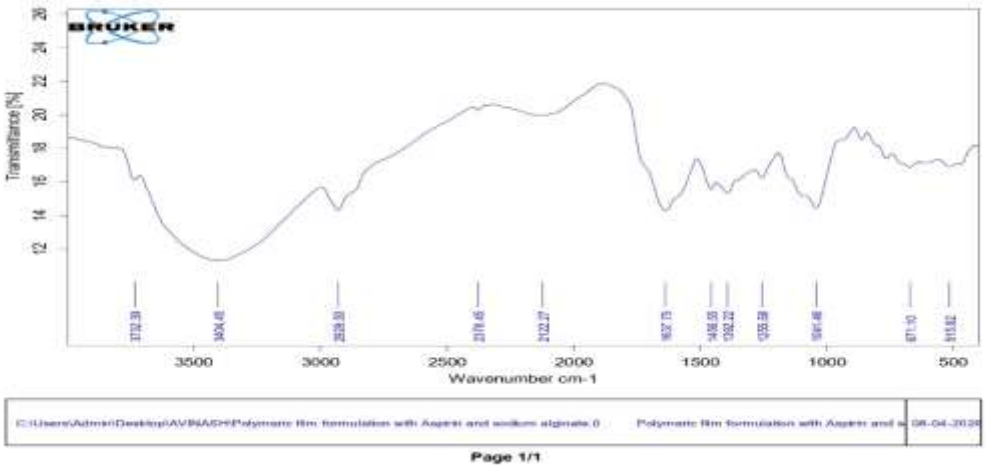

Fig no.8 (FTIR of Polymeric film)

The FTIR spectrum of the drug-loaded polymeric film retained all the main characteristic peaks of aspirin with slight shifts and reduced intensity, indicating physical entrapment of the drug within the polymeric matrix without any significant chemical interaction or incompatibility.[14,26]

Differential Scanning Calorimetry (DSC)

The DSC thermogram of aspirin showed a sharp endothermic peak with an onset at 138.42 °C and a peak temperature at 140.88 °C, corresponding to its melting point. The enthalpy of fusion was 176.61 J/g. The distinct and narrow peak indicates good crystallinity and purity, with no additional thermal transitions observed, confirming the thermal stability of the drug.

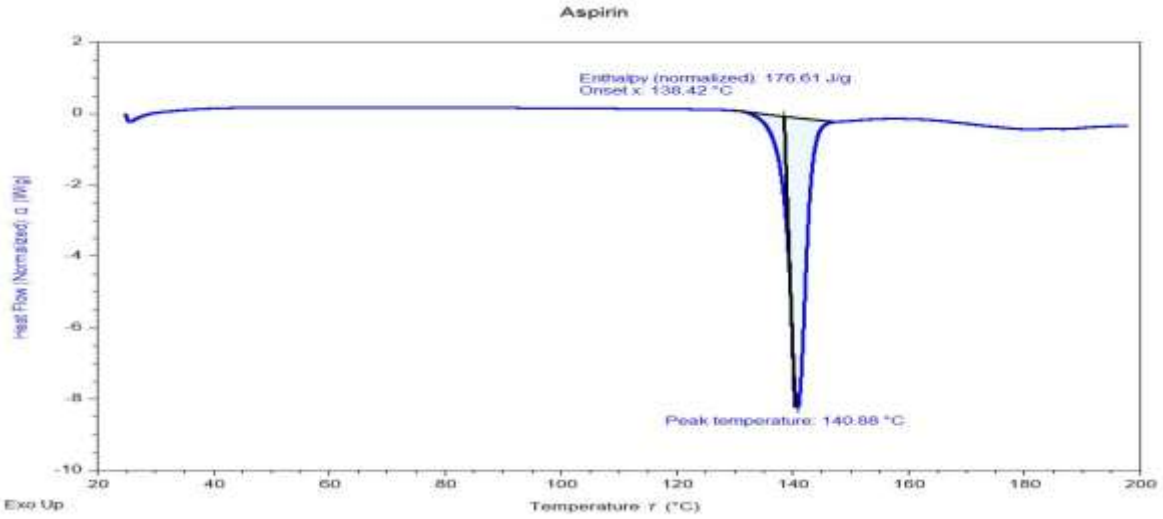

Fig no.9 (DSC graph of aspirin)

The DSC thermogram of sodium alginate displayed a broad endothermic peak with an onset at 44.62 °C and a peak temperature at 88.93 °C. The enthalpy change was recorded as 286.53 J/g. This broad peak is attributed to the loss of bound moisture and the amorphous nature of the polymer. The absence of a sharp melting peak indicates its non-crystalline structure and confirms its typical thermal behaviour as a hydrophilic polymer.

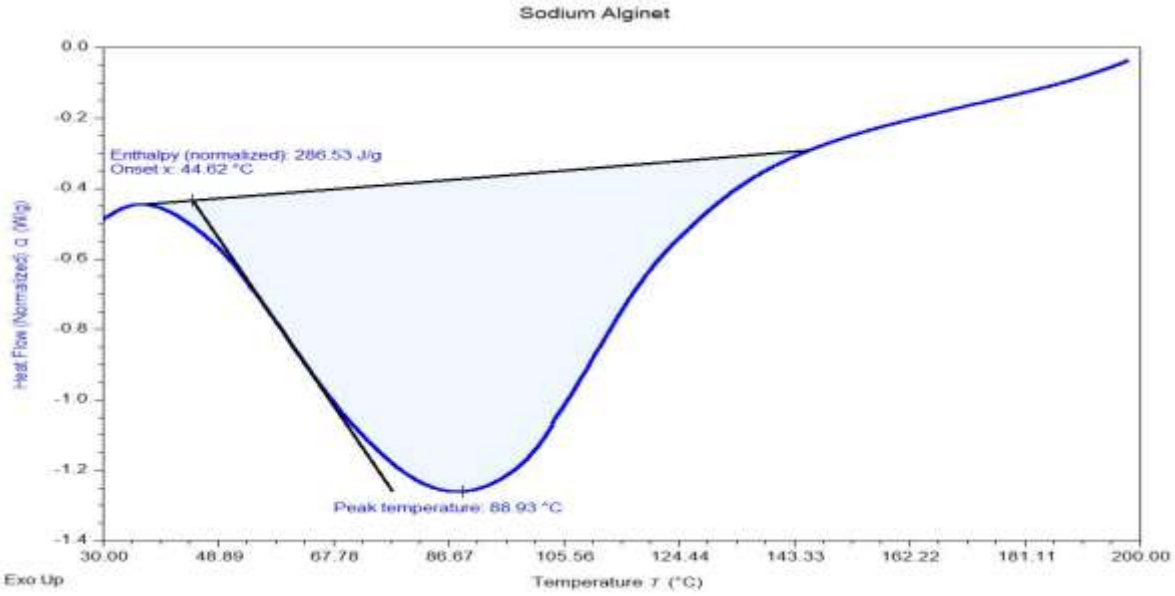

Fig no.10 (DSC graph of sodium alginate)

In the drug-loaded polymeric film, the characteristic melting peak of aspirin was either slightly shifted or reduced in intensity, suggesting partial amorphization or molecular dispersion of the drug within the polymer matrix. This confirms successful incorporation of aspirin into the sodium alginate network without degradation.[25]

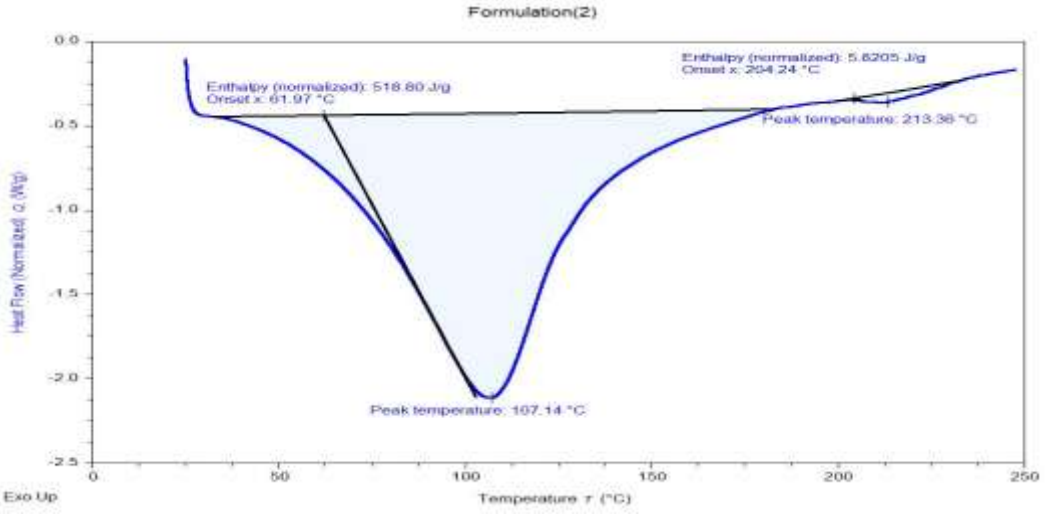

Fig no. 11 (DSC graph of formulation)

Scanning Electron Microscopy (SEM)

SEM analysis revealed that the surface of sodium alginate drug-loaded film showed a slightly rough surface with uniformly distributed drug particles embedded within the polymer matrix. No visible cracks or phase separation were observed, indicating good film integrity and uniform drug dispersion. The porous nature observed in the crosslinked film suggests potential for controlled swelling and drug release in colonic conditions.[4]

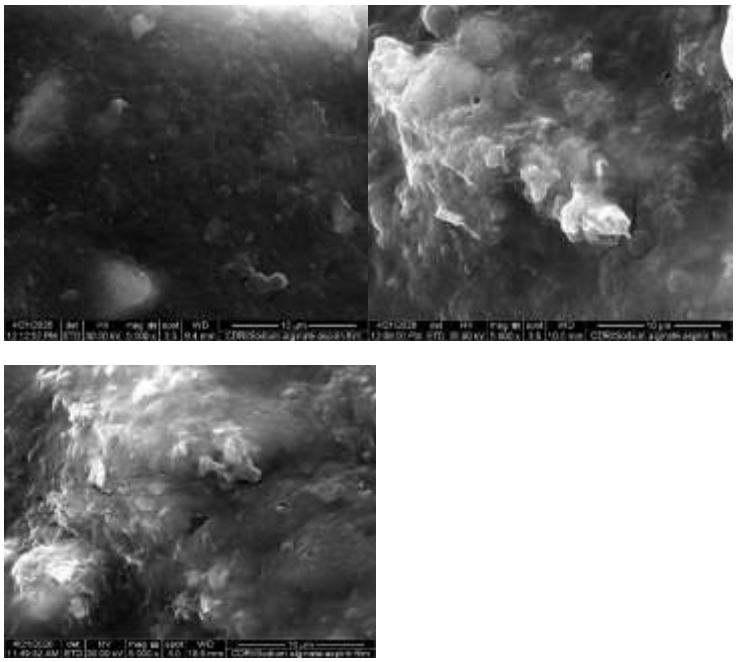

Fig no.12 (SEM images of film)

CONCLUSION

The present study successfully developed sodium alginate-based polymeric films for colon-targeted delivery of aspirin using a solvent casting and ionic crosslinking approach. The formulated films demonstrated desirable physicochemical properties, including uniform thickness, good flexibility, and satisfactory mechanical strength. Drug content analysis confirmed uniform distribution of aspirin, while swelling studies indicated a clear pH-dependent behaviour, with maximum swelling observed under colonic conditions.

In vitro drug release studies revealed minimal drug release in acidic and intestinal environments, followed by a sustained and significant release at colonic pH, confirming

effective site-specific delivery. Spectroscopic and thermal analyses (UV, FTIR, and DSC) verified the compatibility between aspirin and sodium alginate, with no evidence of chemical interaction or drug degradation. SEM analysis further supported uniform drug dispersion within the polymer matrix.

Overall, the findings suggest that sodium alginate-based polymeric films are a promising and efficient system for colon-targeted drug delivery, offering controlled release, improved drug stability, and reduced gastrointestinal side effects. This approach holds potential for enhancing the therapeutic efficacy of aspirin in the treatment of colonic inflammatory conditions.

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