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Formulation And Characterization of Lovastatin Tablets Enteric and Non-enteric Coated with Polymer Blends for Colon-specific Drug Release

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ABSTRACT
The study focused on developing a colon-specific drug delivery system for Lovastatin using β-cyclodextrin inclusion complexes and compression-coated tablets. The inclusion complexes were prepared via a kneading method, where Lovastatin was mixed with β-cyclodextrin in a 1:2 molar ratio. Core tablets were formulated using direct compression, incorporating Lovastatin, β-cyclodextrin, and excipients. These cores were subsequently coated with polymer blends of Inulin with either HPMC or Ethyl Cellulose to achieve colon-specific drug release. The swelling behaviour of the polymers was evaluated in an acidic medium, revealing that HPMC exhibited significant swelling, while Ethyl Cellulose formed a film-like layer. The phase solubility study indicated a 1:2 complex formation between Lovastatin and β-cyclodextrin, enhancing drug solubility. XRD and DSC analyses suggested a transition of Lovastatin to an amorphous state within the complex. Drug release studies demonstrated that selected formulations effectively protected the drug in the upper gastrointestinal tract and ensured release in the colon. This research highlights the potential of the developed system for targeted delivery of Lovastatin to the colon, which could improve therapeutic outcomes for conditions like hypercholesterolemia.

Keywords: *Colon-specific drug delivery, Lovastatin, Inclusion complex, Compression-coated tablets, β-cyclodextrin, Polymer swelling behaviour*

1. INTRODUCTION

The colon, particularly the initial segment of the lower intestine, is vulnerable to a wide range of pathological conditions. These include not only common issues like constipation but also more severe diseases such as Crohn's disease, ulcerative colitis, carcinomas, and various infections. These conditions can significantly affect the quality of life and may lead to serious health complications if not properly managed. The standard treatments for these conditions typically involve the use of anti-inflammatory drugs, chemotherapy agents, and antibiotics, all of which require precise delivery to the colon to be effective (Ashford and Fell, 1994). Delivering these treatments directly

to the colon ensures that the drugs reach the site of disease in effective concentrations, minimizing systemic side effects and improving therapeutic outcomes.

From a medical standpoint, it is not just about delivering any drug to the colon, but rather about delivering specific types of drugs that are best absorbed in this part of the gastrointestinal tract. These include sensitive compounds such as peptides and proteins, which are prone to degradation in the stomach and small intestine (Bai et al., 1995, Watts and Lllum, 1997). Additionally, vermifuges, which are used to expel parasitic worms, and diagnostic agents that help in identifying diseases, benefit from being released directly in the colon. The ability of the colon to absorb these drugs efficiently makes it an ideal site for targeted drug delivery. However, achieving the precise delivery of these drugs is challenging; it requires a formulation that can transport the drug through the upper gastrointestinal tract without any premature release, ensuring that the drug is released in the colon in sufficient concentrations to exert its intended effect.

Since the early 1980s, there has been a concerted effort by pharmaceutical companies and research institutions to develop drug delivery systems specifically designed to release their payload in the colon. These efforts have been driven by the need to improve the effectiveness of treatments for colon-related diseases and to expand the range of drugs that can be delivered orally (Ashford and Fell, 1994). Despite significant advancements, many of these developments have faced challenges. One of the primary obstacles has been the premature release of drugs before they reach the colon, which can significantly reduce their effectiveness and lead to unintended side effects. This issue has spurred ongoing research into more reliable and effective methods of colon-specific drug delivery.

Over the past two decades, the interest in oral drug delivery systems targeting the colon has grown considerably. This is due to several key advantages offered by such systems. One major benefit is the reduced dosing frequency, which enhances patient compliance and convenience. Additionally, colon-targeted delivery systems can achieve higher local drug concentrations, making them particularly effective for treating diseases of the large bowel, such as inflammatory bowel disease. Another significant advantage is the potential for chronotherapeutic drug delivery, where drugs are released in sync with the body's natural rhythms to maximize therapeutic effects and minimize side effects (Van den Mooter, 2006). Furthermore, these systems are well-suited for the delivery of peptides, proteins, and other drugs that are unstable in the harsh environment of the upper gastrointestinal tract.

To achieve colon-specific drug delivery, several strategies have been explored. These include systems that respond to the pH changes in the gastrointestinal tract, time-dependent systems that delay drug release until the colon is reached, and systems that are activated by the bacterial activity in the colon. Pressure-responsive systems, which release drugs in response to the pressure changes within the colon, have also been investigated (Yang et al., 2002, Liu et al., 2009, Singh, 2007). Moreover, researchers have explored combining these approaches to create more sophisticated systems. For example, pH-responsive systems that are also triggered by bacterial activity have shown promise, as have systems that combine time-controlled and microbial-triggered mechanisms (Ibekwe et al., 2008, Sinha et al., 2004). Among the various strategies, drug delivery systems that utilize natural polysaccharides degraded by colonic microflora have been particularly promising. These systems leverage the unique environment of the colon, where specific bacteria can break down polysaccharides, triggering the release of the drug at the targeted site.

In addition to these innovative approaches, advancements have also been made in the methods used to apply protective coatings to tablets designed for colon-specific drug delivery. Traditional dry powder-coating techniques (Pearnchob and Bodmeier, 2003) have been complemented by compression coating, which is especially useful for applying thicker coatings. Compression coating is advantageous because it allows for the application of thick coatings in a relatively short processing time, compared to liquid coating processes, which are often time-consuming and may involve the use of solvents that can compromise the stability of sensitive drugs. For example, hydroxypropyl methylcellulose acetate succinate (HPMCAS) has been used in compression-coated tablets intended for colonic drug delivery. These tablets have been shown to have an extended lag time after undergoing prior acid treatments, which helps ensure that the drug is released only when it reaches the colon, thereby improving the targeting and effectiveness of the treatment (Fukui et al., 2001).

Overall, the ongoing research and development in colon-specific drug delivery systems highlight the potential to significantly improve the treatment of various colon-related diseases. By continuing to refine these systems and explore new approaches, it is possible to achieve more effective, targeted, and patient-friendly therapies that can make a real difference in the management of chronic and debilitating conditions

The purpose of this study was to develop compression-coated tablets suitable to target the drug to the colon in the intact form for the effective treatment of colorectal cancer. Basically, lovastatin is a cholesterol lowering agent but research has shown that it induces apoptosis in colon cancer cells, so an attempt is being made to target lovastatin to colon for the prophylaxis of colorectal cancer. β-cyclodextrin was used to prepare inclusion complex of drug to increase the solubility of drug. Inulin, HPMC and ethyl cellulose are the three major components which were mainly used as a coating material. Inulin is a polysaccharide which is fermented by the colonic micro flora. HPMC and the ethyl cellulose are matrix forming materials. Inulin was mixed with HPMC and ethyl cellulose in different proportions. These mixtures were used as coating materials.

2. MATERIAL AND METHODS

2.1 Materials

Lovastatin was sourced from Glenmark Pharmaceuticals, Mumbai, India. Inulin was obtained from Sensus, The Netherlands. β-Cyclodextrin was provided by Universal Medicament Pvt. Ltd., Nagpur, India. Other excipients used included HPMC E 50, Sodium Lauryl Sulphate, and Talc, which were all procured from Loba Chemie Pvt. Ltd., Mumbai, India. Additionally, Ethyl Cellulose, Lactose, and Magnesium Stearate were supplied by S. D. Fine Chemicals Pvt. Ltd., Mumbai, India. All these materials were utilized as received, without any further modification or purification.

2.2 Methods

2.2.1 Preparation of inclusion complexes

Inclusion complexes of β-cyclodextrin and lovastatin were prepared using the kneading method in a molar ratio of 1:2. To achieve this, a mixture of methanol and water was used as the solvent system. Initially, a suspended solution of lovastatin was prepared and gradually added to a pre-prepared paste of β-cyclodextrin. The mixture was then subjected to continuous grinding for 2 hours, facilitating the interaction between lovastatin and β-cyclodextrin. During this process, solvent evaporation occurred, resulting in the formation of a solid powder. The solid was then pulverized to ensure uniformity and subsequently sieved through sieve no. 120# to obtain the final inclusion complex.

2.2.2 Preparation of tablet cores

The core tablets for the formulation were prepared using the direct compression method. Initially, all ingredients were passed through sieve no. 120# to ensure uniform particle size. The formulation for the lovastatin core tablets, with a diameter of 8 mm, included 40 mg of lovastatin, 80 mg of β-cyclodextrin, 70 mg of lactose, 4 mg of sodium lauryl sulphate, 4 mg of talc, and 2 mg of magnesium stearate. These ingredients were carefully blended and then subjected to direct compression using a Mini Press-II MT tablet press (Rimek). The direct compression method facilitated the efficient and consistent formation of the tablet cores.

2.2.3 Preparation of compression coated tablets

Compression-coated tablets were prepared by coating 8 mm diameter drug cores into 12 mm diameter tablets using blends of Inulin and HPMC, as well as Inulin and Ethyl Cellulose. For the Inulin and HPMC blend, the ratios used were 10:90, 20:80, 30:70, 40:60, 50:50, and 60:40, and these formulations were coded as IH1, IH2, IH3, IH4, IH5, and IH6, respectively. Similarly, another six batches of tablets were prepared with blends of Inulin and Ethyl Cellulose in the same ratios, and these were coded as IE1, IE2, IE3, IE4, IE5, and IE6. Each 200 mg core tablet was coated with 300 mg of the respective coating material. The process for preparing the compression-coated tablets involved filling half of the polymer powder into the die cavity of the tablet press. The 8 mm drug core tablet was then centrally positioned on this initial powder layer. The remaining half of the polymer powder was added on top of the core, ensuring even coverage. Finally, the compression was performed using a Mini Press-II MT tablet press (Rimek), resulting in 12 mm diameter coated tablets. This method ensured that the drug cores were effectively encapsulated within the polymer matrix, providing the desired controlled release characteristics (Fukui et al., 2001).

2.2.4 Swelling behaviour of polymers

To evaluate the swelling behaviour of the polymers, one gram each of hydroxypropyl methylcellulose (HPMC) and Ethyl Cellulose (EC) was placed into three separate graduated stoppered test tubes. The initial height of the solid layer formed by each polymer was measured and recorded. Subsequently, a measured volume of 0.1 N HCl was added to each test tube, after which the heights of both the solid and liquid layers were noted. The test tubes

were then incubated at a temperature of 37ºC to simulate physiological conditions. The experiment involved monitoring the changes in the height of the solid and liquid layers over time. These measurements were taken at 24-hour intervals to observe the extent of swelling and any other relevant changes in the polymer layers. This method allowed for a detailed assessment of the swelling behaviour of HPMC and Ethyl Cellulose in an acidic environment, which is critical for understanding their performance in drug delivery applications (Ibekwe et al., 2008, Sinha et al., 2004).

2.2.5 Phase solubility study

The phase solubility study of the prepared inclusion complex was conducted to assess the solubility behaviour of the drug in the presence of varying concentrations of β-cyclodextrin. In this study, an excess amount of the drug was added to vials containing 25 ml of distilled water (pH 7), with β-cyclodextrin concentrations ranging from 1 to 5 mmol. The vials were then subjected to continuous shaking at a constant temperature of 25°C using an incubator (KI-216, Khera Instruments Private Limited, India). After a 48-hour equilibration period, aliquots were carefully withdrawn from each vial and filtered through a 0.2 µm filter to remove any undissolved particles. The filtered samples were then analyzed using a UV-spectrophotometer (Shimadzu UV-1700, Japan) at a wavelength of 238 nm. A blank solution, prepared with the same concentration of β-cyclodextrin in water, was used as a reference for the spectrophotometric analysis (Fukui et al., 2001).

The apparent stability constant (Kc) of the inclusion complex, assuming a 1:1 stoichiometric ratio between the drug and β-cyclodextrin, was calculated from the phase solubility diagrams. This calculation provides insight into the binding affinity and stability of the inclusion complex, which is crucial for understanding its potential efficacy in drug delivery applications (Fukui et al., 2001).

$K_{1.1}$ = slope / S_0 (1- slope) (1)

2.2.6 X-ray Diffraction analysis of inclusion complex

The X-ray diffraction (XRD) analysis of the inclusion complex was conducted to examine its crystalline structure. Samples were scanned using an automated Philips Holland-PW 1710 X-ray diffractometer, operating at a power input of 35 kV and a current of 20 mA. The goniometer was set to a scanning speed of 1º per minute throughout the study to ensure consistent and accurate data collection. X-ray radiation was generated using a copper (Cu) filter, and the samples were scanned over an angular range of 5-60º on the 2θ scale. This range was selected to capture a comprehensive diffraction pattern, which would provide insights into the crystalline or amorphous nature of the inclusion complex. The resulting X-ray diffraction patterns were graphically recorded by the instrument, offering a detailed representation of the diffraction peaks corresponding to the sample's structure. These patterns are essential for determining whether the drug remains in a crystalline state or has transformed into an amorphous form upon complexation with β-cyclodextrin, which has significant implications for the drug's solubility and bioavailability (Ibekwe et al., 2008, Sinha et al., 2004).

2.2.7 Differential Scanning Calorimetry Study (DSC)

The Differential Scanning Calorimetry (DSC) study was conducted to analyze the thermal behaviour of the drug and its inclusion complexes with β-cyclodextrin. For this analysis, 5 mg of each sample—both the pure drug and the corresponding inclusion complexes—were placed into pierced aluminum containers. The DSC studies were performed using the METTLER TOLEDO SR SYSTEM. The samples were subjected to a controlled heating process under a static air atmosphere. The temperature range for the analysis was set from 20ºC to 400ºC, with a consistent heating rate of 10ºC per minute. During the DSC analysis, the heat flow associated with the thermal transitions of the samples was recorded. The peak temperature, which indicates the specific thermal events such as melting, crystallization, or decomposition, was determined. The DSC instrument was calibrated with standard materials to ensure the accuracy of the temperature measurements. The resulting thermograms provide valuable information regarding the thermal stability and interactions within the inclusion complexes, which are critical for understanding their behaviour in various pharmaceutical applications.

2.2.8 Fourier Transforms Infrared (FT-IR) spectroscopy

Fourier Transform Infrared (FT-IR) spectra of the samples were obtained using a JASCO FT-IR-4100 type A spectrometer. To prepare the samples for analysis, a thin film was created using the press pellet technique, where 2 mg of the sample was finely ground and mixed with 200 mg of potassium bromide (KBr) to form a KBr disc. The scanning range for the FT-IR analysis was set from 400 cm^{-1} to 4000 cm^{-1}, allowing for the detection of various functional groups and molecular interactions within this broad spectrum. The resolution of the

spectrometer was maintained at 4 cm^{-1} to ensure precise and detailed spectral data. The resulting FT-IR spectra provide insights into the molecular structure and potential interactions between the drug and β-cyclodextrin in the inclusion complex. By analyzing the characteristic absorption bands, it is possible to identify specific functional groups and assess any shifts or changes that may indicate successful complexation or other chemical modifications.

2.2.9 Hardness test

A tablet was placed between the two anvils of a hardness tester (Tablet Tester, Campbell, Mumbai). Force was gradually applied to the anvils until the tablet reached its breaking point. The crushing strength, which is the amount of force required to cause the tablet to break, was then recorded. This measurement is critical for assessing the mechanical integrity of the tablet and ensuring it can withstand handling and transportation without breaking apart.

2.2.10 Friability test

Ten tablets were initially weighed and then placed in the friabilator (C-FT 10/20, Thermonik, Campbell Electronics). The friabilator was operated at a speed of 25 rpm for 4 minutes, during which the tablets were subjected to repeated drops from a height of several inches with each revolution. After the operation, the tablets were reweighed, and the percentage friability was calculated. This calculation is used to determine the tablets' ability to resist abrasion and breaking during handling and transportation, ensuring their durability and integrity.

2.2.11 Drug release

The drug release profile was evaluated using a paddle apparatus (USP XXIII) model (TDR-06, Tab Machine, Mumbai, India) under controlled conditions. The experiment was conducted at a rotational speed of 100 rpm, with the temperature maintained at 37ºC. The dissolution medium used was 900 ml of 0.1 N HCl (pH 1.0) for the initial 2 hours, followed by a medium change to Sorensen's phosphate buffer (pH 7.4) to simulate gastrointestinal conditions. The drug release was quantified using High-Performance Liquid Chromatography (HPLC) equipped with a Phenomenex C18 column. Specifically, the stationary phase consisted of a Phenomenex Luna C18 column (250 mm × 4.6 mm i.d., 0.5 µm particle size). The mobile phase used was a mixture of acetonitrile and triethylamine buffer, with a solvent ratio of 5:25. The flow rate was set at 1.1 ml/min, and the detection wavelength was 238 nm. This method allowed for the precise measurement of the drug release from the formulation, ensuring accurate monitoring of the release profile as the medium transitioned from an acidic environment (pH 1.0) to a more neutral pH (7.4), reflecting the conditions from the stomach to the intestines (Ibekwe et al., 2008, Sinha et al., 2004).

2.2.12 Drug release in presence of the rat caecal content

To evaluate the susceptibility of inulin coatings to the enzymatic activity of colonic bacteria, drug release studies were extended using rat caecal content. The experiment was conducted in 100 ml of pH 6.8 phosphate-buffered saline (PBS), which contained 4% w/v of rat caecal contents. This setup was placed in a paddle apparatus (USP XXIII) model (TDR-06, Tab Machine, Mumbai, India), operated at 100 rpm and maintained at a temperature of 37ºC. To enhance the solubility of the drug during the analysis, a slight modification was made by adding 1 ml of acetonitrile to the samples. After this addition, the samples were centrifuged to separate the solid and liquid phases. The supernatant was then carefully filtered through a 0.45 µm membrane filter to remove any particulate matter. The filtered solution was subsequently analyzed to determine the lovastatin content, allowing for the assessment of drug release in the presence of rat caecal content, which simulates the enzymatic conditions within the colon. This approach is particularly useful for understanding how inulin-based coatings behave in the gastrointestinal tract, especially in the presence of the colonic microflora, which plays a crucial role in the degradation of polysaccharide-based coatings, thereby triggering drug release

3. RESULT AND DISCUSSION

The swelling study revealed that hydroxypropyl methylcellulose (HPMC) exhibited significant swelling, reaching a maximum of 152.63% after 72 hours. In contrast, ethyl cellulose (EC) displayed minimal swelling, with only 111.76%, and primarily formed a film-like layer. These findings suggest that in colon-targeted formulations, HPMC is likely to swell and create a matrix-like structure that can effectively control the drug release rate. On the other hand, ethyl cellulose is expected to form an insoluble film, which also plays a crucial role in modulating the drug release rate from these formulations.

The phase-solubility diagram for the inclusion complex between lovastatin and β-cyclodextrin (as illustrated in Figure 1) demonstrated that the aqueous solubility of lovastatin increases linearly with the concentration of β-cyclodextrin. The linear relationship observed, with a slope of less than 1, indicates the formation of a 1:2 complex between lovastatin and β-cyclodextrin. The apparent stability constant (Kc) for this complex was calculated from the slope of the linear phase-solubility diagram and was found to be 0.3346 $mmol^{-1}$. A Kc value in the range of 200-5000 $mmol^{-1}$ is generally considered optimal for enhancing the bioavailability of poorly soluble drugs, suggesting that the inclusion complex formed here could potentially improve the solubility and, consequently, the bioavailability of lovastatin.

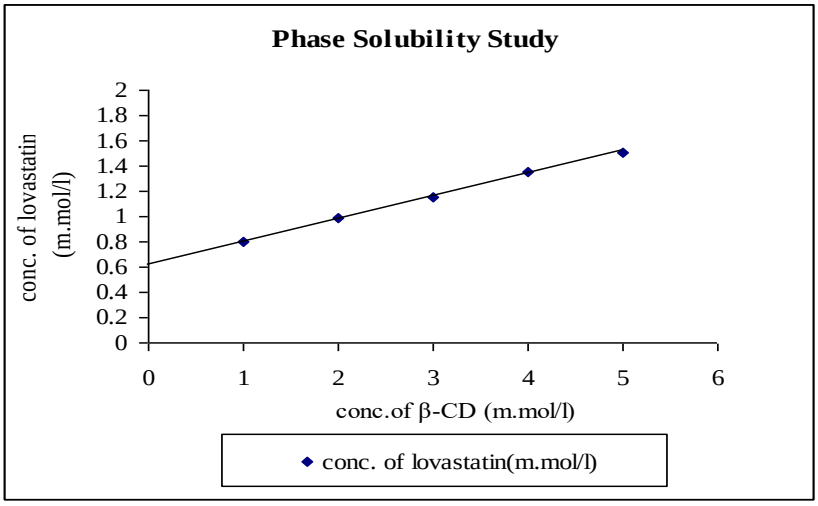


Figure 1. Phase Solubility Diagram of Lovastatin

The results of the X-ray Diffraction (XRD) analysis, as shown in Figures 2a, 2b, and 2c, indicated a noticeable reduction in both the peak intensity and the number of peaks in the inclusion complex compared to the spectra of the pure drug and β-cyclodextrin. These observed changes suggest that a phase transition occurred during the formation of the complex. Specifically, the reduction in crystalline peaks implies that lovastatin, which was originally in a crystalline form, transitioned to an amorphous state within the complex. This transformation to the amorphous form is significant, as it often correlates with enhanced solubility and potentially improved bioavailability of the drug.

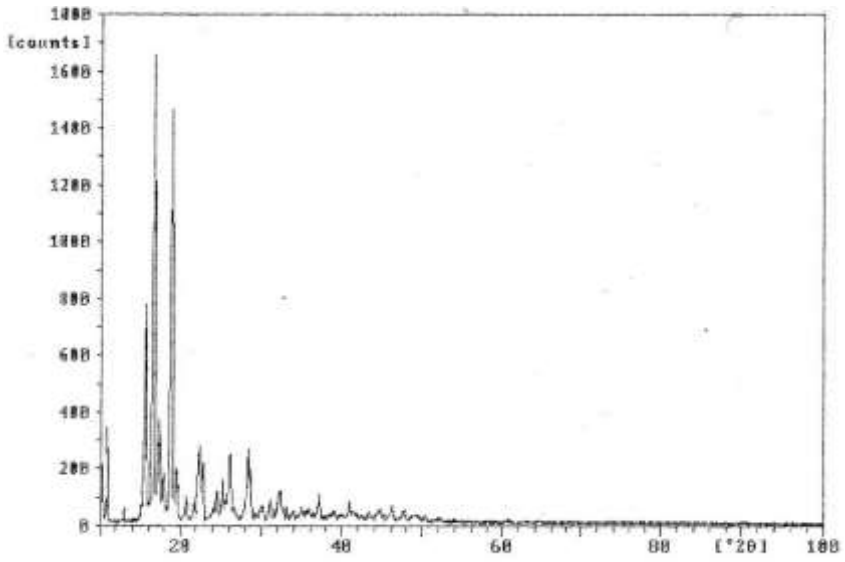


Figure 2a. X-Ray Diffraction pattern of Lovastatin.

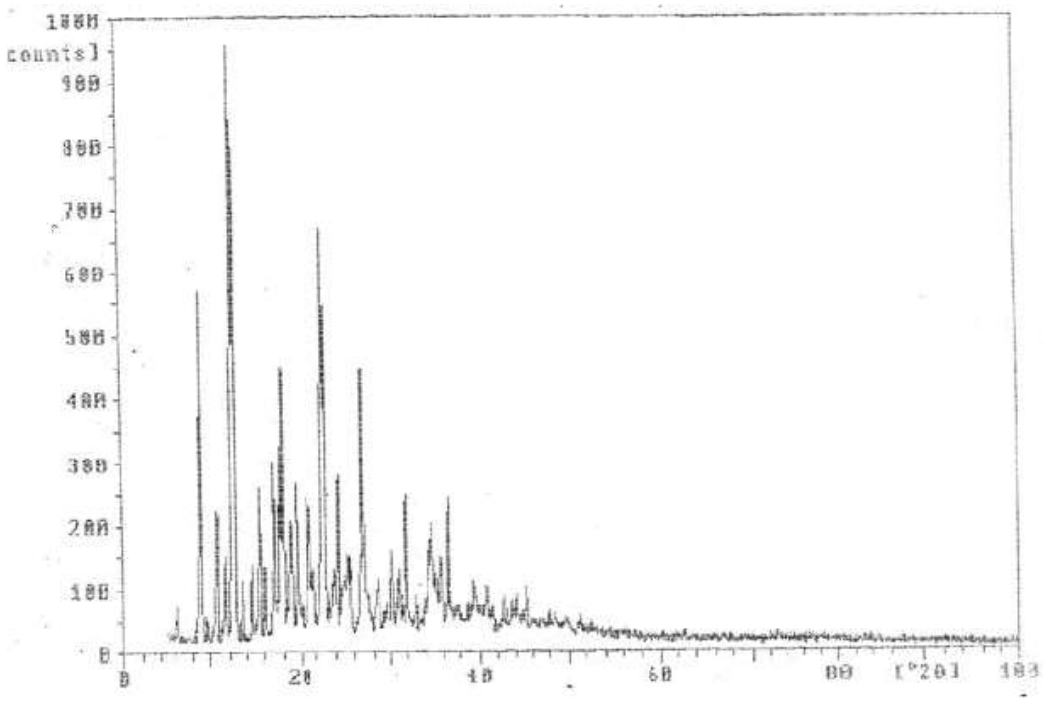


Figure 2b. X-Ray Diffraction pattern of β-Cyclodextrin.

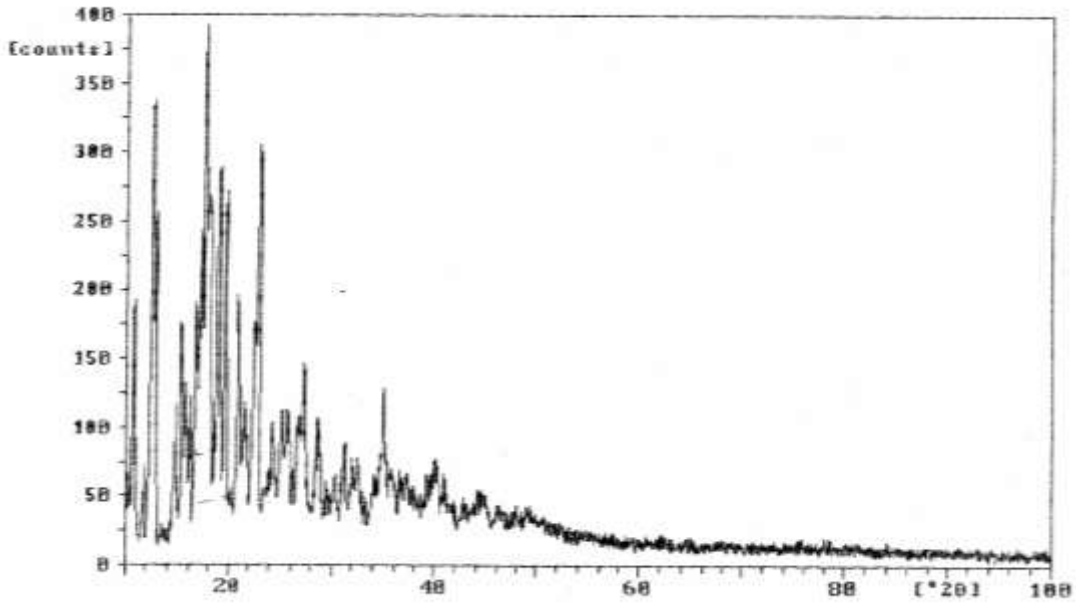


Figure 2c. X-Ray Diffraction pattern of Inclusion Complex.

The DSC thermogram (Figures 3a, 3b, and 3c) of the complexes revealed that the endothermic peak characteristic of lovastatin persisted in the complex prepared by the kneading method. However, in the inclusion complex, the endothermic peak of lovastatin, which is typically observed in the range of 170-175ºC in pure lovastatin (specifically at 171.7ºC), was notably absent. This absence of the endothermic peak in the complex suggests that lovastatin underwent a partial transition to an amorphous state. Furthermore, this observation indicates that lovastatin has likely been encapsulated within the β-cyclodextrin cavity, which interferes with the crystallinity of the drug, further supporting the formation of an inclusion complex where the drug is partially amorphous.

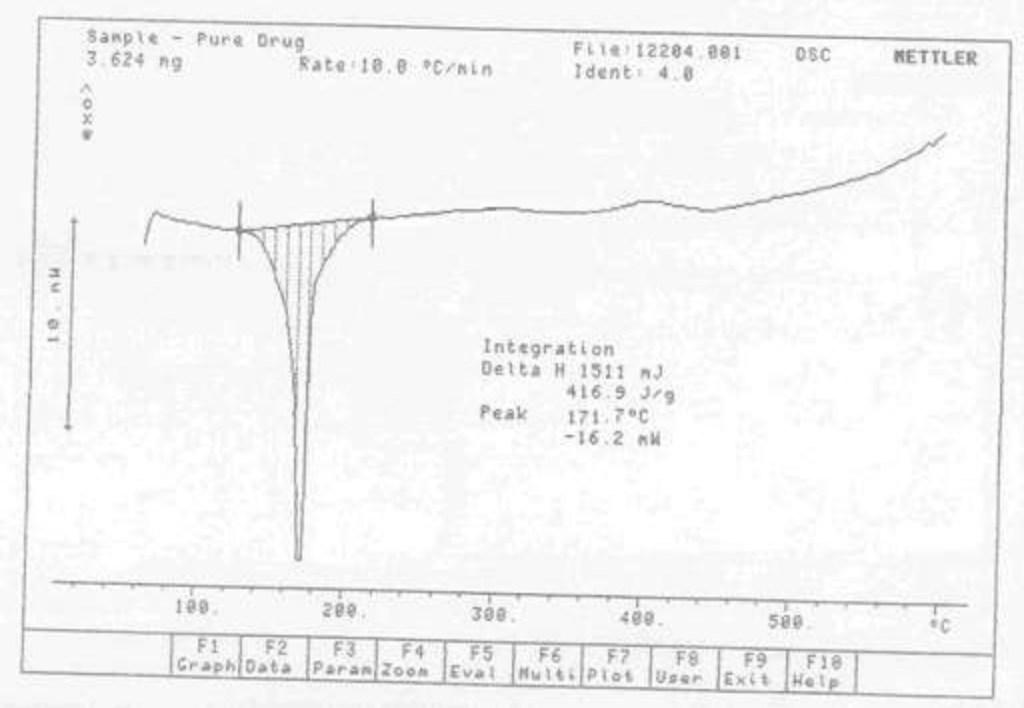


Figure 3a. DSC Thermogram of lovastatin

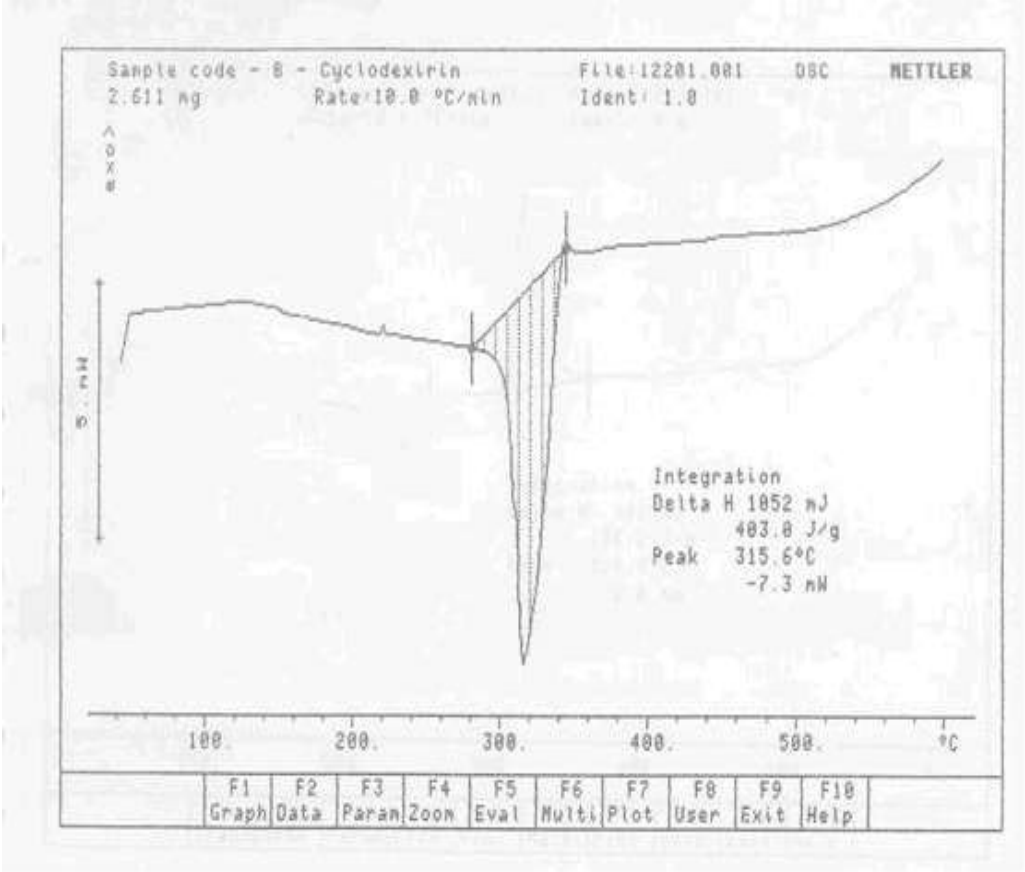
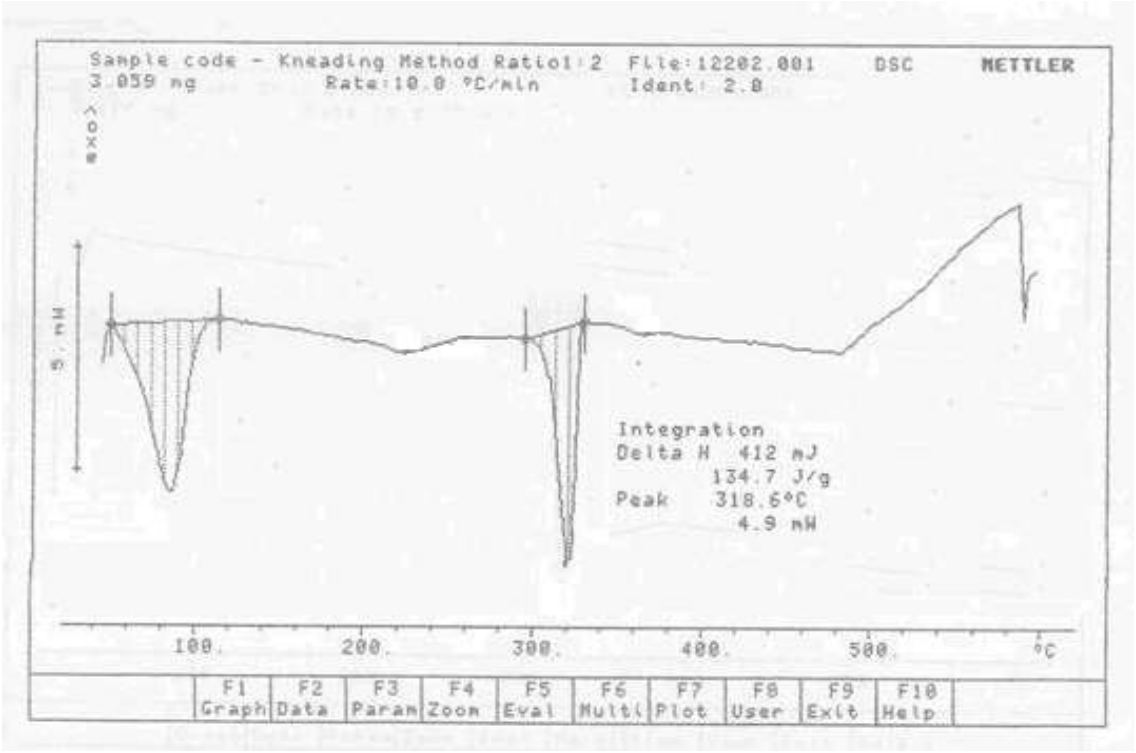


Figure 3b. DSC Thermogram of β-Cyclodextrin



The FT-IR spectrum (Figures 4a, 4b, and 4c) of the complex prepared using the kneading method was analyzed and compared with the spectrum of pure lovastatin. During this comparison, the presence or absence of characteristic peaks corresponding to specific functional groups within the lovastatin molecule was carefully examined. The results indicated that the characteristic peaks of lovastatin remained largely unchanged in the spectrum of the inclusion complex. This suggests that no well-defined chemical interactions occurred between β-cyclodextrin and lovastatin during the kneading process. Therefore, the inclusion complex formation likely involved physical encapsulation of the drug within the β-cyclodextrin cavity rather than the formation of new chemical bonds.

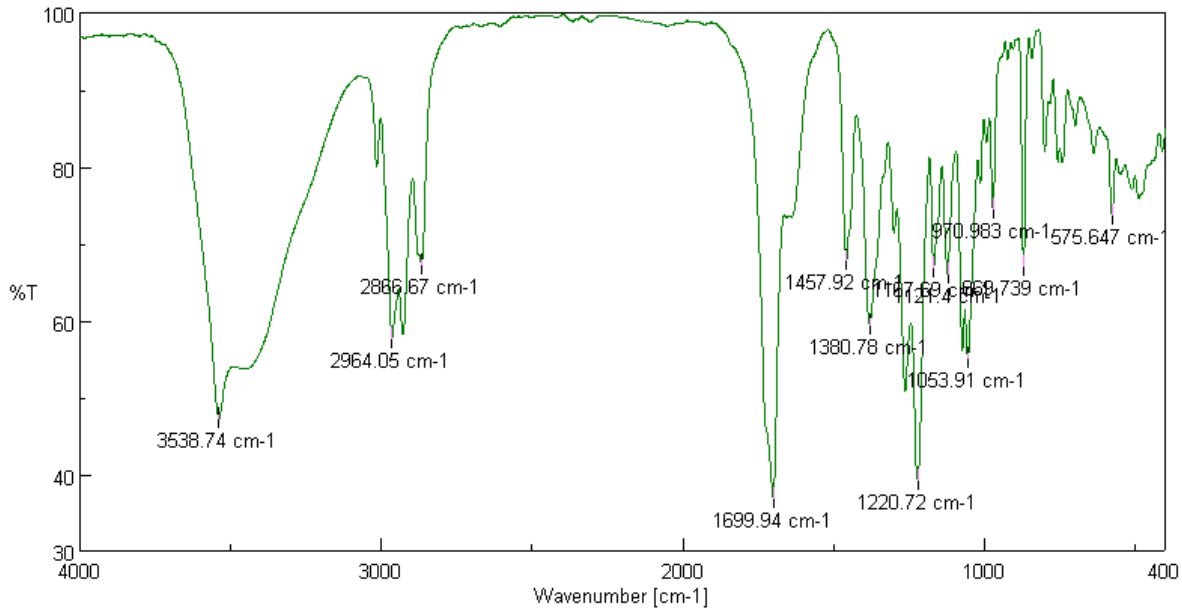


Figure 4a. FT-IR spectra of lovastatin.

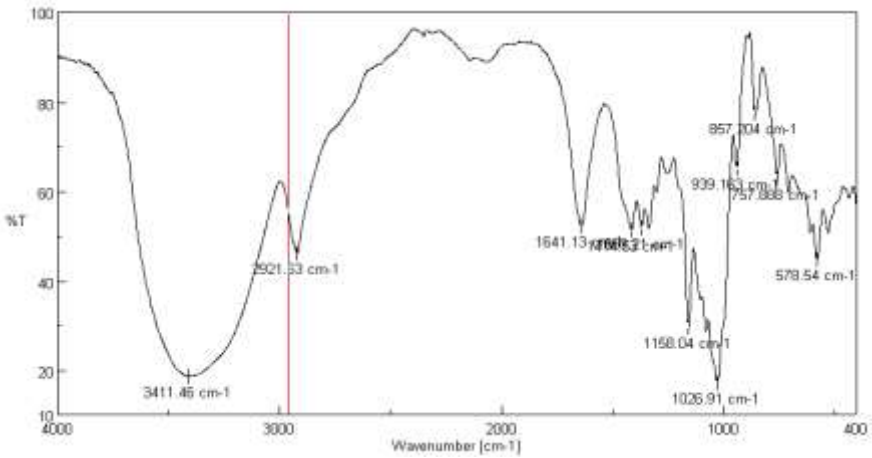


Figure 4b. FT-IR Spectra of β-cyclodextrin

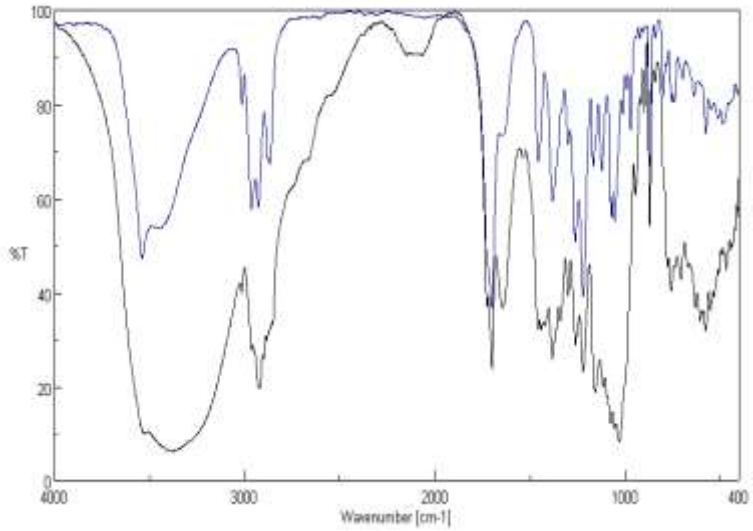


Figure 4c. Overlay spectra of complex and lovastatin.

The drug release study for the uncoated drug cores revealed that they achieved an 85.55% release of the drug within 90 minutes, significantly higher compared to the 30.68% release observed with the pure drug over the same period (Figure 5). This indicates that, in an optimal scenario, a satisfactory drug release could be expected after the erosion of the coating in intestinal fluids. Additionally, the core tablets exhibited a friability of 0.65% and a hardness of 5-6 Kg/cm², demonstrating sufficient mechanical strength to withstand physical abrasion during handling and processing. Following the preparation of the core tablets, they were coated with different ratios of coating material using the direct compression method. The resulting compression-coated tablets showed friability values ranging from 0.17% to 0.93% and hardness between 3.5 and 7 Kg/cm², indicating that these tablets also possessed adequate mechanical integrity. The various formulations of the compression-coated tablets were subsequently subjected to a drug release study. The study was conducted for 2 hours in 0.1 N HCl to simulate the average gastric emptying time of 2 hours (Figures 6a and 6b). The dissolution medium was then replaced with Sorensen's phosphate buffer at pH 7.4, and the study continued for an additional 3 hours to mimic the average small intestinal transit time (Figures 6c and 6d).

Based on the initial drug release results, the formulations IH1, IH2, IH6, IE1, IE2, and IE6 were excluded from further testing in the presence of rat caecal content. These formulations exhibited drug release percentages of 47.42%, 42.8%, 38.95%, 50.53%, 39.43%, and 39.17%, respectively, within the first 5 hours and were not even intact after this period. On the other hand, the formulations IH3, IH4, IH5, IE3, IE4, and IE5 demonstrated much lower drug release within the first 5 hours, with values of 8.49%, 11.56%, 23.62%, 15.65%, 12.23%, and 22.91%,

respectively. Among these, IH5 and IE5 were partially intact, while the formulations IH3, IH4, IE3, and IE4 remained fully intact. Due to their favorable performance, these formulations were selected for further investigation in the presence of rat caecal content to assess their potential for colon-specific drug delivery.

The release study of the compression-coated tablets in a rat caecal content medium was conducted over a period of 4 hours (Figure 7). A successful colon-targeted drug delivery system must not only protect the drug from premature release in the physiological environment of the upper gastrointestinal tract but also ensure effective drug release once it reaches the colon. For this purpose, the formulations that remained intact during the initial testing were selected for further evaluation in pH 6.8 phosphate-buffered saline (PBS) containing 4% w/v of rat caecal contents. This medium simulates the enzymatic conditions present in the colon, where specific enzymes from the colonic bacteria can trigger the release of the drug. Upon continuing the studies in the rat caecal content medium, the formulations IH3 and IE4 demonstrated significant drug release, with 76.89% and 77.58% of the total drug being released, respectively. These results suggest that these formulations are capable of protecting the drug through the upper gastrointestinal tract and effectively releasing it in the colonic environment, making them promising candidates for colon-targeted drug delivery

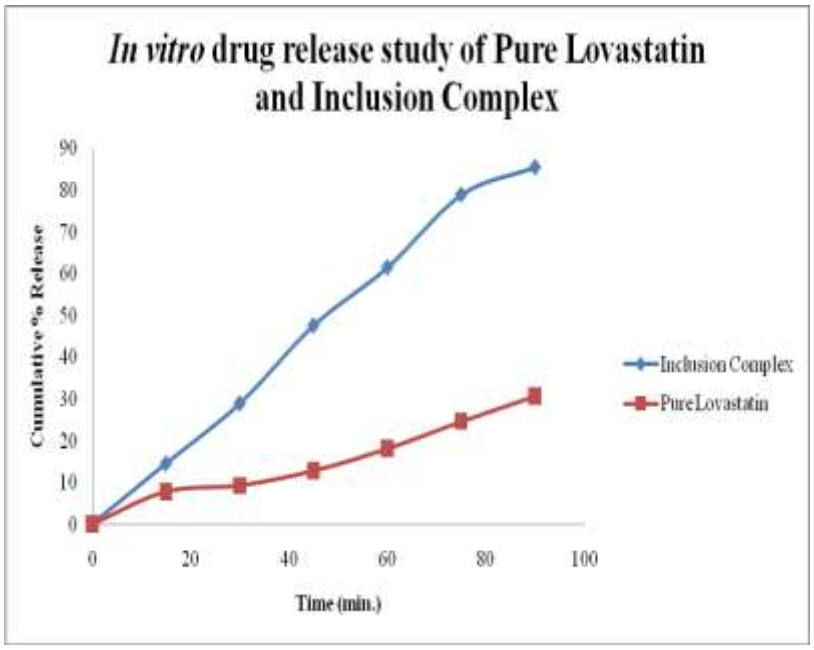


Figure 5. *In vitro* drug release study of lovastatin and inclusion complex.

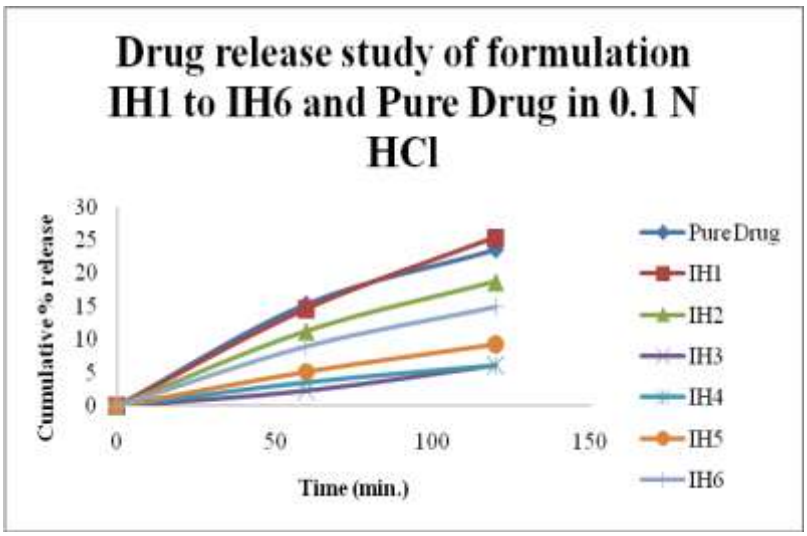


Figure 6a. Drug release study of formulation IH1 to IH6 and Pure Drug in 0.1 N HCl

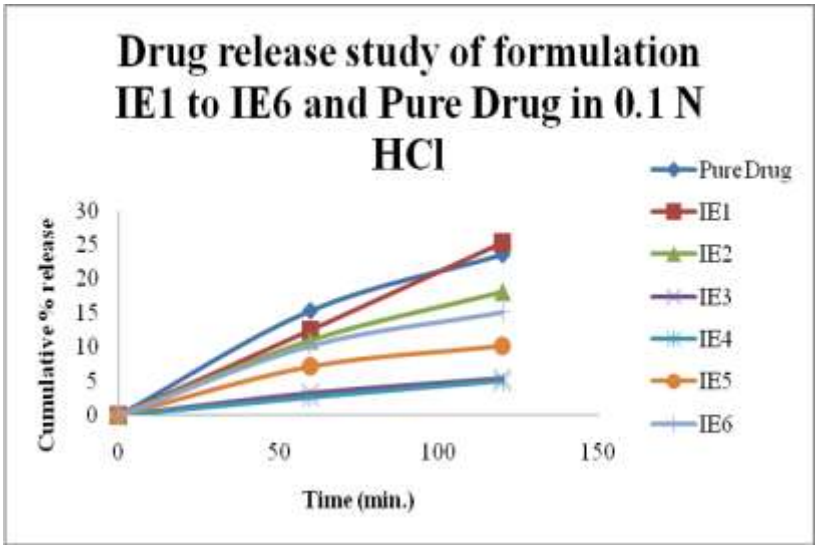


Figure 6b. Drug release study of formulation IE1 to IE6 and Pure Drug in 0.1 N HCl

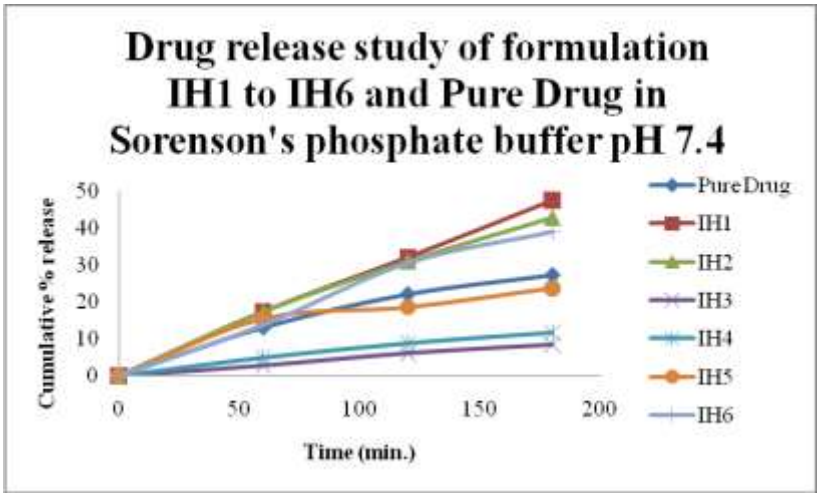


Figure 6c. Drug release study of formulation IH1 to IH6 and Pure Drug in Sorenson's phosphate buffer pH 7.4

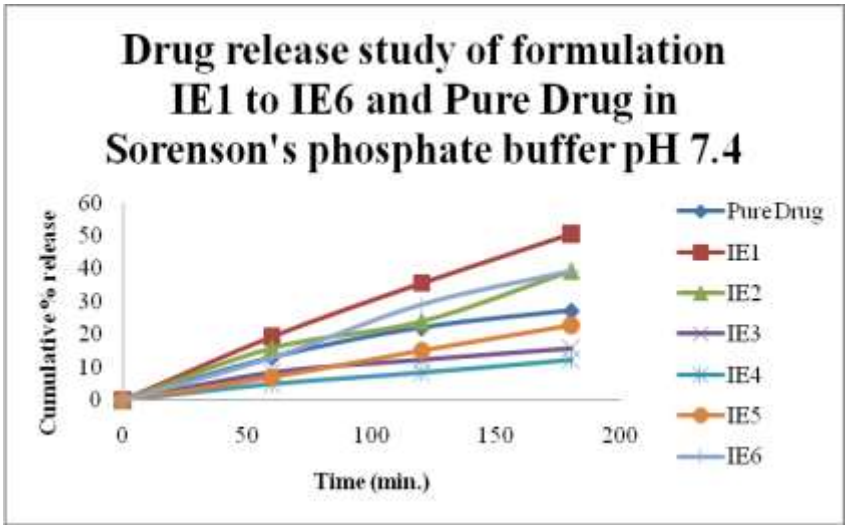


Figure 6d. Drug release study of formulation IE1 to IE6 and Pure Drug in Sorenson's phosphate buffer pH 7.4

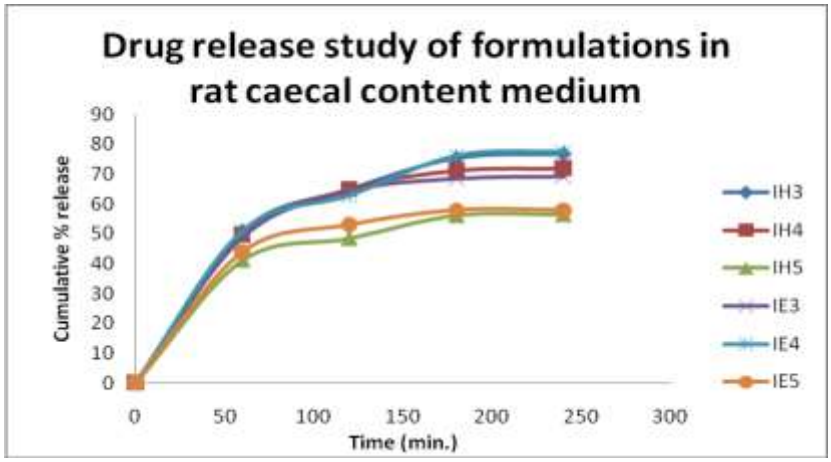


Figure 7. Drug release study of formulations in presence of rat caecal content.

4. CONCLUSION

In conclusion, the tablet formulations compression-coated with blends of Inulin and HPMC [batch IH3 (30:70)] and Inulin and Ethyl Cellulose [batch IE4 (40:60)] emerged as the optimized formulations for a colon-targeted drug delivery system for lovastatin. These formulations demonstrated promising results by ensuring no drug release in the acidic environment of the lower pH media, while allowing for rapid and targeted drug release in the higher pH environment of the colon. This selective release profile is particularly beneficial for the prophylaxis of colorectal cancer, as it maximizes the delivery of lovastatin directly to the colon, where it can exert its therapeutic effects most effectively.

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