# Formulation and Evaluation of solid dispersion based suppositories

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*Abstract :* Mesalamine (5-aminosalicylic acid) is widely used in the treatment of inflammatory bowel diseases, particularly ulcerative colitis. However, its poor aqueous solubility and limited rectal retention can reduce its therapeutic effectiveness when formulated in conventional suppositories. The present study aims to **formulate and evaluate solid dispersion based mesalamine suppositories** in order to enhance drug solubility, dissolution rate, and local therapeutic action.

Solid dispersions of mesalamine were prepared using hydrophilic carriers such as polyethylene glycol (PEG 4000/6000) and polyvinylpyrrolidone (PVP K30) by fusion and solvent evaporation techniques. These solid dispersions were incorporated into suitable suppository bases like cocoa butter and PEG base by the fusion method. The prepared suppositories were evaluated for physical appearance, weight variation, drug content uniformity, hardness, melting point, liquefaction time, and in-vitro drug release using appropriate dissolution media.

The results indicated that solid dispersion based mesalamine suppositories showed significantly improved dissolution and drug release profiles compared to conventional mesalamine suppositories. This study concludes that solid dispersion is an effective strategy to improve the bioavailability and therapeutic efficacy of mesalamine in rectal delivery systems for the management of ulcerative colitis.

**Keywords: suppositories**, polyvinylpyrrolidone, cocoa butter, uv spectroscopy , PEG, mesalamine

**INTRODUCTION**

## Inflammatory Bowel Disease (IBD)

Inflammatory bowel disease is usually characterized as Crohn's disease and Ulcerative colitis which involves spontaneous and uncontrolled inflammation of intestinal mucosa. Ulcerative colitis was first described by the London physician, Sir Samuel Wilksin 1859, in which the inflammation was restricted to the colon. Crohn's disease was first observed by the German surgeon Wilhelm Fabryin 1623, and later described and named after the New York physician Dr. Burril B. Crohn, in which any part of gastrointestinal tract (GIT) can be affected. Recently, global prevalence of IBD has been reached to 36.9 per million persons.2 The incidence and prevalence of IBD are increasing with time and in different regions around the world, indicating its emergence as a global disease.3 Over 1 million people in the United States are affected with IBD. IBD is seen in all races and ethnic groups throughout the world, with the highest prevalence in North America and Europe. The onset of IBD is verifiably associated with a complex and elusive interaction between genetic and environmental factors, such as oral contraceptive use, breastfeeding, infections, microbial agents, smoking, appendectomy, sanitation and stress. The clinical picture of Crohn's disease and ulcerative colitis is associated with a variety of intestinal complaints, such as bloody diarrhoea, fever, weight loss, abdominal pain or vomiting.

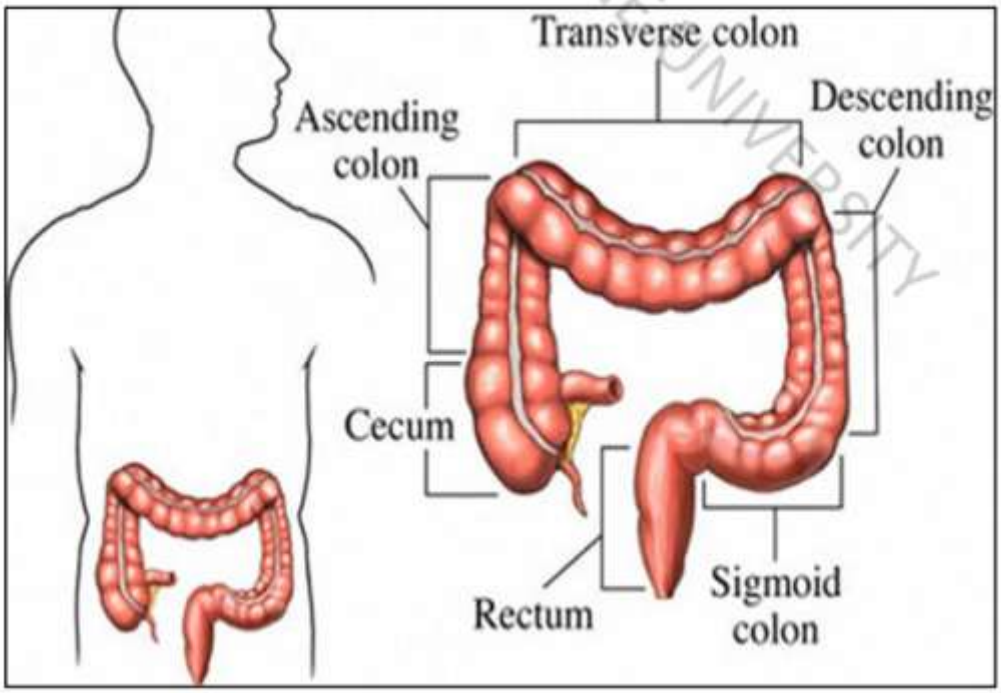



**Figure Location of the colon in the**

## Crohn's disease

Crohn's disease is a chronic inflammatory bowel disease (IBD) that causes inflammation in the digestive tract. It can affect any part of the digestive system, but it most commonly affects the small intestine and the beginning of the large intestine. The symptoms of Crohn's disease can vary, depending where and how severe your inflammation is. The most common symptoms include diarrhea, cramping and pain in your abdomen and weight loss. There is no cure for Crohn's disease, but treatments can decrease inflammation in the intestines, relieve symptoms, and prevent complications. Treatments include medicines, bowel rest, and surgery.

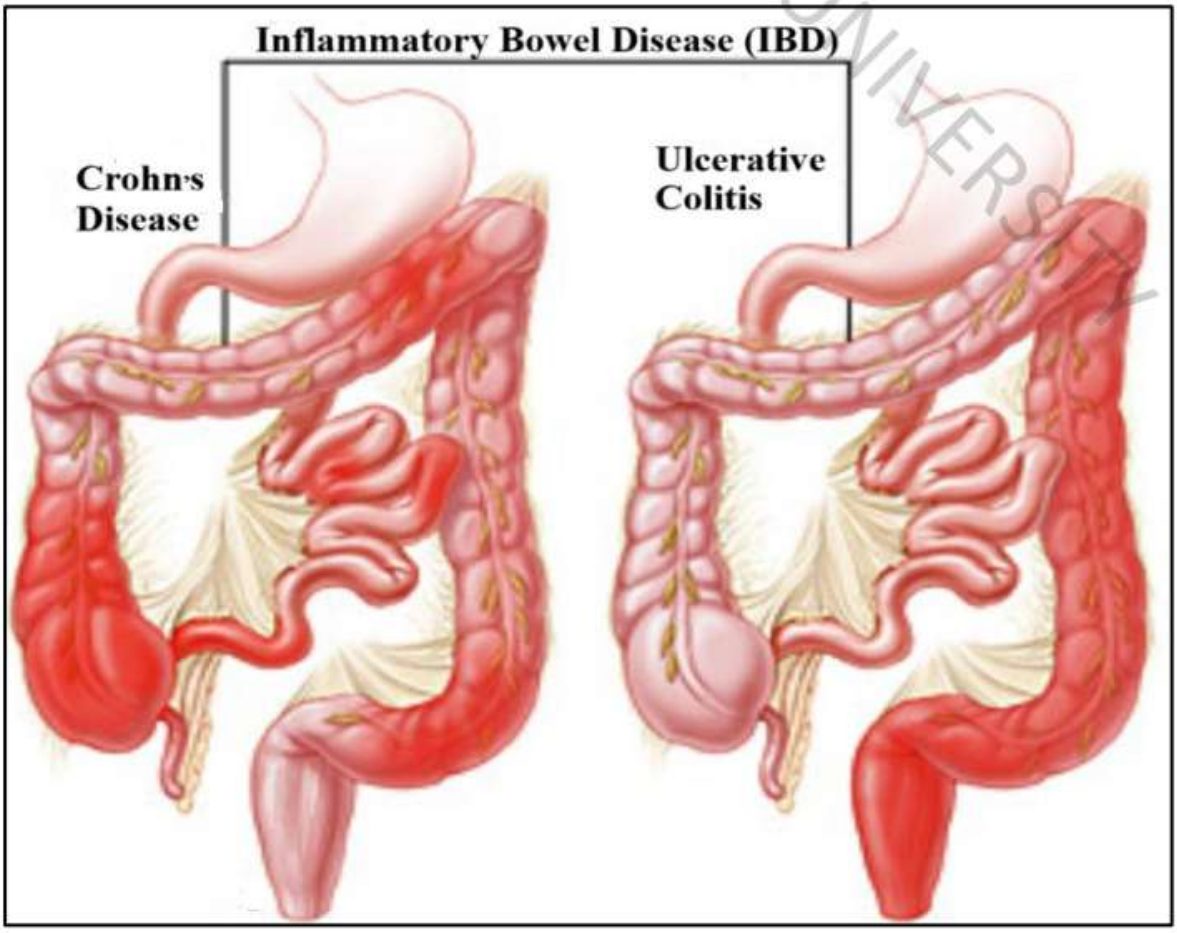



**Figure : Anatomic distribution of Crohn's disease and ulcerative colitis.**

## Ulcerative Colitis

Ulcerative colitis is an idiopathic, chronic inflammatory disorder of the colonic mucosa, which starts in the rectum and generally extends proximally in a continuous manner through part of, or the entire colon. Ulcerative colitis always starts in the rectum, and approximately one third of patients have disease occurring in the rectum alone, referred to as proctitis. Typically, rectal therapies are mainly considered for patients with proctitis, proctosigmoiditis and left-sided colitis. In cases where ulcerative colitis involves the entire colon, rectal therapy can still be an appropriate choice because the disease is often most severe in the rectum.

## Rectal Drug Delivery System

Rectal therapy means medication administered rectally, and includes enemas, foams, and suppositories. Rectally administered preparations are poorly absorbed and deliver high levels of medication directly to the intended site of action, thus minimizing systemic effects. Rectal drug delivery is pivotal when the oral medication is not possible. Rectal route offers potential advantages for drug delivery, they include: rapid absorption of many low molecular weight drugs, partial avoidance of first pass metabolism, potential for absorption into the lymphatic system, possibility of rate controlled drug delivery and absorption enhancement. 15,16 The rectal dosage forms are not common because of cultural and psychological bases, but there are several advantages to administer the drug by rectal route. In cases of nausea and vomiting act of taking medication orally may induce emesis so that drug is vomited before it is absorbed. Irritation to the stomach and small intestine associated with certain drugs can be avoided. Hepatic first pass elimination of high clearance drug may be avoided partially. Contact with digestive fluid isavoided, thereby preventing acidic and enzymatic degradation of some drug. The rectal absorption of drugs have also appeared in the US and Japan where suppositories had not been previously well accepted. The rectum is an interesting area for drug absorption because it is not buffered and has a neutral pH. It also has very little enzymatic activity, thus enzymatic degradation does not occur. The rectal mucus is more capable of tolerating various drug related irritations than the gastricmucosa.

## Advantages of Rectal Administration

**1 Targeted Delivery:** It delivers the drug directly to the site of inflammation in the lower GI tract, leading to localized effects with a lower risk of systemic side effects.

**2 Reduced Systemic Exposure:** Due to the first-pass metabolism and the targeted route of delivery, systemic absorption is minimized, leading to fewer side effects compared to oral formulations.

## Suppositories

Drug treatment for various ano-rectal conditions has been known since ancient times. Suppositories are one of the very feasible modes of administration for medication. Suppositories are a medicated solid dosage form intended for insertion into the body orifices. The term suppositories have its origin in Latin and means, "to place under". Suppositories are a very feasible mode of administration for medication. The medicament is incorporated into a base, which either melts at body temperature or dissolves in the mucus secretions and exerts localized or systemic action.

Suppositories have been employed for three reasons, to (1) promote defecation, (2) introduce drugs into the body, and (3) treat anorectal diseases. Suppositories generally consist of an active drug incorporated into an inert matrix, which may be either a rigid or semi-rigid base. This mixture of the drug and inert matrix must be formulated to be free of any interactions between the two to avoid any alteration either of the active or the inert matrix. After administration, the role of the suppository is to release the drug, either by melting due to body temperature or by dissolving in the local mucosal fluids, and then to release the active ingredient so it is free to produce a local effect or to move to the mucosal barriers into the circulatory system to produce a systemic effect. Rectal suppositories intended for localized action are most frequently used to relieve constipation or pain, irritation, itching, and inflammation associated with hemorrhoids or other anorectal conditions. Drugs to be used in suppository dosage forms must be posses good bioavailability for systemic effect.

### NEED OF THE STUDY.

Mesalmine is BCS Class IV drug, slightly soluble in water. It is first line treatment for ulcerative proctitis. Therapeutic effect of mesalamine is obtained through a local effect on the mucosa rather than by a systemic effect. Problem encountered during the oral administration of mesalamine tablets is that when this dosage form reaches the colon or rectum, it is covered with solid stool and is expelled rapidly from the colon. The clinical aim, therefore, is to maximize delivery of the mesalamine to the colonic mucosa, while minimizing systemic absorption. Mesalamine suppositories induces more prompt and superior clinical, and histologic improvements compared with mesalamine tablets in patients with ulcerative proctitis. Topical therapy delivers a high dosage of the active compound

To formulate and evaluate **mesalamine solid dispersion-based rectal suppositories** for improved solubility, dissolution rate, and local therapeutic efficacy in the treatment of ulcerative colitis.

- Oral mesalamine formulations show **incomplete drug delivery** to the distal colon.
- Poor solubility and limited absorption result in **reduced bioavailability**.
- Rectal suppositories can **target local inflammation directly**, improving effectiveness.
- Solid dispersion can **enhance the solubility and dissolution rate** of mesalamine.
- The combination of both approaches can lead to **optimized local delivery with minimal systemic side effects**.

### RESEARCH METHODOLOGY

### FORMULATION OF SOLID DISPERSIONS OF MESALAMINE WITH B-CYCLODEXTRIN USING ROTARY EVAPORATOR

### ROTARY EVAPORATION METHOD

Drug and β-CD at 1:1, 1:2 and 1:3 w/w concentrations were prepared by addition of β-CD in 25 mLwater and drug in 25 ml ethanol (1:1) solution followed by thorough mixing of these two solutions together with a magnetic stirrer for stirring for 2 hours. This solution was then transferred to round bottom flask of rotary evaporator. The mixture was allowed to heat at 40°C with continuous stirring at a speed of 100 rpm. The resulting SDs in the form of powder were dried in vacuum desiccator for 72 hours at room temperature. Upon hardening, the mixture was triturated using mortar and pestle to get fine powder and then it was passed through sieve number 100. The resulting powder was kept in a closed container at room temperature until it was utilised

## CHARACTERIZATION AND OPTIMIZATION OF SOLID DISPERSIONS

### 1:Drug content

To determine the percentage drug content, solid dispersion equivalent to 10 mg was dissolved in 10 mL pH 7.4 phosphate buffer, mixed and filtered. Stock solution was further diluted with pH 7.4 phosphate buffer and analyzed against blank using a UV spectrophotometer at 305 nm wavelength.

### 2: SATURATION SOLUBILITY STUDIES

Excess SDs and PMs were placed in separate glass-stoppered flasks containing 10 mL of 0.1 N HCl, phosphate buffer pH 6.8. phosphate buffer pH 7.4. Placed in orbital shaker at 37°C at 100 rpm for 24 h. Filtered through Whatman filter paper No 41, diluted appropriately and assayed for drug content by UV-spectrophotometer at 305 nm.

### 3:DISSOLUTION STUDIES OF SOLID DISPERSIONS

*In vitro* release studies from solid dispersions were performed in 900 ml of pH 7.4 phosphate buffer using USP paddle apparatus type (II). The temperature was maintained at 37°C ± 0.5°C throughout the experiment with constant speed of 75 rpm. Samples (10 ml) were withdrawn at 30, 45, 60, 75, 90, 105 and 120 min time interval and same volume of fresh buffer was replaced. The samples were diluted and filtered through a 0.45 µm membrane filter and analysed using UV spectrophotometer at 305 nm wavelength. The experiment was performed in triplicate and average drug release was calculated.

### 4: FTIR STUDIES

Fourier transform infrared spectra of powdered samples of mesalamine, β- cyclodextrin, physical mixture and solid dispersion of mesalamine with β- cyclodextrin 1:3 ratio w/w were obtained using a FTIR spectrophotometer. The scanning range was 400–4000 $cm^{-1}$ and the resolution was 4 $cm^{-1}$.

### 5: SCANNING ELECTRON MICROSCOPY (SEM)

SEM images of mesalamine, β-CD, and SDs containing the optimized ratio prepared via rotary evaporation method were acquired using a JSM 6390 SEM from JEOl, Peabody MA, USA, with an accelerating voltage of 10 kV.

## FORMULATION OF SUPPOSITORIES

Mesalamine suppositories were formulated using two suppository bases, hydrophilic base and lipophilic base. Mixture of PEG 1540 and PEG 4000 in different ratios was used as hydrophilic base, while cocoa butter was chosen as the lipophilic base. Solid dispersion with drug equivalent to 500 mg was incorporated in bases and suppositories were preparedusing melting method and further evaluated. Formulation of mesalamine suppositories is given in Table

### Characterisation of suppositories

**1 Preparation of sample solution (Suppository formulation)**

Twenty suppositories each containing 500 mg of mesalamine were weighed and crushed. Sample equivalent to 10 mg of drug was transferred to 10 ml volumetric flask and volume was made up with methanol to obtain a concentration of 1000 µg/ml and was sonicated for 10 min. Further, dilution with mobile phase was made to get concentration of 10 µg/ml. Concentration of mesalamine was determined using HPLC. Percentage recovery of mesalamine was calculated based on the known concentration of mesalamine in the suppository formulation.

**TABLE FORMULATION OF MESALAMINE SUPPOSITORIES.**

| Base Type | Composition | | |
|---|---|---|---|
| | F1 Cocoa butter | F2 PEG1540: PEG4000 ( 40:60%) | F3 PEG1540: PEG6000 ( 40:60%) |
| PEG 1540 | -- | 40% | 40% |
| PEG 4000 | -- | 60% | -- |
| PEG 6000 | -- | -- | 60% |
| Cocoa Butter | qs | -- | -- |
| Solid Dispersion using β-Cyclodextrin | Drug (equivalent to 500 mg) | Drug (equivalent to 500 mg) | Drug (equivalent to 500 mg) |

## Evaluation of formulated suppositories

Suppositories were visually assessed for surface texture (smooth/rough), clarity (clear/opaque), appearance (dry/oily), cracking and discolouration.

### 1. Uniformity of drug content

Ten PEG suppositories from each batch were selected, weight, average weight calculated and crushed. Weight equivalent to 10 mg of mesalamine dissolved in 10 mL pH 7.4 phosphate buffer mixed and filtered. Further, diluted with pH 7.4 phosphate buffer and analyzed against a blank using a UV visible spectroscopy at 305 nm wavelength. Cocoa butter suppositories were melted in a water bath at 50°C and the same procedure was used. Uniformity of content test was considered acceptable if not more than one suppository was outside the limits of 85 to 115% of the mean drug content, and all samples were within the limits of 75 to 125% of the average drug content.

### 2. Uniformity of weigh

For uniformity of weight, twenty suppositories were individually weighed. The mean, standard deviation and percentage deviation were calculated. In order to pass the uniformity of weight test, no more than two suppositories may have a percentage deviation over 5%, and none may deviate by more than 10% of the mean weight.

### 3.Hardness

For determination of hardness Monsanto hardness tester was used. Hardness of ten suppositories was determined.

### 4. Melting point

Melting point was determined by open capillary method using melting point apparatus. Suppository was taken in a glass capillary and one end of it was sealed by flame. The capillary tube containing drug was dipped in liquid paraffin in the melting point apparatus.

### 5. Disintegration

Disintegration test was performed using disintegration test apparatus. Six suppositories were placed in a basket and lowered into 250 mL deionised water at 37 ± 0.2°C. Time taken for disintegration was recorded.

### *6. In-vitro* release studies of suppositories

*In vitro* release studies from suppositories was performed in 900 mL pH 7.4 phosphate buffer using USP paddle apparatus type (II). The temperature was maintained at 37°C ± 0.5°C throughout the experiment with constant speed of 75 rpm. The samples were withdrawn at 30, 45, 60, 75, 90,105 and 120 min time interval and same volume of fresh buffer was replaced. The samples were diluted and filtered through a 0.45 µm membrane filter and analysed using UV visible spectrophotometer at 305 nm wavelength. The experiment was performed in triplicate and average drug release was calculated.

## 7. *IN- VITRO* COMPARATIVE STUDY WITH MARKETED FORMULATION

*In-vitro* release studies of formulated suppositories were compared with marketed suppositories and plain drug suppositories. Plain drug suppositories were prepared by incorporating 500 mg mesalamine in cocoa butter. *In- vitro* comparative study were conducted as per procedure

## 9. STABILITY STUDIES OF SUPPOSITORIES

The study was done where suppository formulation samples were stored in stability cabinet at temperature of 25°C and relative humidity of 60% for six months. Sample assays were performed at zero-month, third month and the sixth month using HPLC. A photostability chamber with a UV light exposure of at least 200 watt-hours/$m^2$ was used to test the suppository formulation samples. Further the formulations were exposed to at least 1.2 million Lux-Hr of cool white fluorescence light. An accurately weighed suppository sample containing 10 mg of the drug was transferred to a 10 mL volumetric flask and volume was made with methanol and then filtered. With the help of the mobile phase methanol: ammonium acetate buffer (90:10 v/v). the resultant solution was further diluted to a final concentration of 10 µg/mL. The solution was then injected to obtain a chromatogram to determine the content of mesalamine.

## IV. RESULTS AND DISCUSSION

### Formulatiom of solid dispersions of mesalamine with β -cyclodextrin using rotary evaporator

#### Selection of drug concentration

Mesalamine is available in specially formulated oral and rectal forms. Suppositories with 500 mg dose are useful for treatment of ulcerative proctitis. Maximum daily dose recommended is 2-4 gm. Composition of trial batches for mesalamine is given in Table

**Table Composition of trial batches for mesalamine**

| Formulation Code | Carrier | Drug : Carrier | Method |
|---|---|---|---|
| PM 1 | β-Cyclodextrin | 1:1 | Physical mixture |
| PM 2 | β-Cyclodextrin | 1:2 | Physical mixture |
| PM 3 | β-Cyclodextrin | 1:3 | Physical mixture |
| SD 1 | β-Cyclodextrin | 1:1 | Solid dispersion |
| SD 2 | β-Cyclodextrin | 1:2 | Solid dispersion |
| SD 3 | β-Cyclodextrin | 1:3 | Solid dispersion |

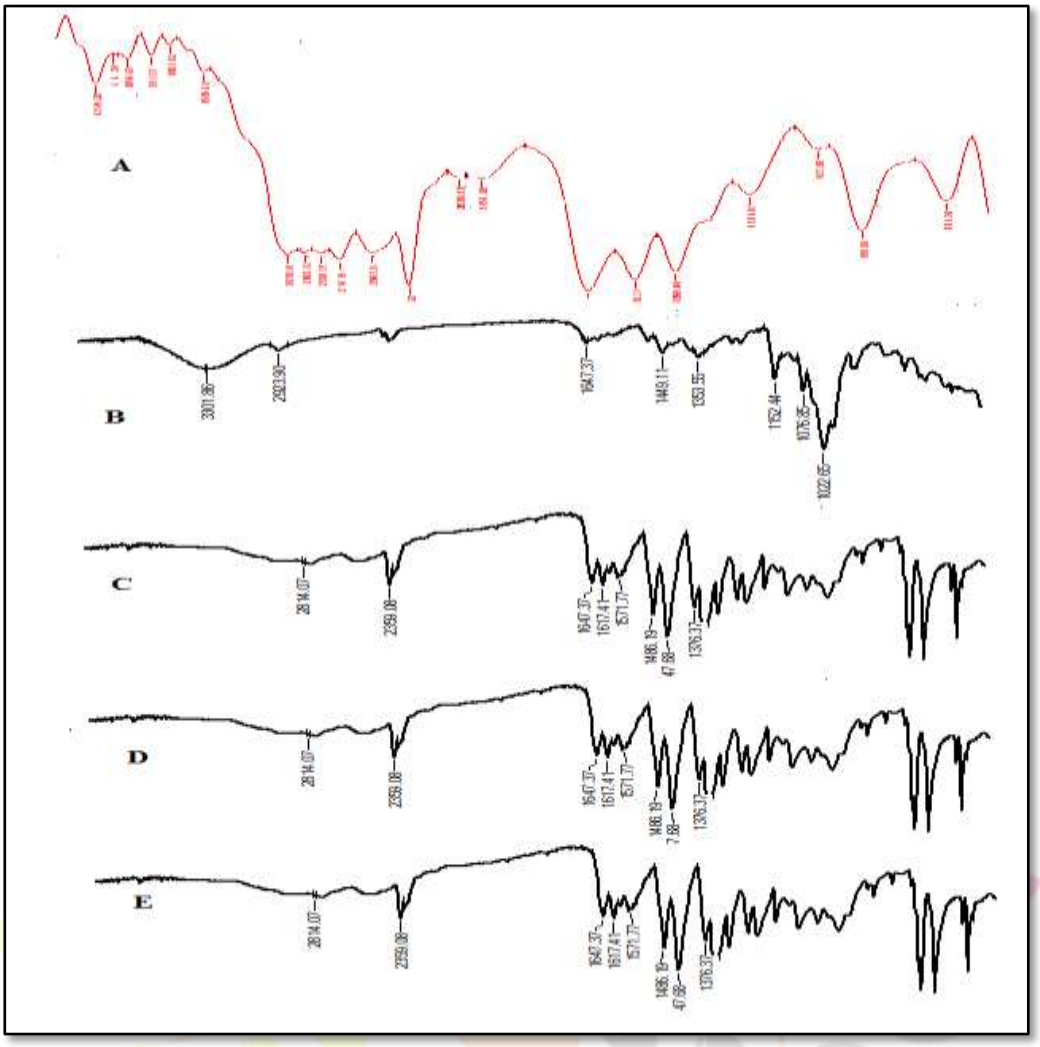



**Figure Compatibility study of mesalamine:β - cyclodextrin.**

**A-Mesalamine, B-β-cyclodextrin, C-Physical mixture [Mesalamine: β - cyclodextrin 1:1], D- Physical mixture [Mesalamine: β -cyclodextrin 1:2], E- Physical mixture [Mesalamine: β -cyclodextrin 1:3].**

## Characterization and optimization of solid dispersions

All the solid dispersions were found to be fine free flowing powders.

### 1. Drug content

The percentage drug content was determined at 305 nm by UV visible spectrophotometer. The drug content was found to be between 94%-99% indicating no or negligible loss of drug during the process.

## 2.Saturation solubility studies

Saturation solubility of mesalamine solid dispersions is given in Table 6.18 and Figure 6.18. Solubility was seen in the following order, phospate buffer pH 7.4 > phospate buffer pH 6.8 > 0.1 N HCl. It was observed that as the concentration of β- cyclodextrin in solid dispersions increases solubility of mesalamine also increases. Graphical presentation of saturation solubility studies.

## 3. Dissolution studies of solid dispersions

The characteristics of mesalamine's *in-vitro* dissolution from different solid dispersions employing β-cyclodextrin, physical mixtures, and pure drug are shown in Figure 6.19 and Table 6.19. Compared to physical mixtures and pure mesalamine, the solubility of mesalamine in all solid dispersion samples was greater. SD of drug and β- CD (1:3 w/w) showed maximum drug release of 97.24%, physical of drug and β- CD (1:3 w/w) showed drug release of 55.28%, pure drug showed 45.47% drug release within 120 min. The enhancement of dissolution is mainly attributed to increased surface area of drug exposed to large carrier molecules, increased

wettability. This also may be attributed to the hydrophilic carriers, which can reduce the interfacial tension between the poorly aqueous soluble drug and the dissolution medium. This observation indicated that the increased dissolution of mesalamine from solid dispersion due to presence of drug in amorphous state as compared to the physical mixtures and pure drug, where drug is present in crystalline state.

## Table Saturation solubility studies.

| Sr.No. | 0.1 N HCl (µg/mL) | Phospate buffer pH 6.8 (µg/mL) | Phospate buffer pH 7.4 (µg/mL) |
|---|---|---|---|
| Drug | 11±0.01 | 15±0.01 | 20±0.01 |
| PM 1:1 | 13±0.01 | 20±0.01 | 25±0.02 |
| PM 1:2 | 16±0.02 | 24±0.03 | 27±0.01 |
| PM 1:3 | 18±0.01 | 27±0.02 | 29±0.03 |
| SD 1:1 | 51±0.03 | 63±0.01 | 75±0.01 |
| SD 1:2 | 62±0.01 | 72±0.04 | 83±0.02 |
| SD 1:3 | 68±0.01 | 87±0.03 | 98±0.01 |

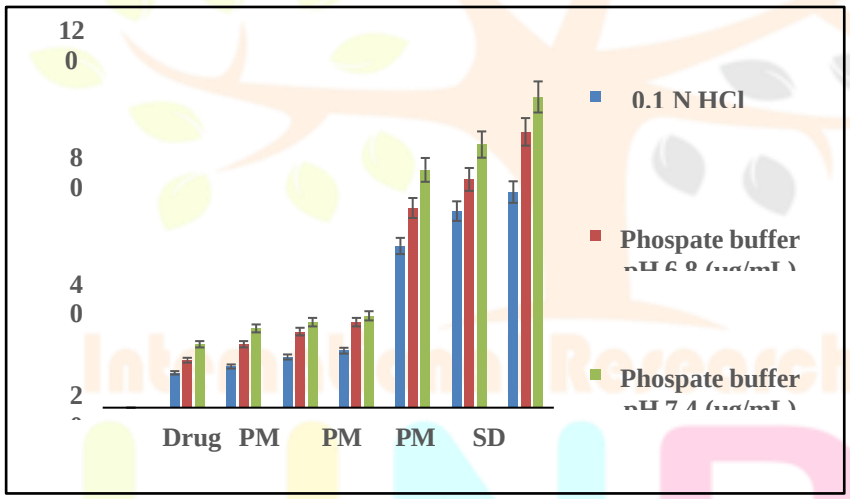



**Figure Graphical presentation of saturation solubility studies.**

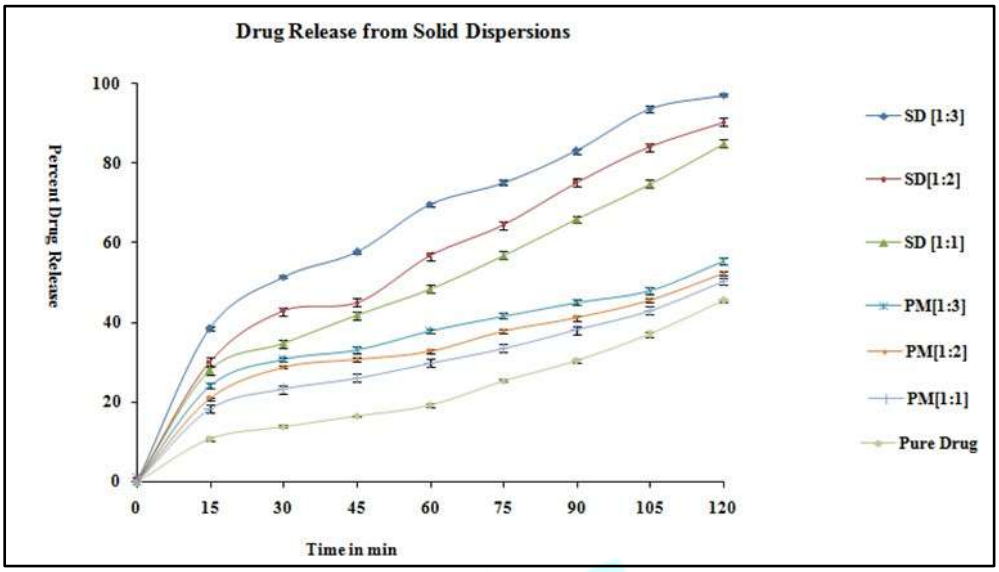



**Figure : Release profile of pure drug, SDs and physical mixture of prepared batches in 1:1, 1:2 and 1:3 w/w ratios using β-CD by rotary evaporation method.**

**Table Percent drug release (%) of prepared batches in 1:1, 1:2 and 1:3 w/w ratios using β-CD by rotary evaporation method.**

| Time in min | Percent drug release (%) | | | | | | |
|---|---|---|---|---|---|---|---|
| | PM [1:1] | PM [1:2] | PM [1:3] | SD [1:1] | SD [1:2] | SD [1:3] | Pure Drug |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 15 | 18.22 ±1.1 | 20.73 ±1.0 | 24.04 ±1.4 | 27.89 ±0.9 | 30.17 ±1.1 | 38.37 ±1.8 | 10.74 ±0.9 |
| 30 | 23.19 ±1.0 | 28.77 ±1.9 | 30.65 ±0.9 | 34.72 ±0.8 | 42.84 ±1.2 | 51.46 ±1.2 | 13.87 ±1.0 |
| 45 | 25.99 ±0.9 | 30.69 ±1.1 | 33.05 ±0.8 | 41.84 ±1.0 | 45.04 ±1.1 | 57.68 ±1.1 | 16.67 ±1.4 |
| 60 | 29.82 ±0.9 | 32.66 ±0.5 | 37.94 ±1.0 | 48.44 ±1.1 | 56.66 ±0.9 | 69.67 ±1.3 | 19.21 ±1.0 |
| 75 | 33.46 ±1.1 | 37.86 ±0.9 | 41.62 ±0.8 | 56.92 ±1.0 | 64.42 ±1.3 | 75.22 ±1.2 | 25.38 ±1.4 |
| 90 | 38.01 ±1.0 | 41.06 ±1.0 | 45.09 ±1.1 | 65.92 ±1.0 | 75.10 ±1.1 | 83.10 ±1.1 | 30.42 ±0.9 |
| 105 | 43.04 ±1.1 | 45.67 ±1.0 | 48.12 ±0.9 | 74.80 ±1.0 | 84.06 ±1.0 | 93.71 ±0.7 | 37.04 ±0.3 |
| 120 | 50.33 ±1.6 | 52.46 ±1.0 | 55.28 ±1.1 | 84.95 ±0.9 | 90.40 ±1.1 | 97.24 ±0.3 | 45.47 ±1.5 |

## FTIR studies

The disappearance of some peaks, overlapping of O-H group and broadening of the peak in the spectra of solid dispersion indicates that mesalamine is molecularly dispersed in the polymer matrix. However, other peaks related to C=0, C-H stretching remains unchanged. This indicates that overall symmetry of the molecule might not be significantly changed. FTIR spectra given in Figure 7.12

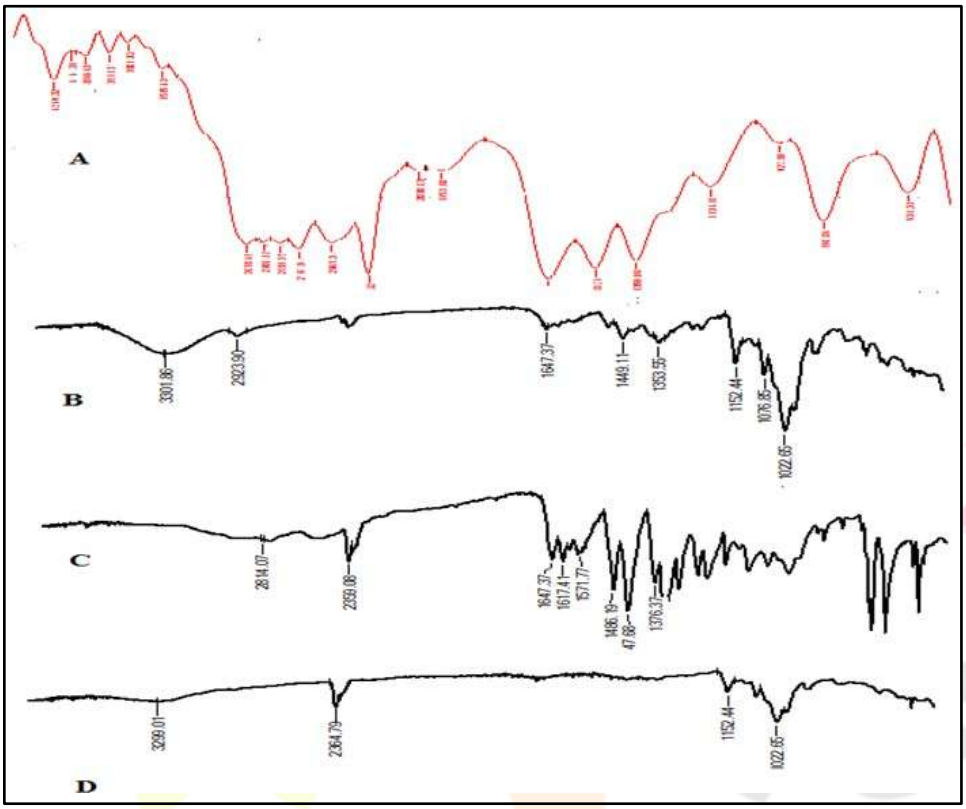
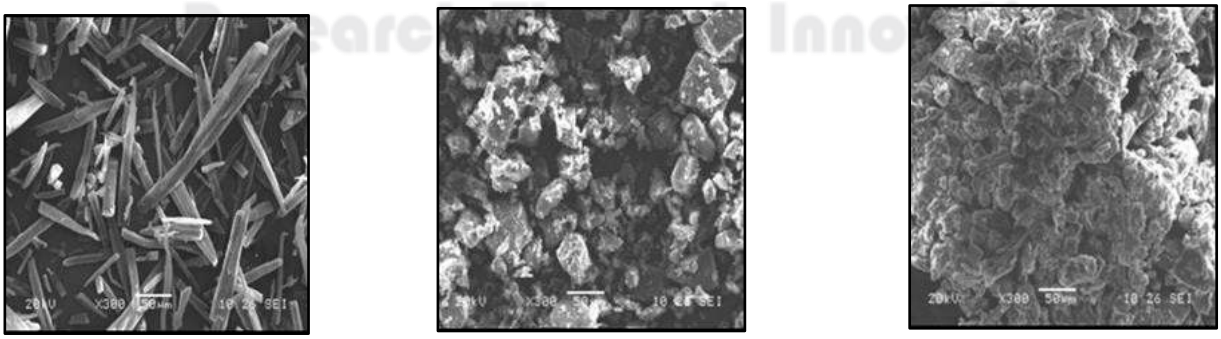



**Figure Infra-red spectra of mesalamine solid dispersion with β- cyclodextrin (1:3 ratiow/w) by rotary evaporation method. (a) mesalamine; (b), β-cyclodextrin; (c) mesalamine: β-cyclodextrin physical mixture (1:3 ratio w/w)(d) mesalamine:β- cyclodextrin – solid dispersion (1:3 ratio w/w).**

## Scanning Electron Microscopy (SEM)

figure shows SEM images of mesalamine crystals, which exhibit a distinctive morphology characterized by longer crystals. The SEM images illustrate the presence of equant-shaped crystals of mesalamine, whereas those of the solid dispersion reveal a polymer matrix form with no visible evidence of drug crystals.



**A** **B** **C**

**Figure 7.13 SEM of (a) Mesalamine; (b), β-cyclodextrin; (c), Mesalamine: β cyclodextrin- solid dispersion (1:3 ratio w/w).**

## Formulation of suppositories

Mesalamine suppositories were formulated using solid dispersions of mesalamine and β-cyclodextrin. Cocoa butter was used as a fatty base and mixtures of polyethylene glycol (PEG) in different ratios were used as water soluble base as given in were as given in formulation Table

# Characterization of suppositories

### 1.Properties of formulated suppositories

**Table . Properties of formulated suppositories.**

[7]

| Parameters | Observed results |
|---|---|
| Size | Uniform |
| Shape | Bullet shaped |
| Colour | Uniform pinkish colour |
| Texture | Smooth |

### 2. Uniformity of content

Uniformity of content was found in between 91.42% to 95.23%, which shows negligible loss of drug, depicted in Table 7.10

### 3. The uniformity of weight

Uniformity of weight was in between 3.55g to 3.75g, depicted in Table 7.10

### 4.Hardness

Hardness of cocoa butter suppositories was found to be less as compared to suppositories formulated using PEG mixture. Hardness was found to be between 1.5 kg/cm$^2$ to 2. kg/cm$^2$, depicted in Table 7.10

### 5.Melting point

Melting point for cocoa butter suppositories was found to be less as compared to suppositories formulated using PEG mixture. Melting ppoint was found within the range of 35°C to 37°C, depicted in Table 7.10

## 6.Disintegration time are summarised in Table 7.10.

Disintegration time for cocoa butter suppositories was found to be less as compared to suppositories formulated using PEG mixture. Disintegration time was found to be between 5 min to 11 min, depicted in Table 7.10

**Table 7.10 Characterization of suppositories.**

| Test | F1 Cocoa butter | F2 PEG1540: PEG4000 ( 40:60%) | F3 PEG1540: PEG6000 ( 40:60%) |
|---|---|---|---|
| Uniformity of weight (g) (± SD), n = 20 | 3.75 ±0.9 | 3.52±0.7 | 3.55±0.3 |
| Uniformity of content % (±SD), n = 10 | 95.23%±0.6 | 93.35%±0.8 | 91.42%±0.4 |

| | | | |
|---|---|---|---|
| Hardness (kg/cm$^2$), n = 10 | 1.5±0.2 | 2±0.3 | 2.2±0.4 |
| Disintegration min (± SD),n = 6 | 5±0.2 | 9 ±0.3 | 11±0.5 |
| Melting point, °C(± SD), n=6 | 35°C±0.1 | 36°C±0.3 | 37°C±0.2 |

## *In-vitro* release studies of suppositories

The release of mesalamine from cocoa butter suppositories [F1], PEG1540: PEG4000 base (ratio 40:60%) suppositories [F2] and PEG1540: PEG6000 (ratio 40: 60%) base suppositories [F3], are illustrated in Figure 7.14. It was observed that the release profile of [F1] was 93.78%, [F2] was 86.32% & [F3] was 48.32%, shown in Figure 7.14. From the drug release data it can be concluded that drug release from cocoa butter suppositories was greater as than mixtures of PEG base suppositories. Faster drug release may be due to less melting point, less hardness, less disintegration time of cocoa butter suppositories as compared to mixtures of PEG base suppositories. Percent drug release has been depicted in Table 7.11

### *In-vitro* comparative study with marketed formulation

Comparative release profile of drug: β-cyclodextrin [1:3] solid dispersions in cocoa butter [F1], marketed suppository [F2] and pure drug in cocoa butter [F3] are shown in Figure 7.15. [F1] showed maximum drug release (93.78%) as compared to marketed (73.42%) and pure drug in cocoa butter (20.41%). From the drug release, it can be concluded that solid dispersions enhanced the solubility of drug. Percent drug release have been depicted in Table 7.12.

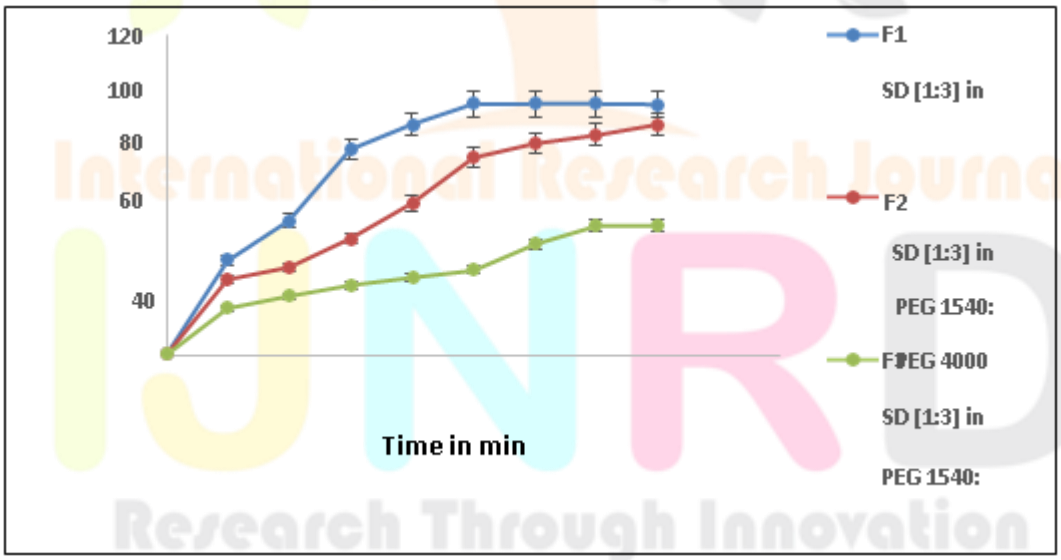



**Figure 7.14 Comparative release profile of F1: SD [1:3] in cocoa butter , F2: PEG 1540: PEG 4000 [40%: 60%], F3: PEG 1540: PEG 6000 [40%: 60%].**

**Table Percent drug release of suppositories.**

| Time in min | Percent Drug Release | | |
|---|---|---|---|
| | F1 SD [1:3] in Cocoa Butter | F2 SD [1:3] in PEG 1540: PEG 4000 [40%: 60%] | F3 SD [1:3] in PEG 1540: PEG 6000 [40%: 60%] |
| 15 | 35.26±0.9 | 28.31±1.1 | 17.41±0.9 |
| 30 | 50.32±0.8 | 32.74±1.0 | 22.08±0.7 |
| 45 | 77.11±1.0 | 43.62±1.8 | 26.10±0.8 |
| 60 | 86.30±0.9 | 56.84±1.1 | 29.10±1.0 |
| 75 | 94.07±0.8 | 73.83±1.0 | 31.73±1.0 |
| 90 | 94.03±1.0 | 79.31±1.0 | 41.42±1.2 |
| 105 | 93.99±1.0 | 82.31±1.0 | 48.32±1.1 |
| 120 | 93.78±1.0 | 86.32±1.1 | 48.32±1.0 |

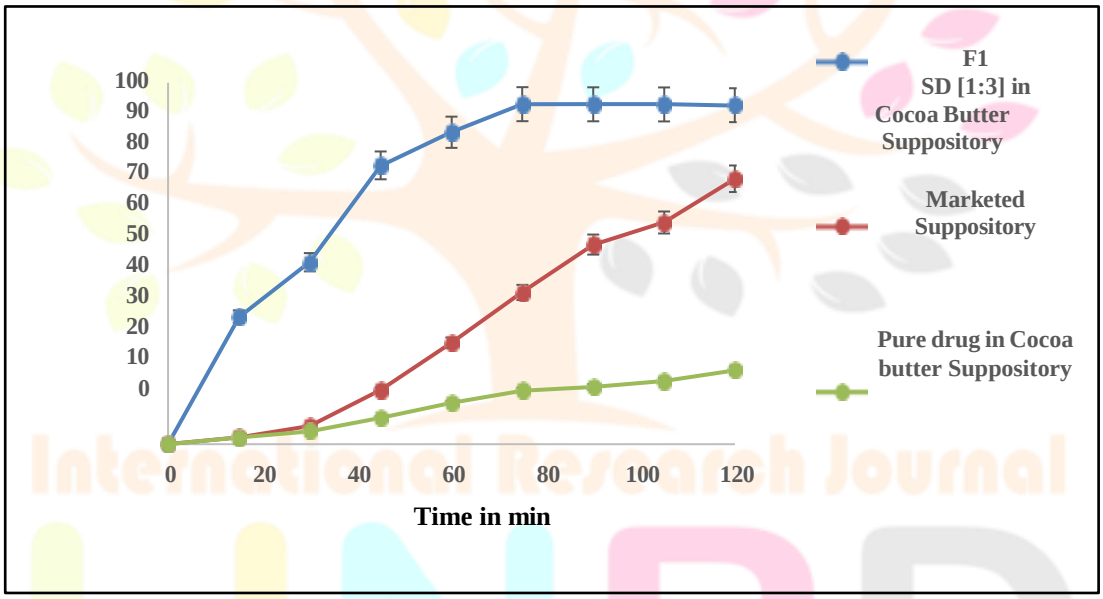



**Figure 7.15 Comparative release profile of F1: drug: β-cyclodextrin [1:3] solid dispersions in cocoa butter, marketed suppository and pure drug in cocoa butter.**

**Table 7.12 Percent drug release of SD by RE Drug: β-CD [1:3] in cocoa butter, marketed suppository and pure drug in cocoa butter.**

| Time in min | Percent Drug Release | | |
|---|---|---|---|
| | F1 SD [1:3] in Cocoa Butter Suppository | Marketed Suppository | Pure drug in Cocoa butter Suppository |
| 15 | 35.26±1.1 | 1.89±1.0 | 1.84±1.9 |
| 30 | 50.32±1.0 | 4.91±1.1 | 3.62±1.0 |
| 45 | 77.11±0.7 | 14.92±1.1 | 7.31±0.4 |

| | | | |
|---|---|---|---|
| 60 | 86.30±1.0 | 28.07±0.9 | 11.42±0.4 |
| 75 | 94.07±1.0 | 41.96±1.0 | 14.85±0.9 |
| 90 | 94.03±0.9 | 55.21±1.0 | 15.83±0.8 |
| 105 | 93.99±1.0 | 61.32±0.8 | 17.47±1.1 |
| 120 | 93.78±1.0 | 73.42±1.1 | 20.41±1.0 |

## Stability Studies

The stability studies at 25°C with relative humidity of 60% were performed for suppository formulations for the period of 6 months. No significant change in assay at 3 and 6 months was observed in comparison to initial assay with minimum % RSD. The formulation was found to be stable during this stability testing period. The formulation was stable with excellent recovery of 99.07% with 0.825% RSD. Overall, the developed formulation had excellent stability which is one of the regulatory requirements, depicted in Table 7.13.

## Table Stability study of formulation.

| **Sr. No.** | **0 Month** | | **03 Month** | | **06 Month** | |
|---|---|---|---|---|---|---|
| | **Peak area** | **% Recovery** | **Peak area** | **% Recovery** | **Peak area** | **% Recovery** |
| Mean | 1410806.3 ±0.148 | 99.648± 0.461 | 1417105.4 ±0.137 | 100.207± 0.528 | 1412096. 6±0.490 | 99.763±0. 251 |
| SD | 7106.00 | 0.630 | 8522.807 | 0.757 | 9684.098 | 0.860 |
| %RSD | 0.504 | 0.633 | 0.601 | 0.755 | 0.686 | 0.862 |

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**REFERENCES**

1. 1 Ghuge A. R., Dhole S. N., Kulkarni N. S. & Medankar T. B. (2025). *Rectal Suppositories for Treatment of Inflammatory Bowel Disease: A Review.* Asian Journal of Pharmacy and Technology, 15(3):261-0. doi:10.52711/2231-5713.2025.00040.

2. Lakshmi, K. M. & Reddy, N. D. (2024). *A Review on Suppositories.* International Journal of Pharmaceutical Sciences, Vol. 2 (2), 668-675. Int. J. Pharm. Sci. Open Access

3. Fazmiya MJA, Sultana A, Heyat MBB, Parveen S, Rahman K, Akhtar F, Khan AA, Alanazi AM, Ahmed Z, Díez IdlT, Ballester JB & Saripalli TSK. (2024). *Efficacy of a vaginal suppository formulation prepared with Acacia arabica gum and Cinnamomum camphora in heavy menstrual bleeding analysed using a machine-learning technique.* Frontiers in Pharmacology, 15:1331622.

4. Dangi, J. S., & Rathore, R. S. (2021). *Formulation and evaluation of paracetamol suppositories. International Journal of Pharmaceutical Research*, 13(1), 451–457.

5. Goyal, R., & Mehta, S. C. (2018). *Development and evaluation of solid dispersion based suppositories for enhanced rectal delivery. Research Journal of Pharmacy and Technology*, 11(9), 3967–

3974.

6. Vishy M. Anatomy of the rectum and anal canal. Surgery. 2017; 35(3): 121-125.

7. Yang L, Chu JS, Fix JA. Colon-specific drug delivery: new approaches and in vitro/in vivo evaluation. Int J Pharm. 2002;235:1-15.

8. Krishnakondamudi P, et al. Drugs as causative agents and therapeutic agents in inflammatory bowel disease. Acta Pharm Sinica B. 2013;3(5):289-296.

9. Molodecky NA, Soon IS, Rabi DM, Ghali WA. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology. 2012;142:46–54.

10. Lautenschlager C, et al. Drug delivery strategies in the therapy of inflammatory bowel disease. Adv Drug Deliv Rev. 2013; 1-19.

11. Mahid SS, Mulhall AM, Gholson RD, Eichenberger MR, Galandiuk S. Inflammatory bowel disease and African Americans: a systematic review. Inflamm Bowel Dis. 2008;14(7):960-967.

12. Carr N, Schofield PF. Inflammatory bowel disease in the older patient. Br J Surg. 1982;69:223-5.

13. Kozuch PL, Hanauer SB. Treatment of inflammatory bowel disease. A review of medical therapy. World J Gastroenterol. 2008; 14(3): 354-377 [PMID: 18200659 DOI: 10.3748/wjg.14.354].

14. Tsianos EV. Risk of cancer in inflammatory bowel disease (IBD). Eur J Intern Med. 2000 ;11(2):75-78. doi: 10.1016/s0953-6205(00)00061-3. PMID: 10745149.

15. Ingrid O, Lars E, Mark T. Ulcerative Colitis. Lancet. 2012; 380: 1606–19.

16. Ulrich K. et al. Topical delivery of therapeutic agents in the treatment of inflammatory bowel disease. Advanced drug delivery reviews. 57 2005; 57:267– 279.

17. Hanauer SB. Advantages in IBD and current developments in the treatment of inflammatory bowel diseases. Gastroenterol Hepatol. 2010; 6(5): 309–316.

18. Carter MJ, Lobo AJ. Guidelines for the management of inflammatory bowel disease in adults. Gut. 2004;53(5):51–56.

19. Gionchetti P. Review article: problematic proctitis and distal colitis. Aliment Pharmacol Ther. 2004; 20 ( 4): 93–96.

20. Boer AG, Breimer DD. Pharmacokinetics of rectal drug administration, Part I. General considerations and clinical applications of centrally acting drugs. Clin Pharmacokinet. 1991 ; 21(1):11-26. doi: 10.2165/00003088-199121010-00002. PMID: 1717195.

21. Prasanna LJ, Deepthi B, Rao RN. Rectal drug delivery: A promising route for enhancing drug absorption. Asian J. Res. Pharm. Sci. 2012; 2(4): 143-149.

22. Baviskara P, Bedsea A, Sadiqueb S. Drug delivery on rectal absorption: suppositories. Int. J. Pharm. Sci. Rev. Res. 2013;21(1): 70-76.

23. Regueiro MA, Loftus EV, Steinhart AH. Clinical guidelines for the medical management of left-sided ulcerative colitis and ulcerative proctitis: summary statement. Inflammatory boweldiseases.2006; 12(10):972978. https://doi.org/10.1097/01.mib.0000231496.92013.

85.

24. Ulcerative Colitis. Improving life for people affected by inflammatory bowel diseases, crohns and colitis, UK, Informa Health Care.

25. Abdul W. Basit, Advances in colonic drug delivery. Drugs. 2005; 65 (14): 1991-2007.

26. Williams A. Double-blind, placebo-controlled evaluation of 5-ASA suppositories in active distal proctitis and measurement of extent of spread using 99mtc-labeled 5-ASA suppositories. Digestive Diseases and Sciences.1987;32(12): 71-75.

27. Sandro A. Comparative tolerability of therapies for ulcerative colitis. Drug Safety. 2002; 25 (8): 561-582.

28. Burger D. Conventional medical management of inflammatory bowel disease. Gastroenterology. 2011; 140:1827–1837.

29. Laszlo LP. Ulcerative proctitis: a review of pharmacotherapy and management, expert opin. Pharmacother. 2008; 9(5):741-749.

30. Malcolm R. Medical therapy of inflammatory bowel disease for the 21st century. Eur J Surg. 1998; 582: 90–98.

31. Ulcerative colitis agents review. Copy Right. 2004 – 2010 Provider Synergies, L.L.C.

32. Loyd V Allen LV. Compounding rectal dosage forms-part ii. Current & Practical Compounding Information For The Pharmacist.2007; 14(4):1-15.

33. Gupta PJ. Suppositories in anal disorders: a review. European Review For Medical and Pharmacological Sciences. 2007; 11: 165-170.

34. Hoag SW. Suppositories. Pharmaceutics. 2002;535 :1-74.

35. Rowe RC, Sheskey PJ, Quinn ME. Handbook of pharmaceutical excipients, 6th ed., Pharmaceutical Press, London. 722.

36. Sridhar I, Doshi A, Joshi A, Vandana. Solid dispersions: an approach to enhance solubility of poorly water soluble drug. Journal of Scientific and Innovative Research. 2013; 2 (3): 685-694.

37. Saffoon N, Uddin R. Enhancement of oral bioavailability and solid dispersion: a review. Journal of Applied Pharmaceutical Science. 2011; 1 (7): 13-20.

38. Arunachalam A, Karthikeyan M, Konam K. Solid dispersions: a review. Current Pharma Research. 2020; 1(1):82-90.

39. Kumar A, Sahoo S, Padhee K. Review on solubility enhancement techniques for hydrophobic drugs. IJCP. 2011; 3 (03):1-7.

40. Padalkar A, Shahi S, Kale A. Formulation and characterization of novel solid dispersions of hydrochlorothiazide by solvent evaporation technique. Asian Journal of Biomedical and Pharmaceutical Sciences. 2012; 2(11) : 49-56.

41. Kapoor B, Kaur R, Kour S, Behl H. Solid dispersion: an evolutionary approach for solubility enhancement of poorly water soluble drugs. Int J Recent Adv Pharm Res. 2012;2(2):1-16.

42. Malkawi R, Malkawi WI, Al-Mahmoud Y, Tawalbeh J. Current trends on solid dispersions: past, present, and future. Adv Pharmacol Pharm Sci. 2022;1(3):59-63.

43. Saffoon N, Uddin R, Huda H. enhancement of oral bioavailability and solid dispersion: a review. Journal of Applied Pharmaceutical Science. 2011; 1 (7): 13-20.

44. Patil JS, Kadam DV, Marapur SC. Inclusion complex system; a novel technique to improve the solubility and bioavailability of poorly soluble drugs: a review. International Journal of Pharmaceutical Sciences Review and Research. 2010; 2 (2): 15-24.

45. Janisse C, Martins T, Veiga. Cyclodextrins and ternary complexes: technology to improve solubility of poorly soluble drugs. Brazilian Journal of Pharmaceutical Sciences. 2011; 47(4): 665-681.