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Research

Formulation And Evaluation Of Mesalazine Solid Dispersion Loaded Suppositories

SK.Musharraf [1], Aukunuru Jitha[1,2]

[1]*Department Of Pharmaceutics, Omega College Of Pharmacy, Edulabad, Hyderabad,Telangana.*
[2]*Technology Consultants, Hyderabad, Telangana, India.*

*Author for Correspondence: SK.Musharraf
Email: skmusharraf303@gmail.com

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Abstract

To increase the drug's solubility, ß -cyclodextrin complexes of Mesalazine were created using a solvent evaporation approach in various ratios. IR spectroscopy was used to describe the complex. No interaction existed between the medication and the carrier. The 1:4 Mesalazine: ß cyclodextrin, drug-carrier ratio was chosen as the optimal batch for suppositories based on physical characteristics and in vitro drug release pattern. Poly ethylene glycol, a water-soluble base, was chosen as the best basis for suppositories. By using a moulding process, the suppositories were made. The perfect batch of solid dispersion was added to the base of the suppository. The hardness, melting point, time required for disintegration, and drug content of the produced suppositories were all measured. All of these qualities were discovered to be perfect. Rotating a dialysis bag method was used to determine the in vitro medication release pattern. When compared to intact bulk drug integrated suppositories, the in vitro release of Mesalazine from its solid dispersion incorporated suppositories was dramatically enhanced.

Keywords: Mesalazine, ß cyclodextrin, PEG 4000 ,PEG 1000, Suppository, FTIR.

INTRODUCTION

Oral bioavailability of a drug depends on its solubility and/or dissolution rate, and dissolution may be the rate determining step for the onset of therapeutic activity. Therefore efforts to increase drug dissolution of drug are often needed. Methods available to improve dissolution include salt formation, micronization and addition of solvent or surface active agents. Solid dispersion (SD) is one of such methods and it involves a dispersion of one or more active ingredients in an inner carrier or matrix in solid state prepared by melting, dissolution in solvent or melting solvent method.

The enhancements of oral bioavailability of such poorly water-soluble drugs often show poor bioavailability because of low and erratic levels of absorption. Drugs that undergo dissolution rate limited gastrointestinal absorption generally show improved dissolution and bio availability as a result of reduction in particle size. However, micronizing of drugs often leads to aggregation and agglomeration of particles, which results in poor wettability. Solid dispersions of poorly water-soluble drugs with water-soluble carriers

have been reduced the incidence of these problems and enhanced dissolution. The development of solid dispersions as a practically viable method to enhance bioavailability of poorly water-soluble drugs overcame the limitations of previous approaches such as salt formation, solubalization by cosolvents, and particle size reduction. Studies revealed that drugs in solid dispersion need not necessarily exist in the micronized state. A fraction of the drug might molecularly disperse in the matrix, thereby forming a solid dispersion. When the solid dispersion is exposed to aqueous media, the carrier dissolves and the drug releases as fine colloidal particles.

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$$\frac{dc}{dt} = \frac{AD(Cs - c)}{h}$$

Where,
dC/dt - is the rate of dissolution,
A -is the surface area available for dissolution,
D - is the diffusion coefficient of the compound,
Cs- is the solubility of the compound in the dissolution medium,
C -is the concentration of drug in the medium at time **t** and
h - is the thickness of the diffusion boundary layer adjacent to the surface of the dissolving compound.

To increase the dissolution rate from equation the following approaches are available.

- To increases the surface area available for dissolution Decreasing the particle size of drug.
- Optimizing the wetting characteristics of compound surface.
- To decrease the boundary layer thickness.
- Ensure sink condition for dissolution.
- Improve apparent solubility of drug under physiologically relevant conditions.
- Drug administered in fed state is a way to improve the dissolution rate.

Of these possibilities, changes in the hydrodynamics are difficult to invoke *in-vivo* and the maintenance ofsink conditions will depend on how permeable the gastrointestinal mucosa is to the compound as well ason the composition and volume of the luminal Fluids. Although some research effort has been directedtowards permeability enhancement using appropriate excipients, results to date have not been particularlyencouraging. Administration of the drug in the fed state may be an option to improve the dissolution rate andalso to increase the time available for dissolution; the likely magnitude of the food effect can be forecastedfrom dissolution tests in biorelevant media.

The dissolution of a drug from its solid oral dosage forms depends upon its release from the dosage form and its subsequent mixing into physiological fluids. It has been estimated that nearly 35-40% of the drugs suffer from poor aqueous solubility, thereby affecting their absorption from the gastrointestinal tract, which leads to poor oral bioavailability, high intra- and inter-subject variability, increase in dose, reduction in therapeutic efficiency and finally failure in formulation development. The development of solid dosage forms for water-insoluble drugs has been a major challenge for pharmaceutical scientists for decades. Various formulation strategies such as micronisation, micellar solubilization, complexation, dendrimers for drug solubilization, formation of solid solutions or dispersions with hydrophilic carriers, self-microemulsifying drug delivery systems, spray drying, nano approaches, pro-drug approaches and salt synthesis have been developed to increase the dissolution rate of water-insoluble drugs. An attractive possibility is employing a simple solid dispersion technique making use of various hydrophilic carriers. Solid dispersions (SDs) are defined as the dispersion of one or more active ingredients in an inert hydrophilic carrier or matrix in a solid state, and are prepared by the fusion, solvent or solvent-fusion method. This technique enables reducing particle size to a nearly molecular level, offers a variety of processing and excipient options that allow for flexibility when formulating oral delivery systems of poor water-soluble drugs that are cost-effective and significantly reduced in dosage. It has been widely demonstrated that a hydrophilic carrier dissolves rapidly, exposing the drug particles to the dissolution medium as fine particles facilitating quick dissolution and absorption[8]. The mechanisms for increased dissolution rate may include reduction of crystallite size, solubilization effect of the carrier, absence of aggregation of drug crystallites, improved wettability and dispersability of a drug from the dispersion, dissolution of the drug in the hydrophilic carrier or conversion of the drug to an amorphous state. Schizophrenia is a severe non-curable illness of the brain with serious consequences if not properly treated and kept under control. It is the most common form of severe mental illness.

Solid dispersions

Solid dispersions(SDs)traditionally have been used as an effective method to improve the dissolution properties and bioavailability of poorly water-soluble drugs. Since 1961,many investigators have studied SDs of poorly water- soluble drugs with various pharmacologically inert carriers to increase the dissolution and oral absorption of poorly water-soluble drug show ever, only a few systems are useful commercially.

Fast or immediate drug dissolution from solid dispersions has been observed due to increased wettability, improved dispersibility of drug particles, existence of the drug in amorphous form with improved solubility and absence of aggregation of drug particles .Literature shows that the solvent evaporation method has been used for the preparation of solid dispersions for dissolution enhancement .Earlier studies show that solid dispersion systems increased the drug dissolution due to improved solubility, wettability and dispersibility using hydrophilic carriers In the present work, physical mixtures, co-grinding and co-precipitation or solvent evaporation method was used to prepare solid dispersions of prednisolone. This method requires the minimal amount of solvent in dissolving the drug. We used various polymeric carriers in this study. Polyvinylpyrrolidone(PVP)and poly ethylene glycol (PEG)were chosen as water-soluble polymers.

Classification of solid dispersion

Based on their molecular arrangement, six different types of solid dispersions can be distinguished. (In Table 1.1) Moreover, in various studies the designation of solid dispersions is based on the method of preparation. However, since different preparation methods can result in the same subtypes or similar preparation methods can result in different subtypes, it can be argued that solid dispersions should preferably be designated according to their molecular arrangement. Moreover, not the preparation method but the molecular arrangement governs the properties of solid dispersions. Therefore, it is essential to use terms that indicate the molecular arrangement in the solid dispersion. Knowledge about the molecular arrangement will enlarge comprehension of the properties and behavior of solid dispersions. Furthermore, it will facilitate optimization of their properties required for a specific application. For example, the mechanism underpinning the dissolution of solid dispersions is poorly understood. Many case studies showed accelerated dissolution of hydrophobic compounds using solid dispersions but mechanisms are rarely discussed. The most important reason for that is the lacking knowledge about the mode of incorporation of the hydrophobic drug in the matrix, despite numerous efforts to clarify this. A question like, “is the drug present as a crystalline phase or as amorphous nano-particles or molecularly dispersed throughout the matrix” is rarely discussed. All three situations result in different drug concentrations at the dissolving interface. Still it has not been fully elucidated how this affects dissolution behaviour of solid dispersions. Secondly, the physical and chemical stability of the matrix or the incorporated drug depends on the mode of incorporation. If drug molecules, for example, are present in amorphous nano-particles, crystallization requires only rotational rearrangement. On the other hand, for a molecularly dispersed drug, translational diffusion is necessary before crystallization can occur by rotational rearrangements.

1. Eutectic mixtures

A simple eutectic mixture consists of two compounds which are completely miscible in the liquid state but only to a very limited extent in the solid state. It is prepared by rapid solidification of fused melt of two components that show complete liquid miscibility but negligible solid-solid solution.

2. Amorphous precipitation in crystalline matrix

This is similar to simple eutectic mixtures but only difference is that drug is precipitated out in an amorphous form.

3.Solid solution

Solid solutions are comparable to liquid solutions, consisting of just one phase irrespective of the number of components. In the case of solid solutions, the drug's particle size has been reduced to its absolute minimum viz. the molecular dimensions14 and the dissolution rate is determined by the dissolution rate of the carrier. Classified according to their miscibility (continuous versus discontinuous solid solutions) or second, according to the way in which the solvate molecules are distributed in the solvendum (substitutional, interstitial or amorphous)[15].

4.Continuous solid solutions

In a continuous solid solution, the components are miscible in all proportions. Theoretically, this means that the bonding strength between the two components is stronger than the bonding strength between the molecules of each of the individual components. Solid solutions of this type have not been reported in the pharmaceutical world till date[16].

5.Discontinuous solid solutions

In the case of discontinuous solid solutions, the solubility of each of the components in the other component is limited. Due to practical considerations it has been suggested by Goldberg et al.14 that the term `solid solution' should only be applied when the mutual solubility of the two components exceeds 5%.

6.Subsitutional solid dispersions

Substitution is only possible when the size of the solute molecules differs by less than 15% or so from that of the solvent molecules15. Classical solid solutions have crystalline structure, in which the solute molecules can either substitute for solvent molecules in the crystal lattice or fit into the intrsticies between the solvent molecule.

7. Interstitial solid solutions

In interstitial solid solutions, the dissolved molecules occupy the interstitial spaces between the solvent molecules in the crystal lattice. Solute molecule diameter should be less than 0.59 times than that of solvent molecular diameter.

8. Glass solution and suspensions

Glass solutions are homogeneous glassy system in which solute dissolves in glass carrier. Glass suspensions are mixture in which precipitated particles are suspended in glass solvent. Lattice energy is much lower in glass solution and suspension.

MATERIALS AND METHODS

Mesalazine -B.M.R.Chemicals,Hyderabad, croscarmellose-S.D FINE CHEMICALS, Eudragit® E100-S.D FINE CHEMICALS, ß-cyclodextrin-B.M.R. Chemicals,Hyderabad, PEG-1000 -B.M.R. Chemicals,Hyderabad, PEG-4000-B.M.R. Chemicals,Hyderabad.

METHODOLOGY

Pre formulation studies

Pre formulation testing is the first step in the rational development of dosage forms of a drug substance.

Definition: It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients.

Objective: Overall objective of preformulation testing is to generate information useful to the formulator in developing stable and bio-available dosage forms.

The following preformulation studies were carried out for Mesalazine

a) Solubility studies

b) Drug–excipient compatibility studies

a) Solubility studies:

Solubility of Mesalazine was carried out in different buffers. Saturated solutions were prepared by adding excess drug to the vehicles and shaking on the shaker for 24 hrs at 25°C under constant vibration. Filtered samples (1ml) were diluted appropriately with suitable buffer and solubility of Mesalazine was determined spectrophotometrically at 332 nm

b) Drug–polymer compatibility studies

In the preparation of tablet formulation, drug and polymer may interact as they are in close contact with each other, which could lead to the instability of drug. Pre formulation studies regarding the drug-polymer interaction are therefore very critical in selecting appropriate polymers. FT-IR spectroscopy was employed to ascertain the compatibility between Mesalazine , and the selected polymers. The pure drug and drug with excipient were scanned separately.

FT-IR studies

Sample/KBr ratio

The concentration of the sample in KBr should be in the range of 0.2% to 1%. The pellet is much thicker than a liquid film, hence a lower concentration in the sample is required (Beer's Law). Too high a concentration usually causes difficulties obtaining clear pellets. The IR beam is absorbed completely, or scattered from the sample which results in very noisy spectra.

Sample preparation

Completely dried potassium bromide was transferred into a mortar. About 2 % of drug sample was weighed in digital balance, mixed and grind to a fine powder. Two stainless steel disks were taken out of the desiccator. A piece of the precut cardboard (in the tin can next to the oven) on top of one disk was placed and cutout hole was filled with the finely ground mixture. The second stainless steel disk was kept on top and transfers the sandwich onto the pistil in the hydraulic press. With a pumping movement, hydraulic pump handle moved downward. The pistil will start to move upward until it reaches the top of the pump chamber. Then, the pump handle moved upwards and continued pumping until the pressure reaches 20,000 prf. Rest for a few seconds and with the small lever on the left side, the pressure was released. Removing of the disks and pulling apart. Obtained film was homogenous and transparent in appearance. Than inserted into the IR sample holder and attach with scotch tape and run the spectrum.

The physical mixtures of drugs were prepared in 1:1 ratio and then passed through sieve # 30. Samples of drug and excipients were placed in vial, closed and labelled.

Experimental Methods

Analytical method development by U.V. Spectroscopy

UV-Visible spectrophotometry is one of the most frequently employed technique in pharmaceutical analysis. It involves measuring the amount of ultraviolet or visible radiation absorbed by a substance in solution. Instrument which measure the ratio, or function of ratio, of the intensity of two beams of light in the U.V-Visible region are called Ultraviolet-Visible spectrophotometers.

In qualitative analysis, organic compounds can be identified by use of spectrophotometer, if any recorded data is available, and quantitative spectrophotometric analysis is used to ascertain the quantity of molecular species absorbing the radiation. Spectrophotometric technique is simple, rapid, moderately specific and applicable to small quantities of compounds. The fundamental law that governs the quantitative spectrophotometric analysis is the Beer -Lambert law.

Scanning of λ_{max} of Mesalazine

Preparation of Stock Solution

10 mg of Mesalazine was taken in a 10ml volumetric flask. To that 2ml of methanol was added and shaken well to dissolve the drug. The solution was made up to the mark with 6.8 pH buffer to give 1000 µg /ml concentration. From the above solution 1ml is diluted to 10ml with 6.8 pH buffer to give 100 µg /ml concentration. From the above solution, take 1ml, and diluted to 10ml with 6.8 pH buffer, to give 10 µg /ml concentration. The prepared solutioni.e.,10µg/ml concentration was scanned for λ_{max} from 200-400 nm in UV/Visible spectrophotometer.

Calibration curve of Mesalazine in 6.8 pH buffer

10mg of Mesalazine was accurately weighed and transferred into 10ml volumetric flask. It was dissolved and diluted to volume with 6.8 pH buffer to give stock solution containing 1000µg/ml. The standard stock solution was then serially diluted with 6.8 pH buffer to get 2 to 12 µg/ml of. The absorbance of the solution was measured against 6.8 pH buffer as blank at 332 nm using UV spectrophotometer. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

PREPARATION OF SOLID DISPERSIONS OF MESALAZINE[87-90]

There are several carriers, which have been reported for the preparation of solid dispersions by using ß-cyclodextrin, croscarmellose various methods of preparation.

Solvent evaporation method

The inclusion complexes were prepared using solvent evaporation technique[2]. The required amount of Mesalazine and ß-cyclodextrin in 1:1, 1:2, 1:3,1:4 and 1:5 ratios were dissolved in N, N-dimethyl formamide (DMF) and allowed to stand overnight. The solvent from the solutions was removed at temperature of 60° under vacuum until the solid dispersion was dry. Solvent was removed by evaporation under reduced pressure and now the obtained product was collected. The dried mass was pulverized, passed through sieve no. 60 and stored in desiccator until used for further studies.

Solid Dispersions

Table 1: Mesalazine: croscarmellose

Formulation code	Drug: polymer ratio (Mesalazine: croscarmellose)
F1	1:1
F2	1:2
F3	1:3
F4	1:4

Table 2: Mesalazine : Eudragit® E100

Formulation code	Drug : Polymer ratio (Mesalazine : Eudragit® E100)
F5	1:1
F6	1:2
F7	1:3
F8	1:4

Table 3: Mesalazine: ß-cyclodextrin

Formulation code	Drug : Polymer ratio (Mesalazine: ß-cyclodextrin)
F9	1:1
F10	1:2
F11	1:3
F12	1:4

RESULT AND DISCUSSION

Solubility

Solubility of was carried out at 25^0C using 0.1 N HCL, 6.8 phosphate buffer, 7.4 pH buffer, methanol and ethanol.

Table 4: Solubility studies data of Mesalazine

MEDIUM	SOLUBILITY (µg/ml)
0.1 N HCL	0.467
6.8 pH phosphate buffer	0.987
7.4 pH phosphate buffer	0.851

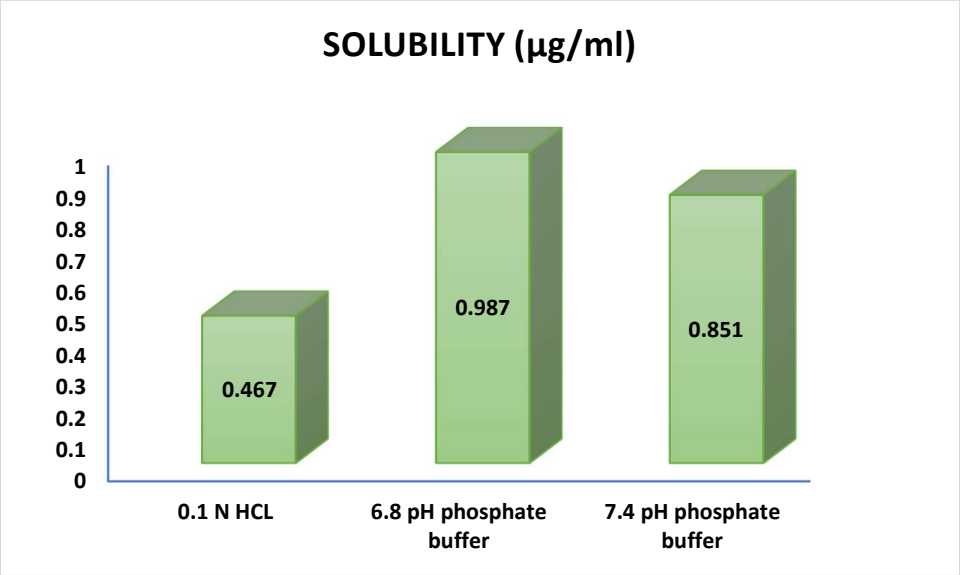

Fig 1: Graphical representation of Mesalazine Solubility studies

From the above conducted solubility studies in various buffers we can say that 6.8 pH Buffer buffer solution has more solubility when compared to other buffer solutions.

Analytical method development by U.V. Spectroscopy
Uv Scan Spectrum of Mesalazine

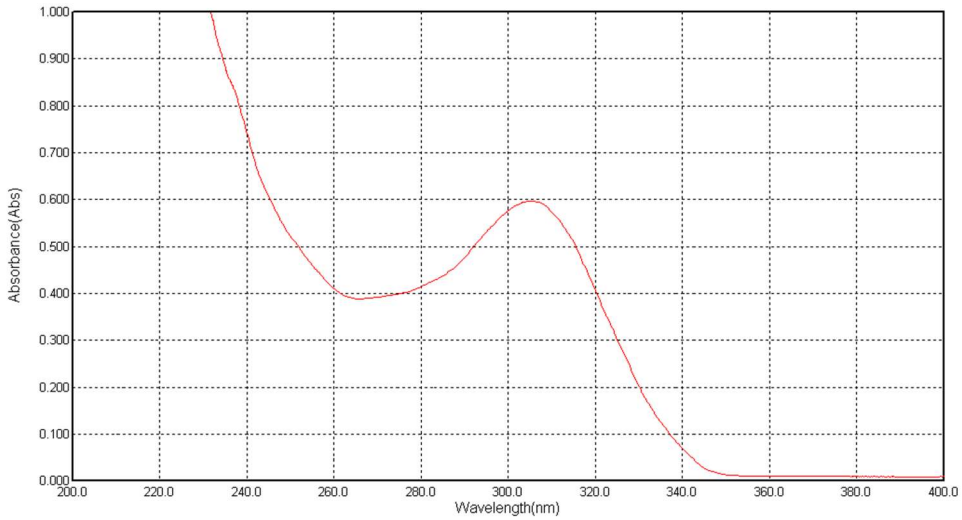

Fig 2: Uv Scan Spectrum of Mesalazine

The λ-max of Mesalazine of 100% solution i.e 8ppm (µg/ml) by using Single Beam Spectrophotometer (YIS-294) was found to be at 332 nm by using pH 6.8 phosphate buffer

Calibration curve of Mesalazine in 6.8 pH

Table 5: Calibration curve of Mesalazine in 6.8 pH Buffer

Concentration (µg/ml)	Absorbance
0	0
2	0.157
4	0.317
6	0.452
8	0.599
10	0.767
12	0.924

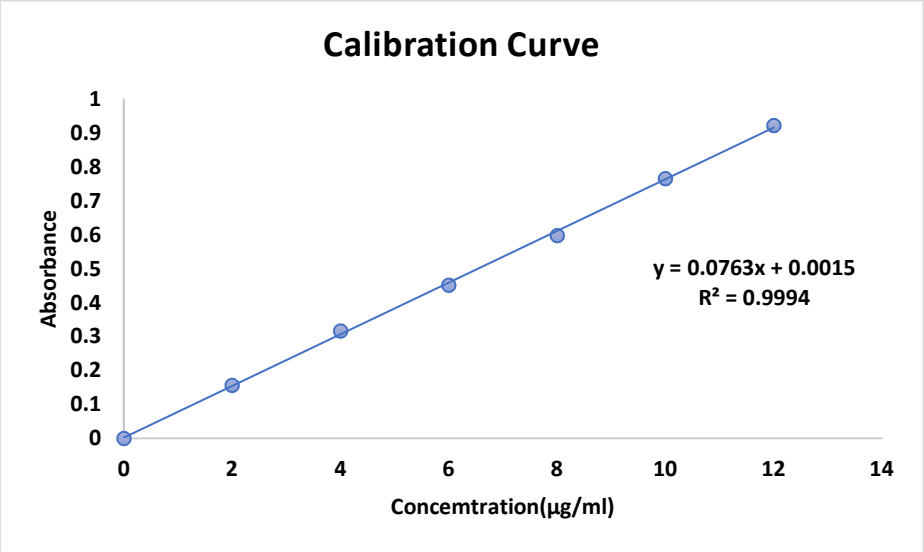

Fig 3: Calibration curve of Mesalazine

The linearity was found to be in the range of 2-12 µg/ml in pH 6.8 phosphate buffer. Regression analysis was selected because it minimizes the deviation and correct the variance heterogeneity. The regression line was defined by its slope (m) and its intercept (C) for normal regression analysis was found as 0.0763 and 0.0015, with regression coefficient of 0.9994 respectively. The regression value was closer to 1 indicating the method obeyed Beer-lamberts' law.

Drug excipient compatibility

Drug and excipient compatibility was confirmed by comparing spectra of FT-IR analysis of pure drug with that of various excipients used in the formulation.

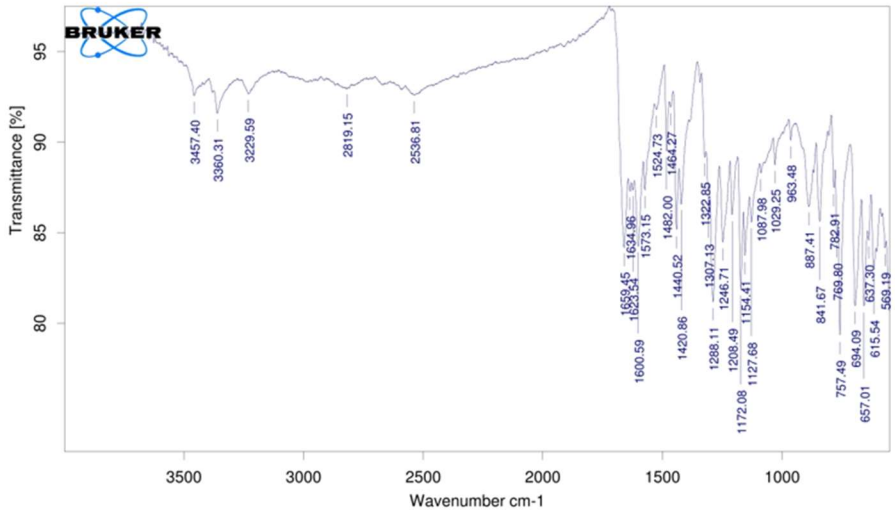

Fig 4: IR spectrum of pure Mesalazine

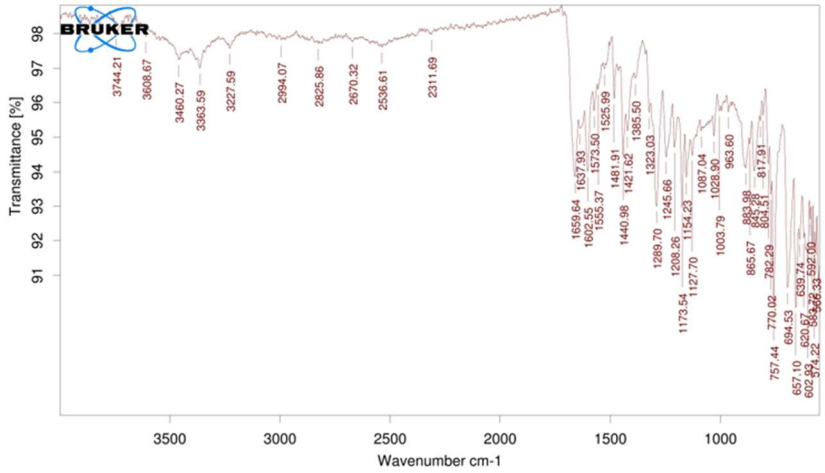

Fig 5: IR spectrum of Mesalazine Optimised Formulation

From the drug excipient compatibility studies we observe that there are no interactions between the pure drug (Mesalazine) and optimized formulation (Mesalazine: excipients) which indicates there are no physical changes.

Percentage Drug Content of Solid Dispersions

Table 6: Percentage drug content of solid dispersions

Formulation code	%Drug content
F1	94.12%
F2	95.02%
F3	96.34%
F4	97.15%
F5	93.36%
F6	94.78%
F7	95.67%
F8	96.02%
F9	95.61%
F10	96.61%
F11	97.61%
F12	98.12%

The percentage Drug content of the formulated solid dispersions was found to be in the range of 93.36%- 98.12% respectively.

INVITRO DRUG RELEASE STUDIES OF SOLID DISPERSIONS

Table 7: *Invitro* drug release studies for formulations (F1-F12)

Time (Min)	Percentage drug releasee											
	Mesalazine : Croscarmellose				Mesalazine : Eudragit® E100				Mesalazine : ß-cyclodextrin			
	1:1 (F1)	1:2 (F2)	1:3 (F3)	1:4 (F4)	1:1 (F5)	1:2 (F6)	1:3 (F7)	1:4 (F8)	1:1 (F9)	1:2 (F10)	1:3 (F11)	1:4 (F12)
0	0	0	0	0	0	0	0	0	0	0	0	0
5	43.42	58.26	44.64	56.21	45.24	56.84	49.53	58.14	54.44	57.14	60.14	65.24
10	50.16	60.63	58.35	64.74	58.24	67.57	56.92	64.21	61.02	65.28	74.12	78.21
15	58.85	65.98	67.03	71.28	67.45	72.18	60.36	72.24	78.48	74.36	81.51	85.46
30	63.32	75.09	78.32	79.64	78.25	86.32	73.62	80.47	85.23	87.24	89.25	89.17
45	78.19	85.32	86.56	86.28	88.29	91.47	86.43	88.21	89.04	91.25	93.36	94.21
60	92.85	93.78	94.36	97.24	94.75	95.12	96.56	97.25	95.45	96.12	98.47	99.45

In-vitro drug release of Mesalazine solid dispersions with Croscarmellose in various ratios were observed which shows at the end of 60 mins , the formulation F1 releases 92.85%, formulation F2 releases 93.78%, F3 releases 94.36%, and formulation F4 releases 97.24% at the end of 60 minutes, while Eudragit® E100 used as carrier shows formulation F5 releases 94.75%, formulation F6 releases 95.12%, and formulation F7 releases 96.56%, and formulation F8 releases 97.25%, while ß-cyclodextrin used as carrier shows formulation F9 releases 95.45%, formulation F10 releases 96.12%, formulation F11 releases 98.47% and formulation F12 releases 99.45%, at the end of 60 mins. Among all formulation F12 formulation shows maximum drug release at the end of 60 minutes so it was chosen as optimized formulation.

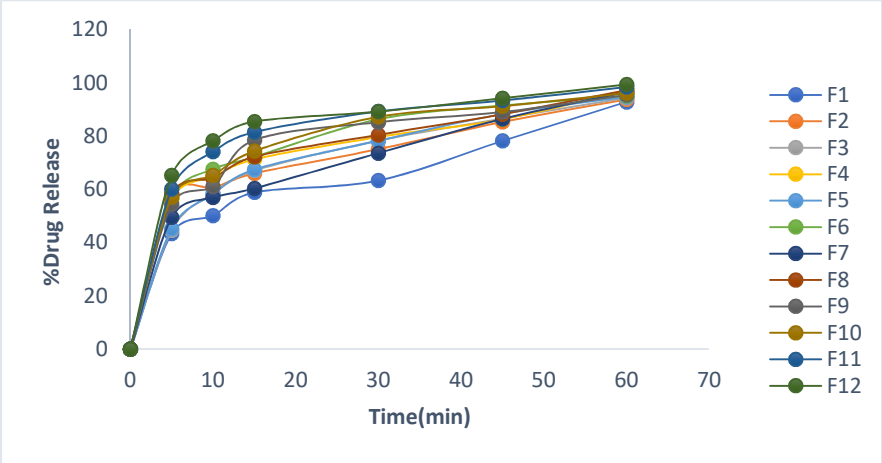

Fig 6: *Invitro* drug release profile for (F1-F12)

Evaluation characteristics of suppositories

Table 8: Evaluation characteristics of suppositories

Parameters	Results
Melting Point	35°C-38°C
Mechanical Strength	4.1 kg/cm^2
Disintegration Time	Completely dissolved within 9 mins
%Drug Content	97.48%

The melting point of the prepared suppository was found in between 35°C-38°C, the Mechanical strength i.e hardness of the suppository was found to be 4.1kg/cm^2, the time of disintegration of solid dispersion loaded was 9 minutes, and the % Drug content of the prepared suppository was found to be 97.48%.

Invitro drug release studies of suppository with pure drug

Table 9: % Drug release comparison for Pure drug loaded Suppository and Solid dispersion loaded Suppository

Time(mins)	Suppository loaded with Pure Drug	Suppository loaded with Solid dispersion
0	0	**0**
40	15.21	**38.23**
80	28.36	**55.48**
120	33.29	**70.98**
160	49.95	**81.29**
200	58.68	**90.15**
240	67.48	**98.85**

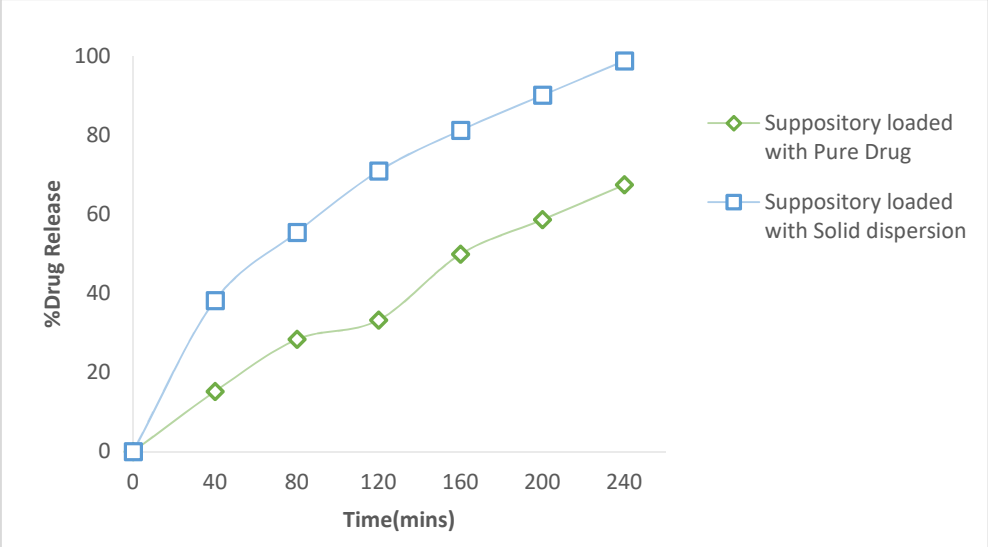

Fig 7: Drug release comparison for Pure drug loaded Suppository and Solid dispersion loaded Suppository

The in vitro dissolution studies were performed by dialysis bag method over a period 4 hrs and the results are shown in fig. At the end of 4 hrs, **98.85**% of drug was released from solid dispersion loaded suppositories with a 50% of drug was released in 40 min, whereas pure drug loaded suppositories released 50% of drug released in 161 min. At the end of 4 h, pure drug loaded suppositories released only 67.48% of drug. The results proved that the solid dispersion incorporated suppository was released maximum amount of drug at the end of 4th Hour.

Kinetics Analysis for Suppository loaded with Solid dispersion

Table 10: Regression values

Kinetics	Zero order	First order	Higuchi	Peppas
Code	R^2	R^2	R^2	R^2
Formulation	0.919	0.864	0.999	0.984

The optimized formulation has coefficient of determination (R^2) values of 0.919, 0.864, 0.999 and 0.984 for Zero order, First order, Higuchi and Korsmeyer Peppas respectively. A good linearity was observed with the Zero order, indicates the rate of drug release through the mode of diffusion and to further confirm the diffusion mechanism. Thus, the release kinetics of the optimized formulation was best fitted into Zero order.

CONCLUSION

Mesalazine is an aminosalicylate drug used to treat mild to moderate active ulcerative colitis and also to maintain remission once achieved. So Mesalazine was chosen as a model drug with an aim to develop a Solid dispersion loaded Suppository. In this research work preparation of Solid dispersion was prepared using super disintegrants like Croscarmellose, Eudragit® E100 and ß-cyclodextrin were selected in the system. The solubility of Mesalazine was is having more solubility 6.8 pH phosphate buffer. All the prepared formulations were analysed for Drug content was found in between 93.36% - 98.12% respectively for F1-F12. From the Invitro drug release data of the Solid dispersion for F1 to F12. it was concluded that the formulation F12 of 1:4 Mesalazine: ß cyclodextrin shows maximum drug release at the end of 60 minutes. So F12 was chosen as Optimized formulation and further transferred for Suppository loading. The suppository was prepared by using PEG 4000 and PEG 1000 in the ratio of 75:25 used as ideal base for suppository is used to prepare suppository. This prepared suppository undergoes through the evaluation parameters like melting point, Drug Content, Hardness, In-Vitro Disintegration, In vitro release profile and release kinetics of the solid dispersion loaded suppository.

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