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Formulation Development and In-Vitro Evaluation of satranidazole Microspheres

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ABSTRACT

Amoebiasis, caused by *Entamoeba histolytica*, is a significant global health concern, with high morbidity and mortality rates. Conventional treatments like metronidazole suffer from poor colonic targeting due to premature absorption in the upper gastrointestinal tract (GIT). This study aimed to develop colon-targeted Satranidazole microspheres using pH-sensitive polymers (Eudragit L100, S100, and their combinations) to enhance drug delivery to the colon. Microspheres were prepared via the oil-in-oil emulsion solvent evaporation method and evaluated for pre-formulation parameters, entrapment efficiency, drug release kinetics, and stability. Optimized formulations (EL3i, ES2i, ELS2i) demonstrated spherical morphology, high entrapment efficiency (up to 85.65%), and controlled drug release (>65% at pH 7.4). Kinetic analysis revealed zero-order release kinetics, with Eudragit S100-based microspheres (ES2i) showing superior colonic targeting. Stability studies confirmed the formulation's robustness under accelerated conditions. These findings suggest that pH-sensitive Satranidazole microspheres are a promising approach for effective amoebiasis treatment by ensuring targeted drug delivery to the colon.IR Study[7]

INTRODUCTION

Amoebiasis, a parasitic infection of the large intestine caused by *Entamoeba histolytica*, affects 34–50 million people annually, resulting in 40,000–100,000 deaths. Current therapies, including metronidazole and Satranidazole, are limited by systemic absorption in the upper GIT, reducing their efficacy against colonic trophozoites. Colon-targeted drug delivery systems (CDDS) using pH-sensitive polymers like Eudragit can overcome this limitation by releasing drugs specifically in the alkaline environment of the colon. Satranidazole, a nitroimidazole derivative, offers advantages such as minimal side effects and better tolerability. However, its bitter taste and upper GIT absorption necessitate a targeted delivery system. Microspheres, with their ability to encapsulate drugs and control release, are ideal for this purpose. This study focused on developing Satranidazole microspheres using Eudragit L100, S100, and their combinations, optimizing formulation parameters, and evaluating their performance in vitro.

MATERIALS

Drug: Satranidazole (Alkem Laboratories). **Polymers:** Eudragit L100, S100 (Degussa, Germany). **Solvents:** Ethanol, acetone, liquid paraffin, n-hexane. **Surfactant:** Span-80. **Instruments:** UV spectrophotometer (Shimadzu), digital pH meter, dissolution apparatus (USP Type II), scanning electron microscope (SEM).

METHODS

Pre-formulation Studies

Drug Characterization:

Melting point, UV spectroscopy (λmax = 318 nm), IR spectroscopy (confirmed functional groups).
Solubility in various solvents (highest in PEG 400).
Partition coefficient (log P = 4.23, indicating hydrophobicity).

Analytical Method Development:

Calibration curves in methanol and pH 7.4 phosphate buffer (linear range: 5–25 µg/mL).

FORMULATION DEVELOPMENT

Microsphere Preparation: Oil-in-oil emulsion solvent evaporation method.

Variables: Drug-polymer ratio (1:1 to 1:5), polymer concentration (5–20% w/v), surfactant concentration (0.5–1.5% w/v).

Process: Polymer and drug dissolved in ethanol/acetone, emulsified in liquid paraffin/Span-80, stirred (1400 rpm), and dried.

Evaluation

1. **Particle Size and Morphology:** Optical microscopy and SEM.
2. **Entrapment Efficiency (EE):** UV analysis of drug content (EE = 65–85%).
3. **In Vitro Drug Release:** USP Type II apparatus (pH 1.2 for 2 h, then pH 7.4).
4. **Kinetic Analysis:** Zero-order, first-order, Higuchi, and Korsmeyer-Peppas models.
5. **Stability Studies:** Accelerated conditions (40°C, 75% RH for 3 months).

RESULTS AND DISCUSSION

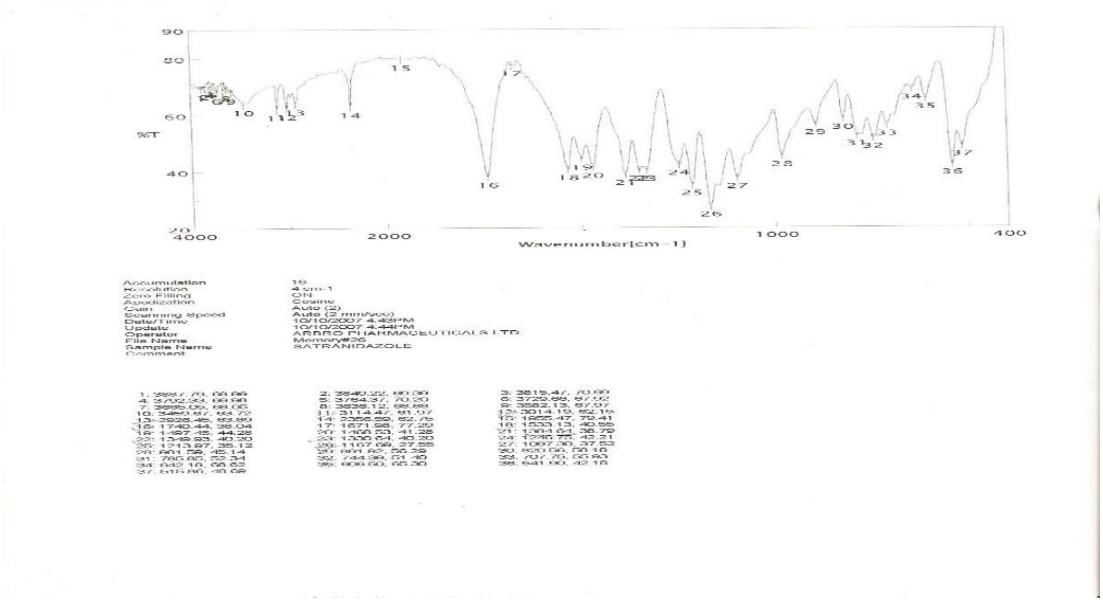

Fig-1 Infra red spectral characteristics of Satranidazole

ANALYTICAL METHOD FOR SATRANIDAZOLE

UV spectrum of Satranidazole in methanol

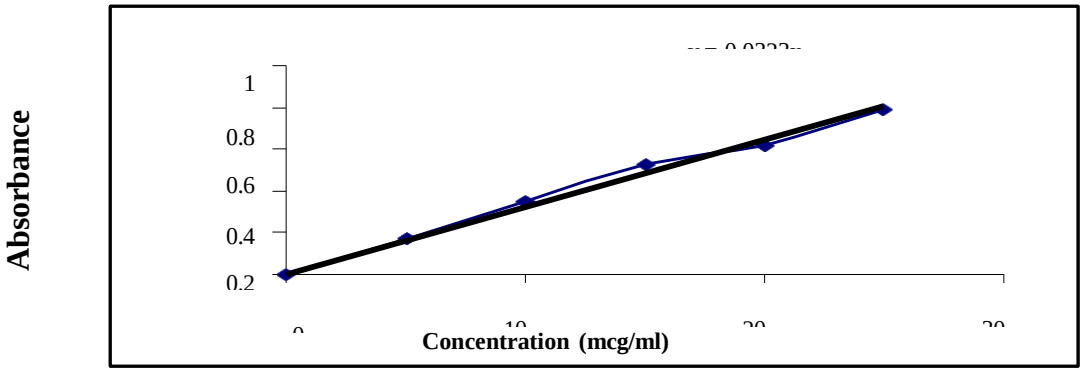

Fig. 2 Calibration curve of Satranidazole in methanol

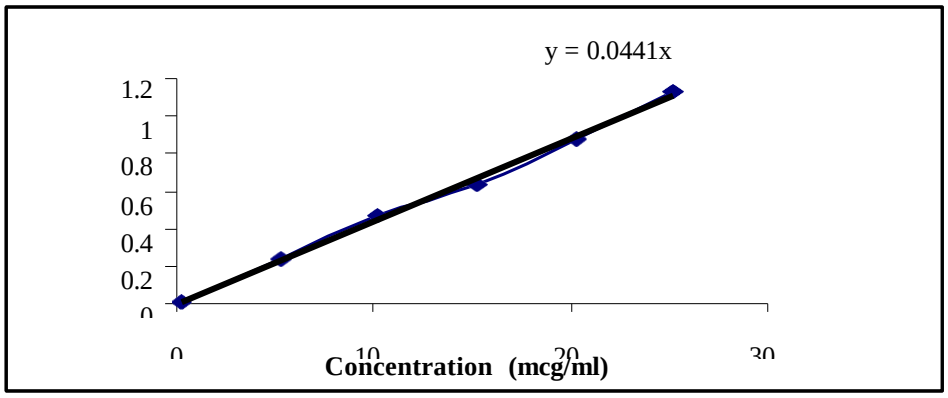

Fig.3 Calibration curve of Satranidazole in pH 7.4 phosphate buffer

Particle Size Distribution

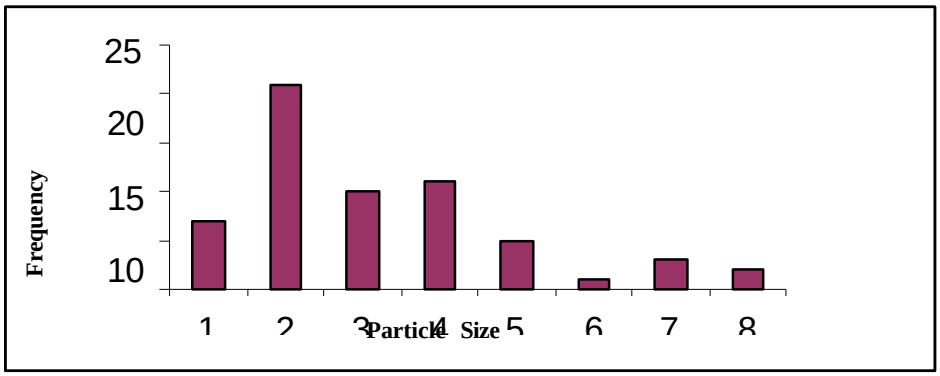

Fig.4: Particle Size Distribution of Satranidazole

Drug – Excipient interaction by DSC Study

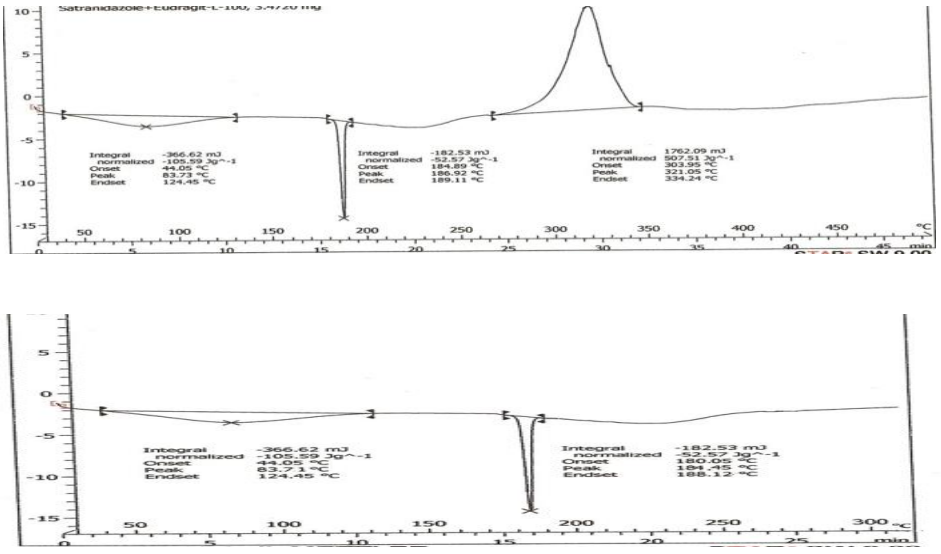

Fig. 5: Drug – Excipient interaction by DSC method

EVALUATION OF PREPARED MICROSPHERES

Evaluation of Eud-L based microspheres:
Size & Shape Determination of Microspheres

Table: 1 Size & Shape of Eud-L based microspheres

S. No.	Code	Mean diameter (µm)±S.D. (n=20)	Shape
1	EL1	53.55±0.08	Irregular and aggregated
2	EL2	55.55±0.08	Spherical and aggregated
3	EL3	56.35±0.06	Spherical and less aggregated
4	EL4	54.34±0.08	Spherical and aggregated
5	EL5	58.54±0.08	Irregular and aggregated

Table: 2 Selected Batch on The Basis of Spherical Shape of Eud-L based microspheres

Batch. No	D:P Ratio	Polymeric solution concentration (%w/v)	Name of surfactant	Surfactant concentration (%w/v)	Stirring speed (rpm)
EL2	1:2	10	Span-80	0.5	1400
EL3	1: 3	10	Span-80	0.5	1400
EL4	1:4	10	Span-80	0.5	1400

Determination of Drug Content and Entrapment efficiency:-

Table: 3 Entrapment Efficiency and Drug Content of Selected Eud-L based microspheres

Batch code	D:P Ratio	Entrapment efficiency (%)	Drug content (%)
EL2	1: 2	74.65	81.35
EL3	1:3	84.78	92.15
EL4	1: 4	65.65	73.46

Table: 4 Selected Batch on The Basis of Size and Entrapment Efficiency of Eud-L based microspheres

Batch. No	D:P Ratio	Polymeric solution concentration (%w/v)	Name of surfactant	Surfactant concentration (%w/v)	Stirring speed (rpm)
EL3	1: 3	10	Span-80	0.5	1400

Max Entrapment Efficiency is Found for Formulation EL3 is 84.78%, Hence it was selected for other parameter variables.

Table: 5 Size and shape of EL3 based formulations

S.No.	Formulation Code	Mean diameter (µm)±S.D. (n=20)	Shape
1	EL3a	55.47±0.04	Spherical & aggregation
2	EL3b	56.65±0.06	Spherical & aggregation
3	EL3c	56.73±0.03	Spherical & aggregation
4	EL3d	56.13±0.08	Spherical & aggregation
5	EL3e	55.69±0.07	Spherical & no aggregation
6	EL3f	57.04±0.05	Spherical & less aggregation
7	EL3g	56.83±0.16	Spherical & no aggregation
8	EL3h	56.39±0.12	Spherical & less aggregation
9	EL3i	56.94±0.09	Spherical & no aggregation
10	EL3j	55.81±0.02	Spherical & less aggregation
11	EL3k	56.28±0.08	Spherical & no aggregation
12	EL3l	55.88±0.06	Spherical & less aggregation

Table: 6 Entrapment Efficiency and Drug Content of EL3 based formulations

S.No.	Formulation Code	Entrapment efficiency (%)	Drug content (%)
1	EL3a	80.24	85.45
2	EL3b	78.25	81.78
3	EL3c	83.45	88.96
4	EL3d	76.12	80.14
5	EL3e	83.12	88.45
6	EL3f	80.45	87.98
7	EL3g	84.48	89.78
8	EL3h	81.96	87.64
9	EL3i	85.12	90.45
10	EL3j	83.45	88.42
11	EL3k	82.78	87.98
12	EL3l	84.56	89.78

EVALUATION OF EUD-S BASED MICROSPHERES

Size & Shape Determination of Microspheres

The diameter of microspheres was determined by using digital microscope.

Table: 7 Size & Shape of Eud-S based microspheres

S.No.	Code	Mean diameter (µm)±S.D. (n=20)	Shape
1	ES1	54.55±0.08	Irregular and aggregated
2	ES2	56.55±0.07	Spherical and less aggregated
3	ES3	57.35±0.06	Irregular and less aggregated
4	ES4	54.34±0.07	Spherical and aggregated
5	ES5	56.54±0.08	Spherical and aggregated

Table: 8 Selected Batch on The Basis of Spherical Shape of Eud-S based microspheres

Batch. No	D:P Ratio	Polymeric solution concentration (%w/v)	Name of surfactant	Surfactant concentration (%w/v)	Stirring speed (rpm)
ES 2	1:2	10	Span-80	0.5	1400
ES 4	1: 4	10	Span-80	0.5	1400
ES 5	1:5	10	Span-80	0.5	1400

Determination of Drug Content and Entrapment efficiency

Table: 9 Entrapment Efficiency and Drug Content of Selected Eud-S based microspheres

Batch code	D:P Ratio	Entrapment efficiency (%)	Drug content (%)
ES2	1: 2	85.65	91.35
ES4	1:3	71.78	82.15
ES5	1: 5	67.65	78.46

Table: 10 Selected Batch on The Basis of Size and Entrapment Efficiency of Eud-S based microspheres

Batch. No	D:P Ratio	Polymeric solution concentration (%w/v)	Name of surfactant	Surfactant concentratio n (%w/v)	Stirring speed (rpm)
ES2	1: 2	10	Span-80	0.5	1400

Table: 11 Size and shape of ES2 based formulations

S.No.	Formulation Code	Mean diameter (µm)±S.D. (n=20)	Shape
1	ES2a	56.72±0.07	Spherical & aggregation
2	ES2b	55.79±0.06	Spherical & aggregation
3	ES2c	56.14±0.03	Spherical & aggregation
4	ES2d	56.77±0.08	Spherical & aggregation
5	ES2e	55.88±0.07	Spherical & no aggregation
6	ES2f	56.32±0.05	Spherical & less aggregation
7	ES2g	56.83±0.16	Spherical & no aggregation
8	ES2h	56.39±0.12	Spherical & less aggregation
9	ES2i	55.81±0.02	Spherical & no aggregation
10	ES2j	56.94±0.09	Spherical & less aggregation
11	ES2k	56.04±0.05	Spherical & no aggregation
12	ES2l	56.33±0.04	Spherical & less aggregation

Table: 12 Entrapment Efficiency and Drug Content of ES2 based formulations

S.No.	Formulation Code	Entrapment efficiency (%)	Drug content (%)
1	ES2a	79.45	83.78
2	ES2b	81.24	86.12
3	ES2c	75.12	80.75
4	ES2d	78.45	84.69
5	ES2e	79.45	85.37
6	ES2f	81.45	87.12
7	ES2g	82.96	89.76
8	ES2h	80.12	88.45
9	ES2i	85.95	92.47
10	ES2j	79.96	84.25
11	ES2k	77.98	83.21
12	ES2l	81.87	86.27

EVALUATION OF EUD-LS BASED MICROSPHERES

Size & Shape Determination of Microspheres

Table: 13 Size & Shape of Eud-L S based microspheres

S. No.	Code	Mean diameter (µm)±S.D. (n=20)	Shape
1	ELS1	55.55±0.03	Spherical & no aggregation
2	ELS2	56.15±0.04	Spherical and less aggregated
3	ELS3	55.25±0.03	Spherical & no aggregation
4	ELS4	56.34±0.09	Spherical and aggregated
5	ELS5	56.64±0.038	Spherical and aggregated

Table: 14 Selected Batch on The Basis of Spherical Shape of Eud-LS based microspheres

Batch. No	D:P Ratio	Polymeric solution concentration (%w/v)	Name of surfactant	Surfactant concentration (%w/v)	Stirring speed (rpm)
ELS 1	1:1	10	Span-80	0.5	1400
ELS 2	1: 2	10	Span-80	0.5	1400
ELS 3	1:3	10	Span-80	0.5	1400

Determination of Drug Content and Entrapment efficiency

Table: 15 Entrapment Efficiency and Drug Content of Selected Eud-LS based microspheres

Batch code	D:P Ratio	Entrapment efficiency (%)	Drug content (%)
ELS 1	1:1	70.12	73.25
ELS 2	1: 2	84.22	74.56
ELS 3	1:3	62.45	68.46

Table: 16 Selected Batch on The Basis of Size and Entrapment Efficiency of Eud-LS based microspheres

Batch No.	D:P Ratio	Polymeric solution concentration (%w/v)	Name of surfactant	Surfactant concentration (%w/v)	Stirring speed (rpm)
ELS2	1: 2	10	Span-80	0.5	1400

Table: 17 Size, Entrapment Efficiency and Drug Content of ELS2 based formulations

S.No.	Formulation Code	Mean diameter (µm)± S.D. (n=20)	Entrapment efficiency (%)	Drug content (%)
1	ELS2a	55.72±0.03	82.78	87.61
2	ELS2b	56.79±0.06	78.25	86.45
3	ELS2c	56.14±0.09	77.84	88.75
4	ELS2d	56.27±0.08	79.65	87.69
5	ELS2e	55.58±0.05	80.78	86.78
6	ELS2f	56.34±0.08	81.61	89.42
7	ELS2g	56.79±0.06	79.86	85.42
8	ELS2h	56.49±0.02	83.46	89.37
9	ELS2i	55.11±0.02	84.45	90.12
10	ELS2j	56.24±0.09	76.49	88.12
11	ELS2k	56.14±0.05	79.86	87.94
12	ELS2l	56.43±0.03	81.46	89.27

Dissolution test

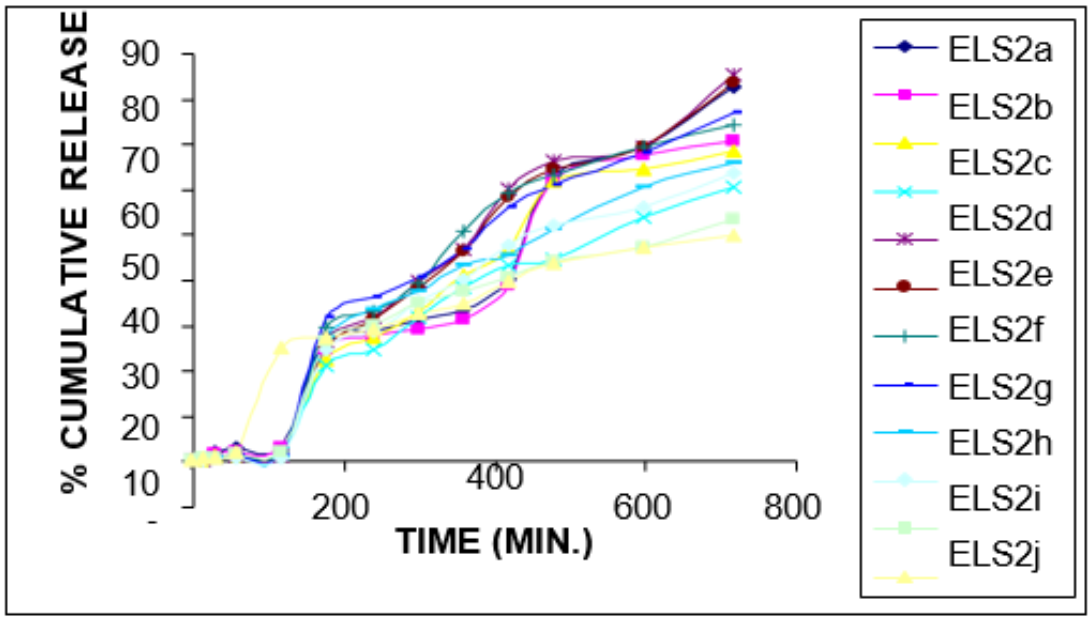

Fig.6: Comparative in vitro dissolution profile of Eud- LS based microspheres

Table 18: Comparative study of *in vitro* dissolution profile of optimized formulations

S.No	Time (mins.)	% Drug Release		
		EL3i	ES2i	ELS2i
1	0	0	0	0
2	15	0.217391	0.217391	0.217391
3	30	0.43599	0.43599	0.43599
4	60	0.655797	0.438406	0.438406
5	120	0.876812	0.658213	0.658213
6	180	22.62077	23.27053	26.96618
7	240	25.78986	29.48671	33.42029
8	300	39.84541	35.95411	37.51812
9	360	47.23913	42.8913	43.15942
10	420	49.67271	51.60507	45.35266
11	480	51.90097	58.40942	51.25242
12	600	61.31401	64.16304	60.22705
13	720	68.82126	70.16425	65.55435

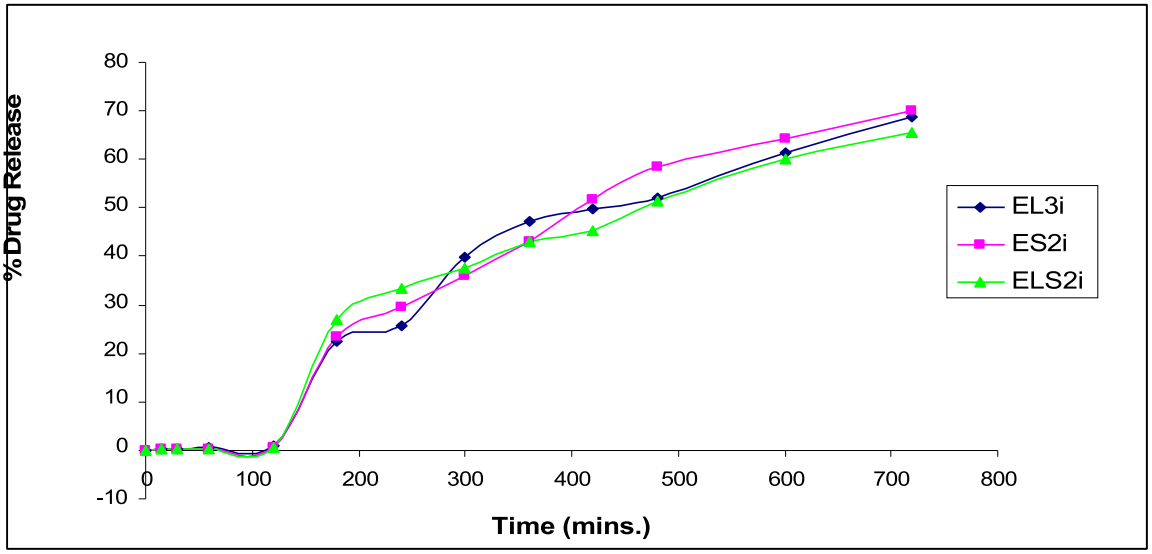

Fig 7: Comparative study of *in vitro* dissolution profile of optimized formulations EL3i, ES2i and ELS2i

Kinetic treatment of dissolution data of Optimized formulations[103,104]

Table:-19 Kinetic treatment of dissolution data of Optimized formulations

Formulation	Zero- order (r^2)	First- order (r^2)	Higuchi (r^2)	Korsmeyer-Peppas (n)
EL3i	0.9478	0.3128	0.9154	0.6705
ES2i	0.9561	0.7312	0.9162	0.9704
ELS2i	0.9344	0.7181	0.9204	0.9109

SEM

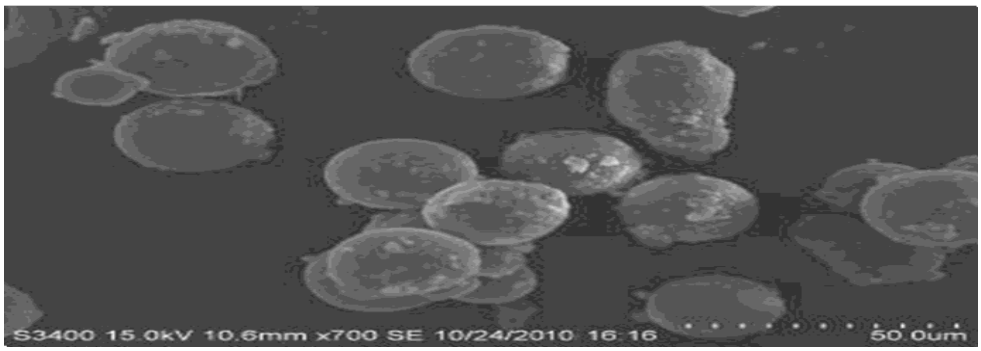

Fig. 8: SEM of optimized formulation ES2i

Stability Study

Batch code	Mean diameter (µm)±S.D. (n=20)	Shape	Entrapment efficiency (%)	Drug content (%)
ES2i	56.32±0.5	Spherical & less aggregated	79.84	87.56

Table 20: *in vitro* release profile of Satranidazole microspheres ES2i

S. No.	Time (Min)	% Cumulative Release
1	0	0
2	15	0.201234
3	30	0.44011
4	60	0.468567
5	120	0.648423
6	180	24.78452
7	240	30.49452
8	300	36.98754
9	360	43.78456
10	420	52.68967
11	480	57.79045
12	600	63.69504
13	720	69.89478

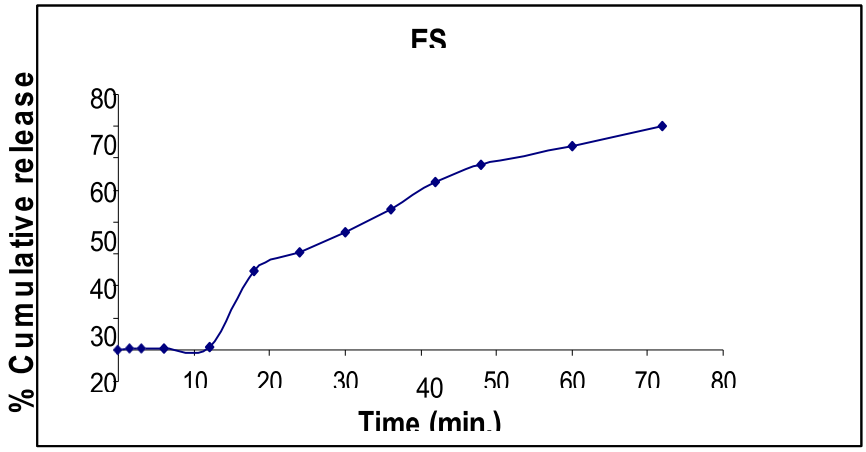

Fig. 9: Stability dissolution graph of optimized formulation ES2i

CONCLUSION

The study successfully developed colon-targeted Satranidazole microspheres using pH-sensitive Eudragit polymers. Eudragit S100-based microspheres (ES2i) demonstrated superior colonic targeting, with high entrapment efficiency, controlled release, and stability. These findings highlight the potential of pH-sensitive microspheres as an effective strategy for treating intestinal amoebiasis by ensuring localized drug delivery, minimizing systemic side effects, and improving patient compliance. Future studies should explore in vivo performance and scalability for clinical translation.

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