



FABRICATION AND PHYSICOCHEMICAL EVALUATION OF MICROSPHERE-BASED TAZAROTENE DELIVERY SYSTEMS

Sumit Kumar Das^{*1}, Prateek Jain², Hemant Agrawal³, Naveen Gupta⁴¹Student- Madhyanchal Professional University (MPU), Bhopal (M.P).^{2,3}Associate Professor - Madhyanchal Professional University (MPU), Bhopal (M.P).⁴Dean - Madhyanchal Professional University (MPU), Bhopal (M.P).

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***Corresponding Author: Sumit Kumar Das**

Student- Madhyanchal Professional University (MPU), Bhopal (M.P).

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ABSTRACT

Tazarotene is a topical retinoid widely used in the treatment of psoriasis, acne, and other dermatological disorders; however, its poor aqueous solubility and instability limit its therapeutic effectiveness and patient compliance. The present study aimed to fabricate and evaluate Tazarotene-loaded microspheres using Eudragit RS100 as a polymeric carrier system to achieve controlled drug release, enhanced stability, and improved topical delivery. Pre-formulation studies were carried out to investigate the physicochemical properties of Tazarotene, including organoleptic characteristics, solubility profile, melting point, pH, λ max determination, calibration curve, and FTIR analysis. The drug exhibited maximum absorbance and showed compatibility with formulation components. Microspheres were prepared by the emulsion solvent evaporation method using Eudragit RS100, sodium CMC, Tween 80, and chloroform. Five formulations (MSF1–MSF5) were developed by varying the polymer concentration. The prepared microspheres were evaluated for physical appearance, particle size, zeta potential, surface morphology, entrapment efficiency, in vitro drug release, release kinetics, and stability studies. Among all formulations, MSF4 was identified as the optimized formulation, exhibiting a particle size of 282.2 nm, zeta potential of 68.9 mV, and entrapment efficiency of 92.83%. SEM analysis revealed that the microspheres were spherical, smooth, porous, and uniformly distributed, indicating successful encapsulation and stable formulation characteristics. The in vitro drug release study demonstrated a sustained and controlled release pattern; with 98.97% cumulative drug release over 12 hours. Release kinetic analysis showed that the formulation predominantly followed the Higuchi diffusion model ($R^2 = 0.991$), indicating diffusion-controlled drug release from the polymeric matrix. Stability studies performed under ICH guidelines for 90 days revealed minimal changes in particle size and entrapment efficiency under both room temperature and accelerated conditions, confirming excellent formulation stability. The findings of the study suggest that Eudragit RS100-based Tazarotene microspheres provide an effective controlled-release topical delivery system with improved physicochemical stability, sustained drug release, and enhanced therapeutic potential for dermatological applications.

KEYWORDS: Tazarotene; Microspheres; Eudragit RS100; Emulsion solvent evaporation; Controlled drug delivery; Entrapment efficiency; Particle size; Zeta potential, Topical formulation.**1. INTRODUCTION**

Topical drug delivery systems have gained considerable attention in recent years due to their ability to provide localized therapeutic action, improved patient compliance, and reduced systemic side effects. Among various dermatological disorders, acne vulgaris,

psoriasis, and other hyperproliferative skin diseases remain major concerns affecting a large population worldwide. Conventional topical formulations such as creams, ointments, and gels often suffer from limitations including poor skin penetration, low drug retention, irritation, and frequent application requirements.

Therefore, the development of advanced carrier systems capable of enhancing drug stability, penetration, and controlled release has become an important area of pharmaceutical research (Prausnitz and Langer, 2008).

Tazarotene is a third-generation topical retinoid widely used in the treatment of acne vulgaris, psoriasis, and photoaging. It acts by modulating gene expression and normalizing keratinocyte differentiation and proliferation. Despite its therapeutic effectiveness, the clinical use of Tazarotene is limited by its poor aqueous solubility, instability in the presence of light and oxygen, skin irritation, and reduced patient compliance associated with conventional formulations (Tang-Liu et al., 1999). These limitations necessitate the development of novel drug delivery approaches that can improve the therapeutic efficacy and tolerability of Tazarotene.

Microsphere-based drug delivery systems have emerged as promising carriers for controlled and targeted topical delivery. Microspheres are free-flowing spherical particles composed of biodegradable or non-biodegradable polymers capable of encapsulating active pharmaceutical ingredients. These systems offer several advantages, including prolonged drug release, enhanced stability, improved drug entrapment, reduced dosing frequency, and minimized irritation at the application site (Jain, 2000). In topical therapy, microspheres help maintain sustained drug concentration on the skin surface, thereby improving therapeutic effectiveness and patient adherence.

Among the various polymers used in microsphere preparation, Eudragit RS100 is widely employed due to its biocompatibility, permeability characteristics, and excellent film-forming ability. The emulsion solvent evaporation technique is one of the most commonly used methods for preparing microspheres because it is simple, reproducible, and suitable for encapsulating lipophilic drugs such as Tazarotene (Jelvehgari et al., 2011). The physicochemical characteristics of microspheres, including particle size, zeta potential, morphology, entrapment efficiency, and drug release behavior, play a crucial role in determining the performance and stability of the final formulation.

The present study was therefore designed to formulate and evaluate Tazarotene-loaded microspheres using Eudragit RS100 by the emulsion solvent evaporation method. Pre-formulation studies were carried out to investigate the physicochemical properties of the drug, followed by characterization of the prepared microspheres for particle size, zeta potential, surface morphology, entrapment efficiency, in vitro drug release, and stability studies. The objective of the research was to develop a stable and effective microsphere-based topical delivery system capable of providing controlled drug release and enhanced therapeutic efficacy of Tazarotene for dermatological applications.

2. MATERIAL AND METHODS

2.1 Pre-formulation Studies

Pre-formulation studies of Tazarotene were carried out to evaluate its physicochemical properties, including organoleptic characteristics, solubility, melting point, pH, λ_{max} , and FTIR analysis. These studies are essential for selecting suitable excipients and developing a stable and effective microsphere formulation (Srinath et al., 2011).

2.1.1 Organoleptic Properties

The organoleptic properties such as color, odor, appearance, and physical state of Tazarotene were evaluated visually under proper lighting conditions. The drug appeared as a white, odorless crystalline powder, confirming its purity and identity (Warne et al., 2021).

2.1.2 Solubility Study

The solubility of Tazarotene was determined in various solvents including water, ethanol, methanol, chloroform, DMSO, and PBS (pH 6.8). The drug was found to be freely soluble in methanol, DMSO, and PBS, while sparingly soluble in water, indicating its lipophilic nature (Alsenj et al., 2007).

2.1.3 Melting Point Determination

The melting point of Tazarotene was determined using the capillary method. The observed melting point was within the reported range, confirming the purity and authenticity of the drug sample (Fule and Amin, 2014).

2.1.4 pH Determination

The pH of the Tazarotene solution was measured using a calibrated digital pH meter. The obtained pH was within the acceptable range for topical formulations, indicating suitability for skin application (Karastogianni et al., 2016).

2.1.5 λ_{max} Determination

The λ_{max} of Tazarotene was determined using UV-Visible spectrophotometry by scanning the drug solution between 200–400 nm. The maximum absorbance was observed at 351.0 nm, which was used for further analytical studies (Bitencourt et al., 2015).

2.1.5.1 Preparation of Standard Stock Solution

A standard stock solution of Tazarotene (1 mg/mL) was prepared in methanol and used for further dilution and calibration studies (Kurane et al., 2024).

2.1.5.2 Calibration Curve

Different concentrations of Tazarotene were prepared from the stock solution, and absorbance was measured at 351 nm. A linear calibration curve obeying Beer-Lambert's law was obtained, confirming the reliability of the analytical method (Shen et al., 2007).

2.1.5.3 FTIR Analysis

FTIR spectroscopy was performed to identify the characteristic functional groups of Tazarotene. The

obtained peaks were consistent with standard reference peaks, confirming the identity and purity of the drug (Nijhawan et al., 2022).

2.2 Preparation of Tazarotene microsphere Formulation

Tazarotene-loaded microspheres were prepared using the emulsion solvent evaporation technique. Eudragit RS100 was used as the polymeric carrier, chloroform as the organic solvent, aqueous sodium CMC as the microencapsulating medium, and Tween 80 as the dispersing agent. For each formulation, the required amount of Eudragit RS100 was dissolved in 10 mL of chloroform to form a uniform polymer solution. Tazarotene (100 mg of the total polymer solution) was added to the polymer solution and mixed thoroughly.

This polymer drug solution was then added dropwise into 10 mL of 0.3% w/v aqueous sodium CMC containing 0.5% v/v Tween 80 under constant stirring at 1000 rpm. Continuous stirring at room temperature for 3 hours allowed complete evaporation of chloroform, resulting in the formation of spherical microspheres.

The microspheres were collected by vacuum filtration, washed repeatedly with distilled water and petroleum ether to remove residual solvent and impurities, and dried at room temperature for 24 hours to obtain microspheres. The five different formulations (F1–F5) were prepared by varying the polymer-to-drug ratio to study its effect on microsphere characteristics such as particle size, encapsulation efficiency, and drug release (Jelvehgari et al., 2011).

Table 1: Composition of microsphere Formulation.

Batch	Tazarotene (mg) (0.1%)	Eudragit RS100	Chloroform	Sodium CMC (%)	Tween 80 (%)	Aqueous Solution (ml)
MSF1	100 mg	200 mg	10 mL	0.3	0.5	10
MSF2	100 mg	250 mg	10 mL	0.3	0.5	10
MSF3	100 mg	300 mg	10 mL	0.3	0.5	10
MSF4	100 mg	350 mg	10 mL	0.3	0.5	10
MSF5	100 mg	400 mg	10 mL	0.3	0.5	10

2.3 Evaluation of Microspheres

2.3.1 Physical Appearance

The prepared microspheres were spherical, smooth, free-flowing, and off-white in color, indicating successful formulation.

2.3.2 Particle Size

Particle size analysis was carried out using dynamic light scattering (DLS). The microspheres showed uniform particle size distribution suitable for topical delivery.

2.3.3 Zeta Potential

Zeta potential analysis was performed using a Malvern Zetasizer to evaluate formulation stability. Higher zeta potential values indicated good stability of microspheres (Deepak et al., 2025, Bhattacharjee et al., 2015).

2.3.4 SEM Analysis

Scanning Electron Microscopy (SEM) confirmed the spherical shape and smooth surface morphology of the microspheres, indicating successful encapsulation (Ural et al., 2021).

2.3.5 Entrapment Efficiency

Entrapment efficiency was determined by UV spectrophotometric analysis and calculated using the standard formula. High drug entrapment indicated efficient incorporation of Tazarotene within the polymer matrix (Were, 2003).

2.3.6 In-vitro Drug Release Study

Drug release studies were performed using a Franz diffusion cell with phosphate buffer pH 6.8. The release data were fitted into different kinetic models including Zero-order, First-order, Higuchi, and Korsmeyer–Peppas models to determine the drug release mechanism (Patel, 2017).

2.7 Stability Studies

Stability studies were conducted according to ICH guidelines at $25 \pm 2^\circ\text{C}/60 \pm 5\% \text{ RH}$ and $40 \pm 2^\circ\text{C}/70 \pm 5\% \text{ RH}$ for three months. The formulation showed no significant changes in particle size and entrapment efficiency, indicating good stability (Mundada and Borate, 2025).

3. RESULT AND DISCUSSIONS

3.1 pre-formulation study of drug

3.1.1 Organoleptic properties of Tazarotene

Table 2: Organoleptic properties of Tazarotene.

Drug	Organoleptic properties	Observation
Tazarotene	Color	White
	Odor	Odorless
	Appearance	Crystalline powder
	State	Solid

3.1.2 Solubility study

Table 3: Solubility study of Tazarotene.

Drug	Solvents	Observation
Tazarotene	Water	Sparingly soluble
	Ethanol	Soluble
	Methanol	Freely soluble
	Chloroform	Soluble
	DMSO	Freely soluble
	PBS 6.8	Freely soluble

3.1.3 Melting point

Table 4: Melting point of Tazarotene.

S. No.	Drugs	Observed	Reference
1	Tazarotene	104 °C	100°C to 106°C

3.1.4 pH determination

Table 5: pH of Tazarotene.

S. No.	Drug Name	Observed	Reference
1	Tazarotene	6.9 pH	5.0 – 7.0 pH

3.2 Determination of λ max by UV spectroscopy of Tazarotene

Table 6: Lambda max of Tazarotene.

S. No	Drug	UV absorption maxima (Lambda max)
1.	Tazarotene	351.0 nm

3.3 Calibration curve analysis of Tazarotene drug

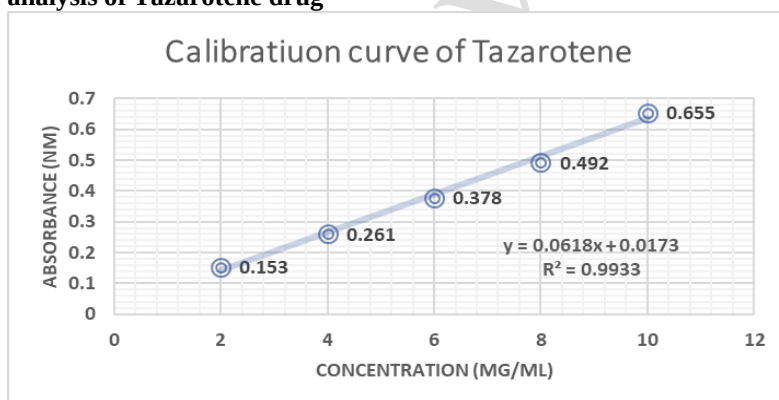


Figure 1: Calibration curve of Tazarotene.

3.4. FTIR of Tazarotene

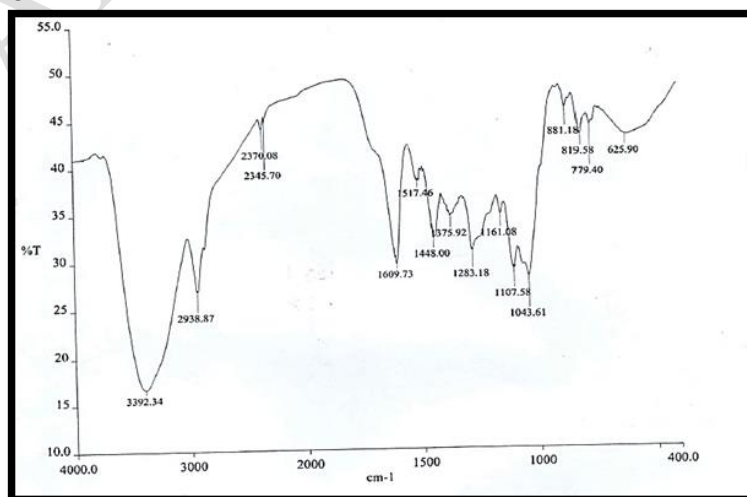


Figure 2: FTIR of Tazarotene.

Table 7: Interpretation of IR spectrum of Tazarotene.

S. No.	Peak obtained	Reference peak	Functional group	Name of functional group
1	3392.34	3400-3300	N-H stretching	aliphatic primary amine
2	2938.87	3000-2840	C-H stretching	alkane
3	2370.08	2600-2550	S-H stretching	Thiol
4	1609.73	1650-1600	C=C stretching	α , β -unsaturated ketone
5	1448.00	1450	C-H bending	alkane
6	1375.92	1390-1310	O-H bending	phenol
7	1107.53	1124-1087	C-O stretching	Secondary alcohol
8	1043.61	1050-1040	CO-O-CO stretching	anhydride

3.5 Characterization of drug loaded Microsphere formulation

3.5.1 Physical Appearance of Microsphere

Table 8: Physical Appearance of Drug loaded Microsphere.

S. No.	Formulation	Parameters	Observation
1.	Microsphere	Colour	off-white
2.		Odour	odorless
3.		Appearance	Solid



Figure 3: Microsphere formulation.

3.5.2 Particle Size Evaluation of Tazarotene-Loaded Microsphere Formulations

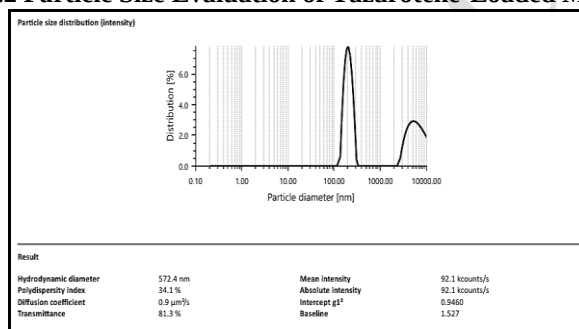


Figure 4: Particle Size MSF1

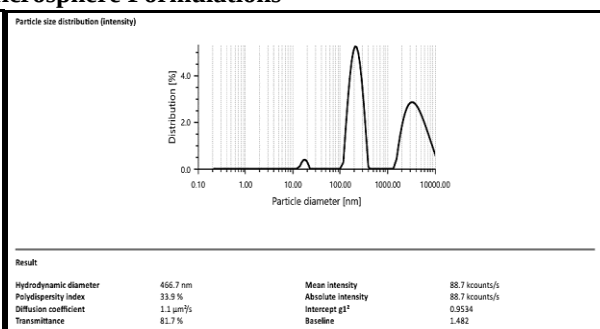


Figure 5: Particle Size MSF2

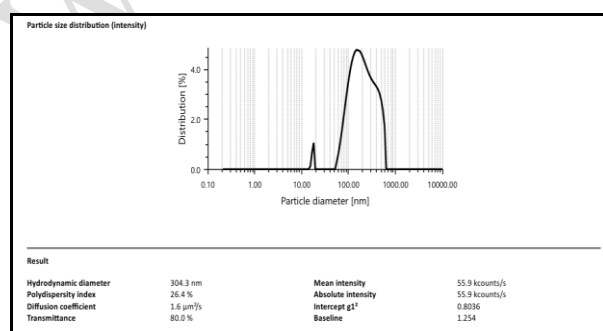


Figure 6: Particle Size MSF3

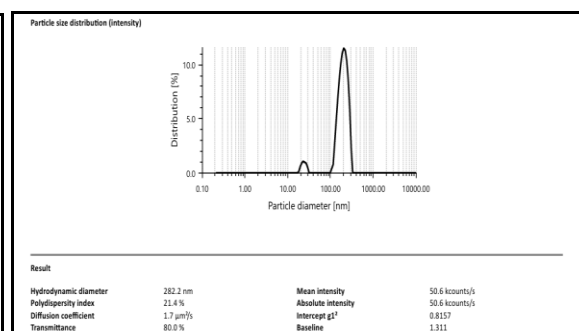


Figure 7: Particle Size MSF4

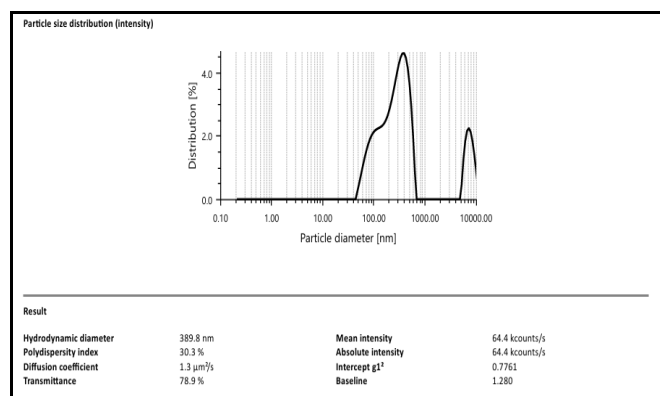


Figure 8: Particle Size MSF5.

3.5.3 Zeta potential evaluation of Tazarotene-Loaded Microsphere Formulations

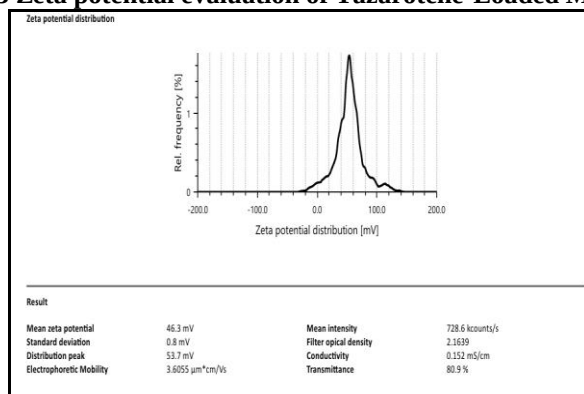


Figure 9: Zeta potential MSF1.

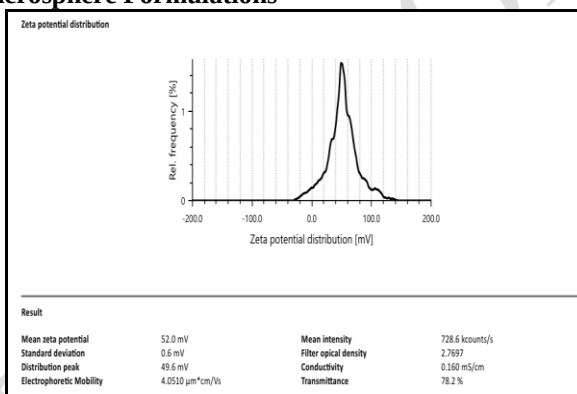


Figure 10: Zeta potential MSF2.

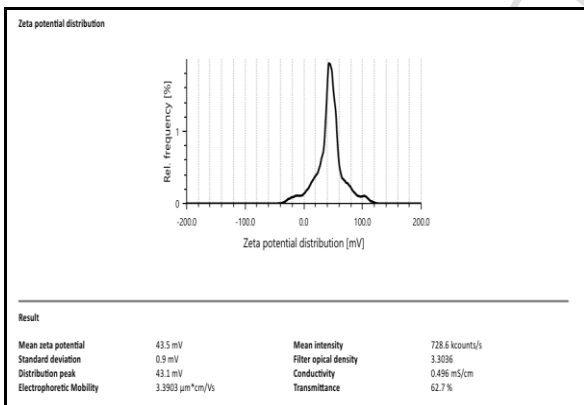


Figure 11: Zeta potential MSF3.

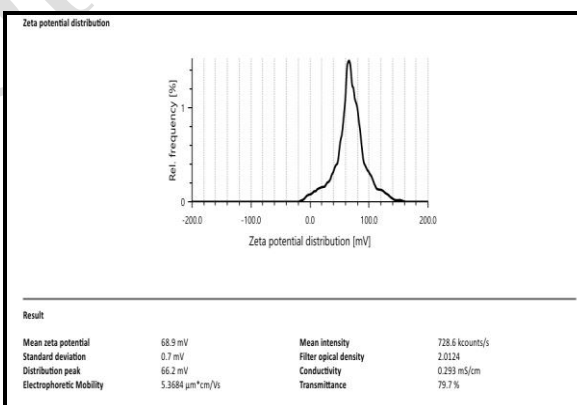


Figure 12: Zeta potential MSF4.

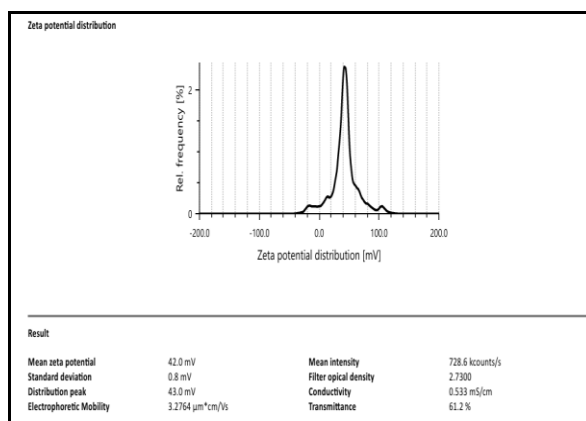


Figure 13: Zeta potential MSF5.

Table 9: Zeta potential of Microspheres formulation.

S. No	Formulation	Zeta potential (mV)	Particle size (nm)	Entrapment efficacy (%)
1.	MSF1	46.3	572.4	75.35
2.	MSF2	52.0	466.7	83.39
3.	MSF3	43.5	304.3	89.47
4.	MSF4	68.9	282.2	92.83
5.	MSF5	42.0	389.8	90.61

3.5.4 Scanning electron microscope (SEM)

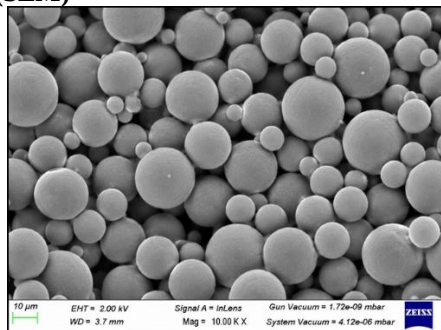


Figure 14: Scanning electron microscope (SEM).

3.6 In Vitro drug release study of optimized microsphere formulation

Table 10: In-vitro drug release studies.

Time (Hr)	cumulative % drug released	% drug remaining	Square root time	log Cumu % drug remaining	log time	log Cumu % drug released
0	0	100	0.000	2.000	0.000	0.000
1	21.12	78.88	1.000	1.897	0.000	1.325
2	31.88	68.12	1.414	1.833	0.301	1.504
3	44.78	55.22	1.732	1.742	0.477	1.651
4	56.33	43.67	2.000	1.640	0.602	1.751
6	67.8	32.2	2.449	1.508	0.778	1.831
8	78.66	21.34	2.828	1.329	0.903	1.896
10	87.25	12.75	3.162	1.106	1.000	1.941
12	98.97	1.03	3.464	0.013	1.079	1.996

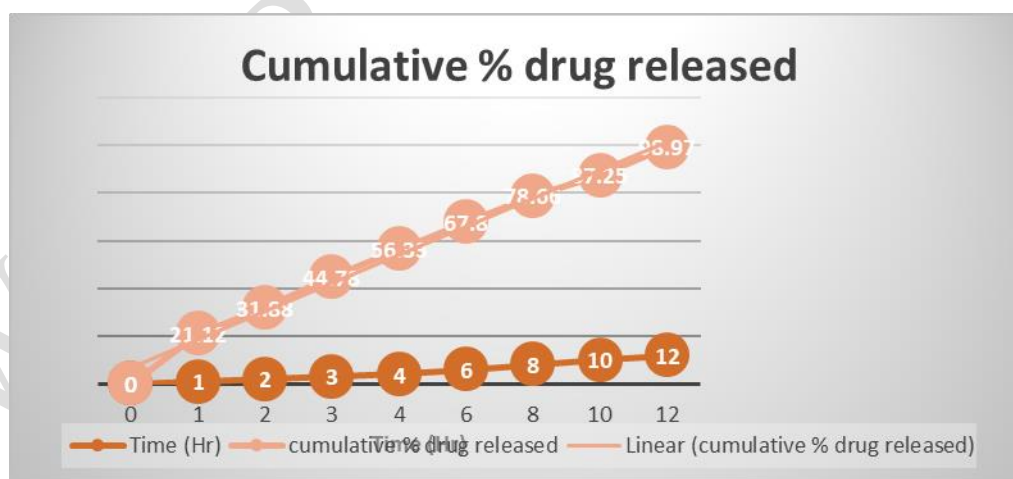


Figure 15: Drug release study.

Table 11: Correlation value (R^2 value).

Formulation	Model	Kinetic parameter values
Microspheres Formulation	Zero Order	$R^2 = 0.938$
	First Order	$R^2 = 0.749$
	Higuchi	$R^2 = 0.991$
	Korsmeyerpeppas	$R^2 = 0.622$

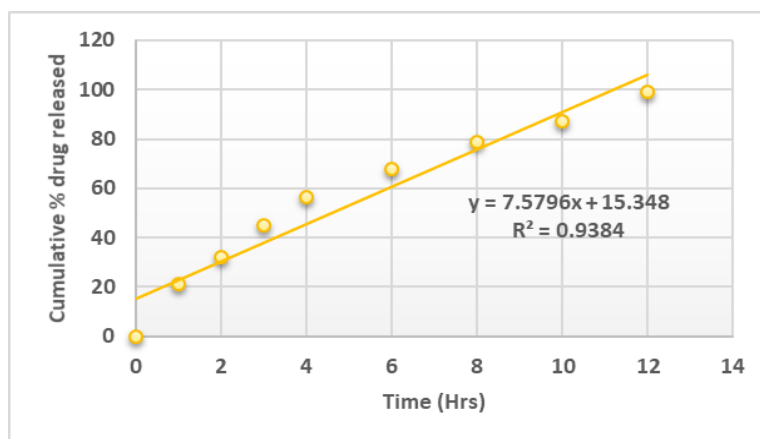


Figure 16: Zero order.

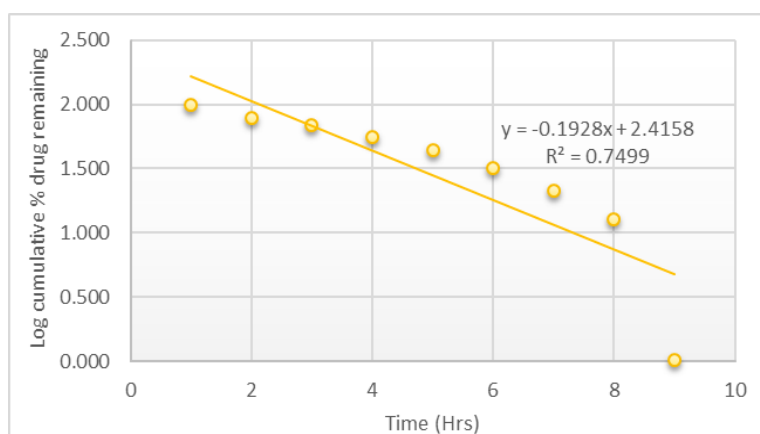


Figure 17: First Order.

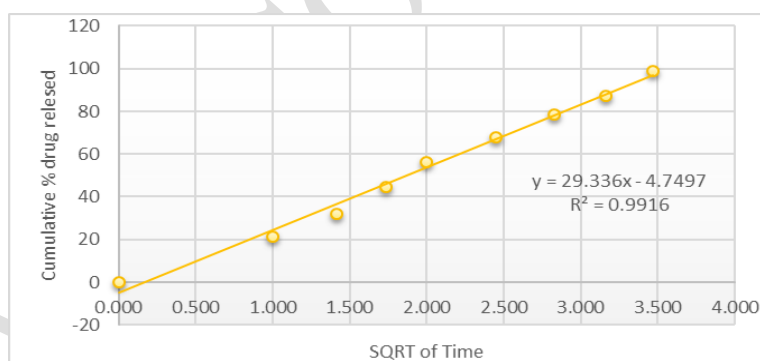


Figure 18: Higuchi.

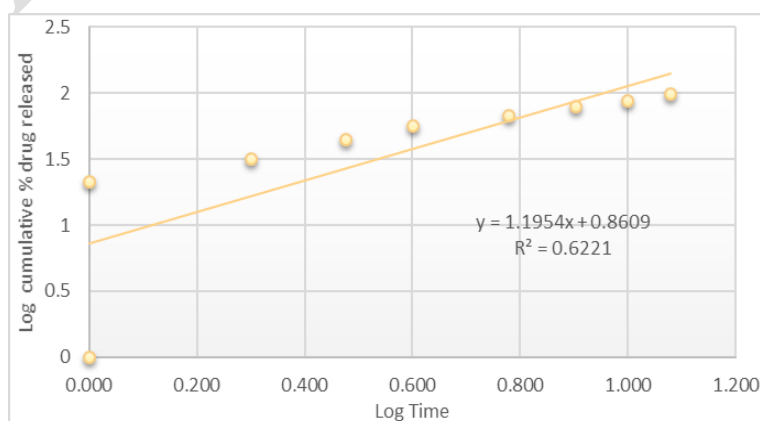


Figure 19: Korsmeyer peppas.

3.7 Stability study

Table 12: Stability Study of optimized formulation of microspheres.

S. No	Time (Days)	25°C±2 °C and 60 ± 5% RH		40°C±2 °C and 70 ±5% RH	
		Particle size (nm)	Entrapment efficacy (%)	Particle size (nm)	Entrapment efficacy (%)
1.	0	282.2	92.83	282.2	92.83
2.	30	282.5	92.83	280.1	92.80
3.	45	283.1	92.80	281.5	92.81
3.	60	283.2	92.81	279.9	92.75
4.	90	282.3	92.79	280.5	92.75

DISCUSSION

The present study successfully developed Tazarotene-loaded microspheres using the emulsion solvent evaporation method with Eudragit RS100 as the polymer. Pre-formulation studies confirmed the purity, compatibility, and suitability of Tazarotene for microsphere formulation. The prepared microspheres showed spherical shape, smooth surface, good stability, and high entrapment efficiency. Among all formulations, MSF4 showed the best results with optimum particle size (282.2 nm), highest zeta potential (68.9 mV), and maximum entrapment efficiency (92.83%). In-vitro drug release studies demonstrated sustained drug release up to 12 hours. Drug release followed the Higuchi model ($R^2 = 0.991$), indicating diffusion-controlled release. Stability studies revealed that the optimized formulation remained stable under different storage conditions.

4. CONCLUSION

Tazarotene-loaded microspheres were successfully prepared and evaluated. The optimized formulation (MSF4) showed excellent stability, high drug entrapment, and sustained drug release characteristics. The study concluded that microsphere formulation can serve as an effective topical drug delivery system for Tazarotene with improved therapeutic efficacy and prolonged drug release.

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