

FORMULATION AND CHARACTERIZATION OF IGURATIMOD LOADED GLYCEROSOME FOR ARTHRITIS

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Abstract

Iguratimod is an anti-inflammatory drug with therapeutic potential in the management of inflammatory disorders; however, its delivery may be improved through the use of advanced vesicular drug-delivery systems. The present study aimed to formulate and characterize Iguratimod-loaded glycerosomes using the thin-film hydration method. Glycerosomes were prepared using soya lecithin, cholesterol, glycerol, ethanol and phosphate buffer pH 7.4, with variations in formulation composition and sonication time. Nine formulations (F1–F9) were prepared and evaluated for particle size, polydispersity index (PDI), zeta potential, drug content, entrapment efficiency, surface tension, morphology, in-vitro drug release, deformability, elasticity and stability. Among the formulations, F9 exhibited the most desirable characteristics, with a particle size of 137.9 ± 4.3 nm, PDI of 0.168 ± 0.008 and zeta potential of -32.8 ± 1.7 mV. The drug content and entrapment efficiency were found to be $99.1 \pm 0.7\%$ and $93.6 \pm 0.9\%$, respectively, while the surface tension was 36.6 ± 0.3 mN/m. F9 also demonstrated the highest deformability ($82.8 \pm 1.3\%$) and elasticity index (0.81 ± 0.02), indicating improved vesicular flexibility. SEM and TEM studies confirmed the formation of discrete glycerosomal vesicles with a defined morphology. In-vitro release studies demonstrated prolonged drug release from the glycerosomal formulations, with F9 showing $90.8 \pm 0.8\%$ cumulative drug release at 12 h compared with a faster release from the marketed formulation. Release kinetics indicated that the Higuchi model provided the best fit, suggesting diffusion-controlled drug release. Stability studies showed no significant physical changes and only a minor decrease in drug content during storage. The findings indicate that Iguratimod-loaded glycerosomes can serve as a promising vesicular delivery system, with F9 exhibiting favourable physicochemical characteristics, high drug entrapment, enhanced deformability and sustained drug release.

Keywords: Iguratimod, Glycerosomes, Thin-film hydration, Soya lecithin, Vesicular drug delivery, Entrapment efficiency, Deformability, Sustained drug release.

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Introduction

Inflammatory disorders are characterized by persistent inflammation, pain, swelling, and progressive tissue damage, which can adversely affect the quality of life of affected individuals (Chen et al., 2017).

Iguratimod is a disease-modifying anti-rheumatic and anti-inflammatory drug used in the management of inflammatory joint disorders (Long et al., 2024). Although conventional drug therapy can provide therapeutic benefits, systemic administration may be associated with limitations such as gastrointestinal exposure, systemic adverse effects, and inadequate drug concentration at the desired site (Adepu et al., 2021). Therefore, development of an effective topical drug-delivery system may provide an alternative approach for localized drug administration (Jeong et al., 2021).

Topical drug delivery offers several advantages, including avoidance of gastrointestinal degradation, reduction of first-pass metabolism, improved patient

compliance, and the potential for localized drug action (Zhao et al., 2024). However, the stratum corneum, the outermost layer of the skin, represents a major barrier to the penetration of many therapeutic agents. Vesicular drug-delivery systems have therefore gained considerable attention because they can improve drug localization, enhance skin permeation, and provide controlled or sustained drug release (Jain et al., 2014).

Glycerosomes are novel lipid-based vesicular systems containing phospholipids along with a relatively high concentration of glycerol (Sharma et al., 2023). The presence of glycerol can improve vesicle flexibility and deformability, allowing glycerosomes to interact more effectively with the skin and potentially enhance drug penetration (Abdallah et al., 2025). Compared with conventional liposomes, glycerosomes may provide improved vesicular stability, elasticity, skin hydration, and drug delivery characteristics. Their ability to encapsulate drugs within lipid vesicles also offers the possibility

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of prolonged drug release and improved therapeutic performance (Natsheh et al., 2020).

In the present study, Icuratimod-loaded glycosomes were developed using the thin-film hydration method with soya lecithin, cholesterol, glycerol, ethanol, and phosphate buffer pH 7.4. The formulations were optimized by varying formulation composition and sonication conditions. The prepared glycosomes were characterized for particle size, polydispersity index, zeta potential, drug content, entrapment efficiency, surface tension, morphology, deformability, elasticity, in-vitro drug release, and stability. The study was undertaken to develop a stable and flexible vesicular system capable of providing sustained release and improved topical delivery of Icuratimod.

Material and Methods

Material

Icuratimod was procured from Yarrow Chem Products, Mumbai, India. Soya lecithin and cholesterol were obtained from Loba Chemie Pvt. Ltd., Mumbai, India. Glycerol, ethanol, and phosphate buffer pH 7.4 were obtained from Merck Life Science Pvt. Ltd., Mumbai, India.

Methods

Formulation of glycosomes by Thin-Film Hydration Method

Glycosomes containing Icuratimod were prepared by the thin-film hydration method with suitable modifications. Accurately weighed quantities of soya lecithin, cholesterol, and Icuratimod were dissolved in a suitable organic solvent system consisting of chloroform and ethanol. The resulting solution was transferred to a round-bottom flask and subjected to rotary evaporation under reduced pressure at approximately 40–45°C until the organic solvents were completely removed and a thin, uniform lipid film was formed on the inner wall of the flask.

An aqueous glycerol solution containing the required concentration of glycerol was prepared separately. The dried lipid film was subsequently hydrated with the prepared glycerol solution at approximately 40–45°C with gentle rotation and continuous stirring until a homogeneous vesicular dispersion was obtained. The resulting dispersion was further subjected to probe or bath sonication for the specified duration according to the formulation design to reduce vesicle size and obtain uniform glycosomal dispersion. The prepared formulations were allowed to equilibrate before further characterization and evaluation (Jahanfar et al., 2021).

Table 1: Formulation of Glycosomes by

Thin-Film Hydration Method							
For mula tion	Igur atim od (mg)	Cho leste rol (% w/v)	So ya Le cit hin (% w/ v)	Gl yce rol (% w/ v)	Et ha nol (% v/v)	Son icat ion Tim e (mi n)	Pho sph ate Buf fer pH 7.4
F1	50	0.5	2	5	5	10	q.s.
F2	50	0.5	3	5	5	20	q.s.
F3	50	0.5	4	5	5	30	q.s.
F4	50	0.5	2	10	5	10	q.s.
F5	50	0.5	3	10	5	20	q.s.
F6	50	0.5	4	10	5	30	q.s.
F7	50	0.5	2	15	5	10	q.s.
F8	50	0.5	3	15	5	20	q.s.
F9	50	0.5	4	15	5	30	q.s.

Note: q.s. = quantity sufficient.

Characterization Parameters of Glycosomes Vesicle Size and Size Distribution

The vesicle size and size distribution of the prepared glycosomes were determined using dynamic light scattering (DLS). An appropriate quantity of glycosomal dispersion was diluted with filtered distilled water or a suitable dispersion medium to minimize multiple scattering effects. The diluted sample was transferred into a suitable cuvette and analyzed using a particle-size analyzer. The polydispersity index (PDI), which represents the uniformity of vesicle size distribution, was determined simultaneously with the vesicle size. The measurements were performed in triplicate to ensure reproducibility (Rani et al., 2022).

Zeta Potential

The zeta potential of the glycosomal formulation was determined using a zeta-potential analyzer based on electrophoretic light scattering. The glycosomal dispersion was appropriately diluted using a suitable low-conductivity medium and transferred into a disposable or folded capillary cell. The sample was analyzed at a controlled temperature, and the zeta potential was recorded as an indicator of the surface charge and physical stability of the glycosomal dispersion (Suzuki et al., 2018).

Vesicle Morphology

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The morphology and surface characteristics of the glycosomal vesicles were examined using transmission electron microscopy (TEM) and scanning electron microscopy (SEM). An appropriately diluted glycosomal dispersion was placed on a suitable grid or specimen holder and subjected to the required sample preparation procedure. The prepared samples were subsequently examined under the respective microscopes to determine the shape, surface characteristics, and morphological integrity of the vesicles (Begum et al., 2016).

Entrapment Efficiency

The entrapment efficiency of the glycosomal formulation was determined by separating the entrapped drug from the untrapped drug. A known quantity of glycosomal dispersion was centrifuged at an appropriate speed to separate the vesicles from the free drug present in the dispersion medium. The supernatant containing the untrapped drug was carefully collected and analyzed using a suitable analytical method, such as UV-visible spectrophotometry or HPLC. The percentage entrapment efficiency was calculated to determine the amount of drug successfully incorporated within the glycosomal vesicles (Gupta et al., 2020, Zhua et al., 2022).

Vesicle Deformability

Vesicle deformability is an important characterization parameter of glycosomes, particularly when the formulation is intended to enhance drug penetration through biological barriers. A known quantity of glycosomal dispersion was extruded through a membrane having a defined pore size under constant pressure. The quantity of formulation that passed through the membrane within a specified period was measured. The deformability index was calculated to assess the ability of the glycosomal vesicles to undergo deformation while passing through pores smaller than their original diameter. A higher deformability index indicates greater vesicular flexibility (Rani et al., 2016).

Vesicle Elasticity

The elasticity of glycosomal vesicles was evaluated by passing the glycosomal dispersion through a membrane containing pores smaller than the vesicle diameter under constant pressure. The vesicle size before and after extrusion was determined using DLS. The ability of the vesicles to pass through smaller pores while maintaining their structural integrity was considered an indication of their elasticity. The presence of glycerol and other membrane-modifying components may enhance the flexibility and elasticity of the vesicular membrane,

thereby facilitating improved penetration through biological barriers (Manca et al., 2017)

Surface Tension

The surface tension of the glycosomal dispersion was determined using a stalagmometer or tensiometer under controlled temperature conditions. Surface tension is an important physicochemical property that can influence the spreading, wetting, and interaction of the formulation with biological surfaces. The measured value was recorded for evaluating the surface characteristics of the prepared glycosomal formulation (Zhang et al., 2022; Zaru et al., 2014).

Drug Content

The drug content of the glycosomal formulation was determined by accurately weighing a known quantity of the formulation and dissolving it in a suitable solvent. The resulting solution was appropriately diluted, and the drug concentration was determined using a validated analytical method, such as UV-visible spectrophotometry or HPLC. The drug content was expressed as a percentage of the theoretical drug content present in the formulation (Zaru et al., 2014).

In-vitro Drug Release

The in-vitro drug release profile of the glycosomal formulation was evaluated using a dialysis membrane method or an appropriate diffusion cell system. A known quantity of glycosomal formulation was placed inside the dialysis membrane and immersed in a suitable release medium maintained at a controlled temperature. The release medium was continuously stirred to maintain uniform drug distribution. Samples were withdrawn at predetermined time intervals and immediately replaced with an equal volume of fresh release medium to maintain sink conditions. The withdrawn samples were suitably diluted and analyzed spectrophotometrically for drug concentration. The cumulative percentage of drug released was calculated at each sampling interval and plotted against time to obtain the drug-release profile (Zaru et al., 2014).

Stability Study

Stability studies are an important aspect of the development and evaluation of pharmaceutical formulations because they provide information regarding the physical and chemical stability of the developed dosage form during storage. Accelerated stability studies are performed under controlled temperature and humidity conditions to facilitate the detection of possible formulation changes within a shorter period.

The stability study of the optimized glycosomal formulation was conducted according to the applicable ICH guidelines. The optimized formulation was suitably packed using polyethylene

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caps and aluminum foil and stored in a stability chamber maintained at $40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ relative humidity (RH) for 30 days. Samples were withdrawn after the specified storage period and evaluated for the following parameters:

1. Physical appearance
2. Drug content

The results obtained before and after storage were compared to determine any significant changes in the formulation and to assess its stability under accelerated storage conditions.

In-vitro Drug Release of Iguratimod-Loaded Glycrosomes and Marketed Formulation

The in-vitro drug release study of the optimized Iguratimod-loaded glycosomal formulation and the marketed Iguratimod formulation was performed using a Franz diffusion cell equipped with a suitable semipermeable membrane. Prior to the experiment, the membrane was adequately soaked in the release medium and carefully positioned between the donor and receptor compartments.

The receptor compartment was filled with a suitable release medium, such as phosphate buffer pH 7.4, and maintained at $37 \pm 0.5^\circ\text{C}$ using a thermostatically controlled system. Continuous stirring was provided using a magnetic stirrer to ensure uniform distribution of the released drug throughout the receptor medium.

An accurately weighed quantity of the optimized Iguratimod-loaded glycosomal formulation, equivalent to a known amount of Iguratimod, was carefully placed in the donor compartment over the membrane. An equivalent quantity of the marketed Iguratimod formulation containing the same amount of drug was used as the reference formulation. Both formulations were evaluated under identical experimental conditions.

Samples were withdrawn from the receptor compartment at predetermined time intervals of 0.5, 1, 2, 3, 4, 6, 8, 10, and 12 h. An equal volume of fresh, pre-warmed release medium was immediately added after each withdrawal to maintain a constant receptor volume and sink conditions. The collected samples were suitably diluted and analyzed spectrophotometrically at the predetermined absorption maximum (λ_{max}) of Iguratimod.

The amount of drug released at each time interval was calculated, and the cumulative percentage of Iguratimod released was plotted against time. The release profiles of the optimized glycosomal formulation and marketed formulation were compared to evaluate the influence of glycosomal encapsulation on the in-vitro drug-release behavior of Iguratimod (Zaru et al., 2010).

Results and Discussion

Glycrosomes containing Iguratimod were successfully prepared by the thin-film hydration method using soya lecithin, cholesterol, glycerol, ethanol and phosphate buffer pH 7.4. The lipid components were dissolved in an organic solvent system followed by solvent evaporation to form a uniform lipid film. Hydration of the lipid film with an aqueous glycerol solution and subsequent sonication resulted in the formation of glycosomal vesicles. The formulation composition of F1–F9 is presented in Table 1. Increasing concentrations of soya lecithin and glycerol and variation in sonication time were used to obtain glycrosomes with desirable vesicular characteristics.

The particle size and polydispersity index (PDI) of the prepared glycrosomes are presented in Table 2. The particle size decreased progressively from 613.4 ± 8.6 nm for F1 to 137.9 ± 4.3 nm for F9. Similarly, the PDI decreased from 0.482 ± 0.021 for F1 to 0.168 ± 0.008 for F9. The reduction in particle size with increasing formulation variables may be attributed to improved vesicle formation and the size-reducing effect of sonication. The lower PDI observed in F9 indicates a relatively narrow particle-size distribution and greater uniformity of the vesicular system. Among all formulations, F9 exhibited the smallest particle size and lowest PDI and was therefore considered the optimized glycosome formulation. The particle-size distribution of optimized formulation F9 is illustrated in Figure 1.

The zeta potential, drug content and entrapment efficiency of the prepared glycrosomes are shown in Table 3. The zeta potential values ranged from -17.6 ± 1.2 mV to -32.8 ± 1.7 mV. F9 exhibited the highest negative zeta potential (-32.8 ± 1.7 mV), suggesting improved electrostatic repulsion between vesicles and consequently better physical stability of the dispersion. The progressive increase in negative surface charge from F1 to F9 may be associated with changes in the lipid composition and vesicular surface characteristics.

Drug content was found to increase from $87.4 \pm 1.5\%$ in F1 to $99.1 \pm 0.7\%$ in F9. The high drug content of F9 indicates efficient incorporation of Iguratimod during glycosome preparation. Entrapment efficiency also showed a marked increase from $66.8 \pm 1.8\%$ for F1 to $93.6 \pm 0.9\%$ for F9. The higher entrapment efficiency may be related to the optimized lipid-to-drug ratio and improved vesicle formation. Thus, F9 demonstrated the most desirable combination of zeta potential, drug content and entrapment efficiency among the tested formulations. The surface tension values of the glycosomal formulations are presented in Table 4. Surface tension decreased from 44.8 ± 0.6 mN/m for F1 to

RESEARCH PAPER

36.6 ± 0.3 mN/m for F9. The gradual reduction in surface tension may be attributed to the increasing concentration of surface-active lipid components and glycerol in the formulation. The lower surface tension observed for F9 may facilitate better interaction of the vesicular system with the biological interface and may contribute to improved spreading and penetration characteristics. F9 exhibited the lowest surface tension among all formulations, further supporting its selection as the optimized formulation.

The morphology of the optimized glycosomes was investigated by scanning electron microscopy (SEM) and transmission electron microscopy (TEM). The SEM photograph is presented in Figure 3, while the TEM photograph is presented in Figure 4. The microscopic examination confirmed the formation of discrete glycosomal vesicles with a defined vesicular structure. The morphological findings were consistent with the particle-size results obtained by particle-size analysis and supported the successful formation of the glycosomal delivery system.

The in-vitro drug-release profiles of the glycosomal formulations are presented in Table 5. All formulations demonstrated a progressive increase in cumulative drug release with increasing time. At 12 h, the cumulative drug release values were 95.6%, 94.3%, 94.5%, 93.6%, 96.5%, 95.8%, 96.7%, 95.9% and 89.5% for F1 to F9, respectively. The formulations showed sustained release behaviour over the study period, indicating that incorporation of Igaratimod into glycosomal vesicles modified the release pattern compared with rapid drug diffusion from a conventional system. The release behaviour may be associated with diffusion of the drug through the lipid bilayer and gradual erosion or reorganization of the vesicular structure.

The regression coefficients obtained from different kinetic models are presented in Table 6. The Higuchi model showed high correlation coefficients for all formulations, ranging from 0.981 to 0.993, while the Korsmeyer–Peppas model also demonstrated high R^2 values ranging from 0.960 to 0.986. The comparatively lower R^2 values obtained for the first-order model indicate that first-order kinetics provided a less suitable description of the release behaviour. The high R^2 values for the Higuchi model suggest that diffusion played an important role in drug release from the glycosomal formulations. Among the formulations, F7 and F8 showed particularly high Higuchi correlation coefficients of 0.993 and 0.990, respectively.

The deformability and elasticity of the glycosomes are presented in Table 7. Vesicle deformability increased progressively from $48.6 \pm 2.1\%$ for F1 to

$82.8 \pm 1.3\%$ for F9. Similarly, the elasticity index increased from 0.42 ± 0.03 for F1 to 0.81 ± 0.02 for F9. The enhanced deformability and elasticity observed with F9 indicate that the optimized glycosomal vesicles possessed greater flexibility. Such vesicular flexibility may be advantageous for passage through biological barriers and may facilitate improved interaction with the skin or other biological membranes. F9 demonstrated the highest deformability and elasticity among the tested formulations, supporting its selection as the optimized formulation.

The comparative in-vitro drug-release profile of optimized F9 glycosomes and the marketed formulation is presented in Table 8. The optimized F9 formulation exhibited a slower and more prolonged drug-release pattern than the marketed formulation. At 1 h, F9 showed $12.8 \pm 0.9\%$ drug release compared with $24.6 \pm 1.2\%$ for the marketed formulation. At 6 h, the drug release from F9 was $64.3 \pm 1.6\%$, whereas the marketed formulation showed $92.4 \pm 1.3\%$ release. The cumulative drug release from F9 gradually increased to $90.8 \pm 0.8\%$ at 12 h. These findings demonstrate the ability of the glycosomal system to provide prolonged drug release compared with the marketed formulation.

The stability data of the optimized formulation stored at $4 \pm 1^\circ\text{C}$ and room temperature are presented in Table 9. No physical changes were observed during the storage period. Drug content remained relatively constant at both storage conditions, with values of $99.10 \pm 0.16\%$ and $99.07 \pm 0.22\%$ initially and $98.45 \pm 0.14\%$ and $98.41 \pm 0.76\%$, respectively, at the final observation. The relatively small decrease in drug content together with the absence of visible physical changes indicates satisfactory stability of the optimized glycosomal formulation under the tested storage conditions.

The results demonstrate that the glycosomal system successfully incorporated Igaratimod and exhibited desirable vesicle characteristics, high drug entrapment, high drug content, improved deformability and sustained drug release. Formulation F9 showed the most favourable overall characteristics, including a particle size of 137.9 ± 4.3 nm, PDI of 0.168 ± 0.008 , zeta potential of -32.8 ± 1.7 mV, drug content of $99.1 \pm 0.7\%$, entrapment efficiency of $93.6 \pm 0.9\%$, surface tension of 36.6 ± 0.3 mN/m, deformability of $82.8 \pm 1.3\%$ and elasticity index of 0.81 ± 0.02 . These findings support F9 as the optimized Igaratimod glycosomal formulation.

Table 2: Particle Size and PDI of Glycosomes

Formulation	Particle Size (nm)	PDI
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F1	613.4 ± 8.6	0.482 ± 0.021
F2	547.7 ± 7.9	0.421 ± 0.018
F3	485.3 ± 6.8	0.362 ± 0.016
F4	522.8 ± 7.3	0.398 ± 0.019
F5	437.6 ± 6.2	0.315 ± 0.014
F6	373.5 ± 5.7	0.258 ± 0.012
F7	322.8 ± 6.4	0.298 ± 0.015
F8	217.6 ± 5.1	0.214 ± 0.010
F9	137.9 ± 4.3	0.168 ± 0.008

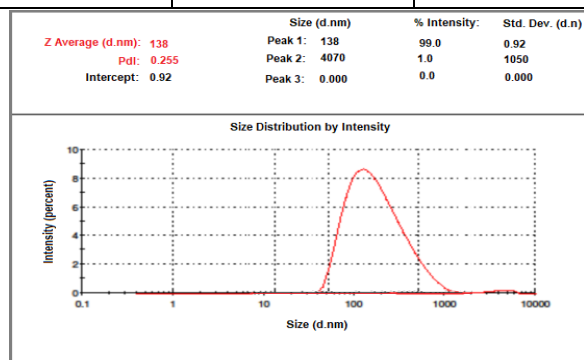


Figure 1: Particle size distribution of optimized F9 glycosome

Table 3: Evaluation Parameters of Glycosomes

Formulation	Zeta Potential (mV)	Drug Content (%)	Entrapment Efficiency (%)
F1	-17.6 ± 1.2	87.4 ± 1.5	66.8 ± 1.8
F2	-21.4 ± 1.1	91.2 ± 1.3	72.6 ± 1.5
F3	-23.8 ± 1.3	93.5 ± 1.2	74.4 ± 1.6
F4	-20.7 ± 1.2	92.3 ± 1.4	72.2 ± 1.4
F5	-23.6 ± 1.0	94.6 ± 1.1	78.8 ± 1.3
F6	-26.8 ± 1.1	95.7 ± 1.0	83.6 ± 1.2
F7	-25.4 ± 1.1	93.2 ± 1.0	81.1 ± 1.4

	1.2	1.1	
F8	-30.6 ± 0.9	95.3 ± 0.9	87.7 ± 1.1
F9	-32.8 ± 1.7	99.1 ± 0.7	93.6 ± 0.9

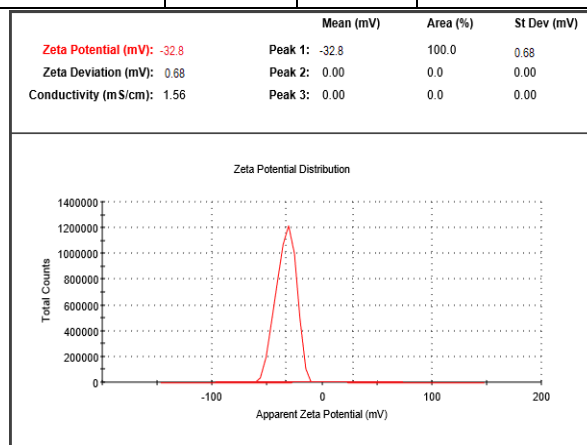


Table 2: Surface Tension of Glycosome Formulations

Table 4: Surface Tension of Glycosome Formulations

Formulation	Surface Tension (mN/m)
F1	44.8 ± 0.6
F2	43.9 ± 0.5
F3	41.1 ± 0.5
F4	41.3 ± 0.4
F5	40.6 ± 0.5
F6	38.8 ± 0.4
F7	39.1 ± 0.4
F8	37.4 ± 0.3
F9	36.6 ± 0.3

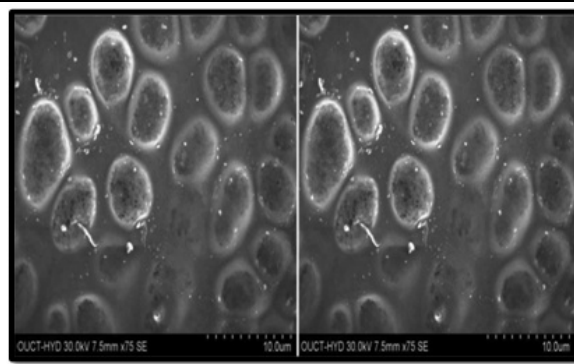


Figure 3: Photograph of Glycosomes through SEM study

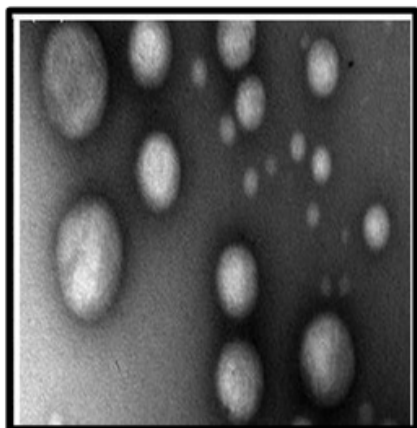


Figure 4: Photograph of Glycrosomes through TEM study

Table 5: In-vitro Drug Release of Glycrosomes

Time (h)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)	F8 (%)	F9 (%)
0	0	0	0	0	0	0	0	0	0
1	18.7	17.3	16.5	16.7	15.2	14.5	14.7	13.7	12.5
2	32.7	30.2	29.5	30.2	27.7	26.8	27.2	24.3	22.6
4	52.3	49.5	47.4	48.8	44.5	42.7	43.6	40.4	37.7
6	68.6	65.3	62.7	64.3	59.3	57.5	58.4	54.5	50.5
8	80.2	77.5	74.4	76.5	71.2	69.2	70.3	65.7	62.3
10	89.1	86.4	83.8	85.2	81.5	78.4	80.2	75.5	78.5
12	95.6	94.3	94.5	93.6	96.5	95.8	96.7	95.9	89.5

Table 6: Regression Coefficient (R²) Obtained from Various Kinetic Models

Batch Code	Zero-Order Kinetics	Higuchi Kinetics	Korsmeyer–Peppas Kinetics	First-Order Kinetics

G1	0.883	0.984	0.986	0.759
G2	0.888	0.981	0.978	0.745
G3	0.909	0.982	0.960	0.746
G4	0.936	0.984	0.980	0.629
G5	0.946	0.988	0.982	0.638
G6	0.944	0.985	0.984	0.659
G7	0.910	0.993	0.971	0.781
G8	0.890	0.990	0.978	0.772
G9	0.884	0.990	0.981	0.784

Table 7: Vesicle Deformability and Elasticity

Formulation	Vesicle Deformability (%)	Vesicle Elasticity*
F1	48.6 ± 2.1	0.42 ± 0.03
F2	53.8 ± 2.0	0.47 ± 0.03
F3	58.4 ± 1.8	0.53 ± 0.02
F4	57.2 ± 1.9	0.51 ± 0.03
F5	63.7 ± 1.7	0.59 ± 0.02
F6	69.8 ± 1.6	0.66 ± 0.02
F7	66.4 ± 1.8	0.63 ± 0.02
F8	74.6 ± 1.5	0.72 ± 0.02
F9	82.8 ± 1.3	0.81 ± 0.02

*Elasticity values are expressed as a relative elasticity index.

Table 8: Comparative In-vitro Drug Release Study of Optimized F9 and Marketed Formulation

Time (h)	Optimized Glycrosome F9 (% Cumulative Drug Release)	Marketed Formulation (% Cumulative Drug Release)
0	0.00 ± 0.00	0.00 ± 0.00
1	12.8 ± 0.9	24.6 ± 1.2
2	23.7 ± 1.1	39.8 ± 1.4
3	34.9 ± 1.3	52.7 ± 1.6
4	45.8 ± 1.5	63.9 ± 1.7
5	55.6 ± 1.4	79.8 ± 1.5

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6	64.3 ± 1.6	92.4 ± 1.3
7	71.8 ± 1.5	100.2 ± 1.2
8	74.6 ± 1.3	-
9	79.4 ± 1.2	-
10	83.5 ± 1.1	-
11	87.7 ± 1.0	-
12	90.8 ± 0.8	-

Table 9: Drug content at 4 ± 1°C and room temperature during storage

Sr. No.	Day	Physical Change	Drug Content at 4 ± 1°C (%)	Drug Content at Room Temperature (%)
1	0	No Change	99.10 ± 0.16	99.07 ± 0.22
2	15	No Change	99.08 ± 0.22	99.05 ± 0.32
3	30	No Change	98.99 ± 0.06	98.97 ± 0.04
4	45	No Change	98.58 ± 0.27	98.67 ± 0.49
5	60	No Change	98.52 ± 0.09	98.53 ± 0.07
6	90	No Change	98.45 ± 0.14	98.41 ± 0.76

Conclusion

Iguratimod-loaded glycosomes were successfully developed by the thin-film hydration method. Among the nine formulations, F9 was optimized based on its small particle size, low PDI, high entrapment efficiency, suitable zeta potential, and excellent deformability. F9 showed 90.8 ± 0.8% drug release over 12 h with Higuchi diffusion-controlled kinetics and satisfactory stability. F9 demonstrated promising potential as a flexible and sustained vesicular drug-delivery system. Further in-vivo and permeation studies are required to confirm its therapeutic applicability.

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