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PREPARATION, CHARACTERIZATION AND EVALUATION OF PRAZOSIN HYDROCHLORIDE LOADED PRONIOSOMES BY SLURRY METHOD

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Abstract

Background: The primary objective of the present study was to develop and evaluate a proniosomal formulation of prazosin hydrochloride for oral drug delivery. Prazosin hydrochloride, a selective α1-adrenoceptor antagonist, is widely used in clinical practice for the treatment of hypertension and congestive heart failure.

Method: Proniosomes containing prazosin hydrochloride were prepared using the slurry method with Tween 80, Span 60, maltodextrin, and cholesterol. The formulations were evaluated for short-term stability, in vitro drug release, release kinetics, entrapment efficiency, and particle size. The type and concentration of non-ionic surfactants significantly influenced vesicle size and drug entrapment efficiency. Vesicle sizes ranged from 3.28 ± 0.43 µm to 8.92 ± 0.41 µm, with a trend of increasing size corresponding to higher surfactant concentrations. Morphological analysis revealed smooth, spherical vesicles without signs of aggregation. Drug release from proniosomal formulations (F1–F8) after 30 minutes ranged between $87.48 \pm 0.33\%$ and $99.12 \pm 0.32\%$. Notably, formulation F4 (Tween 80: Cholesterol in a 1:4 ratio) exhibited the highest release at $99.12 \pm 0.32\%$, outperforming the marketed tablet formulation. Drug release kinetics followed a super case II transport mechanism and conformed to Higuchi kinetics. Stability studies indicated no significant changes in drug content, release percentage, or physical appearance over the test period.

Conclusion: Prazosin hydrochloride-loaded proniosome formulations were successfully prepared using the slurry method with cholesterol, non-ionic surfactants, and maltodextrin. These proniosomal systems offer a promising alternative to conventional dosage forms for the effective management of hypertension.

Key words: Prazosin Hydrochloride, Proniosome, oral drug delivery, Drug release, slurry method, Hypertension

I. INTRODUCTION

Prazosin hydrochloride, a derivative of quinazoline, functions as a selective and competitive α1-adrenoceptor blocker. It is widely prescribed for managing hypertension, benign prostatic hyperplasia, post-traumatic stress disorder (PTSD)-associated nightmares, and Raynaud's disease. Due to its relatively short plasma half-life of about 2–3 hours, dosing must be adjusted according to the patient's blood pressure response.

Dosage Guidelines:

- **Initial Dose:** 1 mg administered two or three times daily.
- **Maintenance Dose:** Gradually increased to a total of up to 20 mg per day in divided doses.
- **Common Therapeutic Range:** 6–15 mg per day, divided into multiple doses.
- **Maximum Dose:** Although doses above 20 mg/day typically do not enhance efficacy, some patients may benefit from titration up to 40 mg per day, also in divided doses.
- **Dosing Frequency:** After initial titration, some patients may be adequately maintained on a twice-daily regimen.[1,2]

Topical drug delivery systems have gained considerable attention for their ability to administer therapeutic agents through the skin in a controlled and sustained fashion. Despite this, the skin's inherent barrier function limits the permeability of most drugs, preventing them from reaching optimal therapeutic levels. To overcome this limitation, several innovative and non-invasive techniques have been developed to boost transdermal drug absorption. Among these, vesicular drug delivery systems have emerged as a key area of focus for formulation scientists in both diagnostic and therapeutic applications within biomedicine. These systems work by enclosing drug molecules within vesicle-like structures, offering the potential to improve the effectiveness of both novel and existing pharmaceutical agents. This method of encapsulation enhances drug stability and bioavailability while enabling site-specific delivery. As a result, it minimizes systemic toxicity and extends the duration of drug action in the bloodstream, making it a promising strategy for future topical and transdermal treatments

Various vesicular systems have been developed, such as liposomes, niosomes, pharmacosomes, transferosomes, and sphinosomes. These carriers are engineered to improve drug delivery by enabling targeted absorption, reducing adverse effects, and enhancing overall therapeutic effectiveness.[3]

Novel drug delivery systems (NDDS) are innovative therapeutic platforms that adopt multidisciplinary strategies blending molecular biology, bio-conjugate chemistry, polymer science, pharmaceutics, and advanced technologies. These systems have evolved to overcome the shortcomings of traditional drug delivery methods, which frequently fall short in meeting the efficacy, targeting precision, and controlled release demands of modern pharmaceutical agents.

The advancement of NDDS has been driven by emerging technologies and specialized instrumentation that allow for more accurate and efficient delivery of therapeutic compounds. These systems function through physical processes such as diffusion, osmosis, erosion, dissolution, and electrotransport, or through biochemical methods, including monoclonal antibody targeting, site-specific controlled release, dose interval regulation, and maintenance of steady plasma concentrations. By enhancing drug bioavailability, precision targeting, and reducing adverse effects, NDDS are reshaping pharmaceutical treatments and significantly improving therapeutic outcomes for patients.[4]

Proniosomes are vesicular systems based on non-ionic surfactants, specifically designed to address the physical instability seen in aqueous niosomal dispersions, such as fusion, aggregation, and drug leakage—issues often encountered in vesicle-based drug delivery. These formulations are prepared in a dry, free-flowing granular state that can be readily rehydrated with warm water to form niosomes just before administration. Proniosomes provide notable advantages, including high drug loading capacity and compatibility with drugs of diverse solubility types hydrophilic, amphiphilic, and lipophilic. Moreover, they offer controlled particle size distribution and superior physical and chemical stability, without the need for specialized storage environments like nitrogen atmospheres. Owing to these attributes, proniosomes represent an effective and adaptable drug delivery platform, making them suitable for integration into various pharmaceutical products.[5,6]

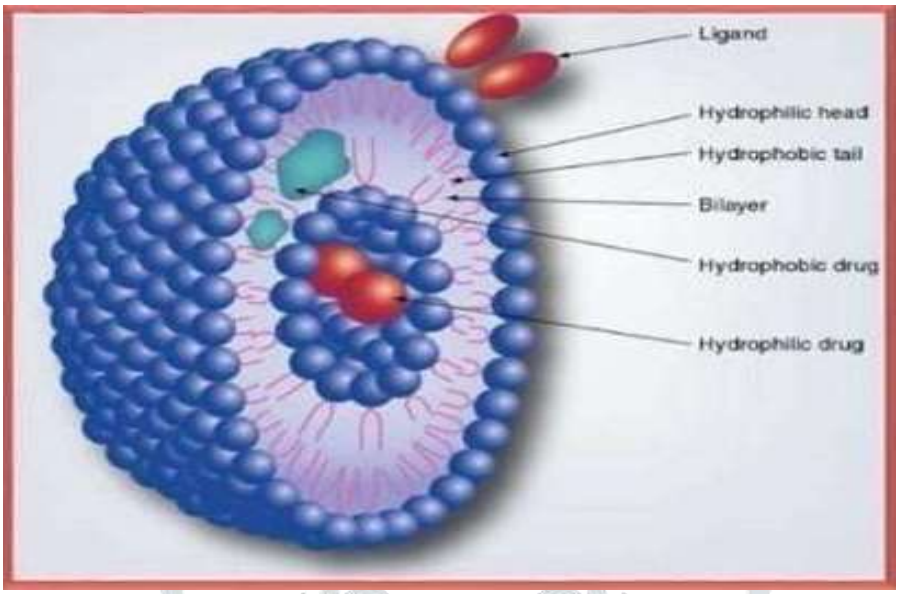

Figure 1: Structure of Proniosome

1.1 ADVANTAGES OF PRONIOSOMES:

- **Enhanced Stability:** Effectively address issues like sedimentation, fusion, aggregation, and drug leakage during storage.
- **Protection of Drug Integrity:** Shield encapsulated drugs from hydrolysis, helping maintain their therapeutic potency.
- **Ease of Handling and Storage:** The dry, free-flowing nature of proniosomes makes them easy to manage, store, and transport.
- **Facilitated Processing:** Easier to sterilize, scale up, distribute, and store long-term compared to traditional vesicular systems.
- **Controlled Drug Delivery**: Enable controlled, delayed, and sustained drug delivery, enhancing efficacy and patient adherence.

1.2 CLASSIFICATION OF PRONIOSOMES:

Proniosomes are classified into two main types based on their physical state and preparation method:

(a) Granular Proniosomes (Dry Form)

Granular proniosomes are dry, free-flowing powders that convert into niosomes when hydrated with hot water. They are usually created by coating a water-soluble carrier such as sorbitol or maltodextrin—with a non-ionic surfactant layer. Upon hydration, the carrier dissolves, triggering spontaneous niosome formation. This form offers excellent stability, ease of handling, and is well-suited for large-scale manufacturing processes.

(b) Liquid Crystalline Proniosomes

These proniosomes are formulated by combining lecithin, alcohol, and non-ionic surfactants. The components are melted together, followed by the addition of a small volume of water and reheating to produce a uniform gel-like consistency. When hydrated with hot water, the gel converts into niosomes. Owing to their semi-solid nature, this type of proniosome is particularly well-suited for transdermal drug delivery applications.

These formulations exhibit several favorable characteristics:

- High physical and chemical stability
- Excellent entrapment efficiency
- Use of biocompatible and non-irritating excipients
- Act as penetration enhancers due to the presence of non-ionic surfactants
- Do not damage the stratum corneum
- Their evaluation and analytical methods are largely similar to those of niosomes [7,8]

1.3 MECHANISM OF DRUG TRANSFER FROM PRONIOSOMES

Figure 2 demonstrates the drug delivery pathway, starting from proniosomes converting into niosomes, followed by transdermal absorption. This transformation is triggered by hydration through skin moisture, which is essential for drug release and penetration. The efficiency of drug release and skin permeation is influenced by various factors, including the drug's physicochemical characteristics and the specific composition of the proniosomal formulation. Excipients—especially non-ionic surfactants and phospholipids commonly incorporated in proniosomes, significantly contribute to enhancing the drug's ability to cross the skin barrier.

After formation, niosomes engage with the stratum corneum by merging with skin lipids, disrupting their organized structure. This disruption leads to fluidization of the lipid bilayers, thereby enhancing the skin's permeability. As a result, the encapsulated drug diffuses more effectively through the skin, improving transdermal delivery efficiency.[9]

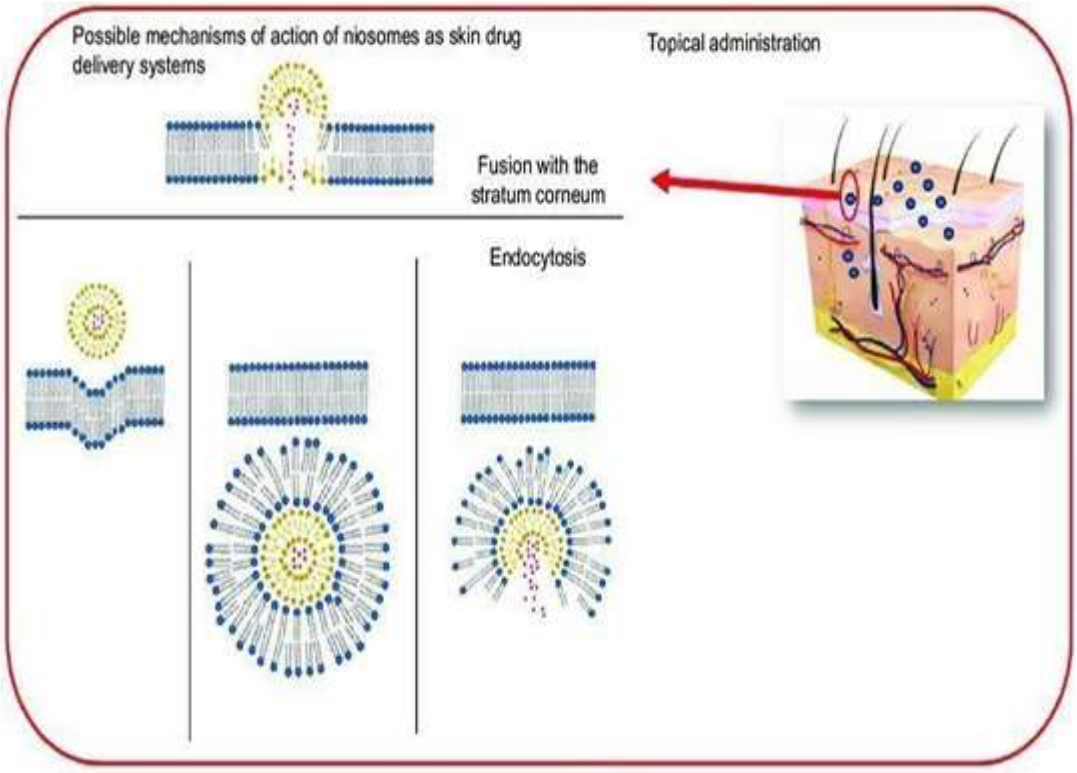

Figure 2: Mechanism of action of niosomes/proniosomes through TDDS

1.4 APPLICATION OF PRONIOSOMES[10]:

The following list includes a few uses for proniosomes:

a. Targeted drug delivery

b. Cancer treatment

c. Leishmaniasis treatment

d. Peptide drug delivery

e. Analysis of immune response

f. Localized and prolonged drug release

g. Transdermal drug delivery systems

h. Hemoglobin carriers

2. MATERIALS AND METHODOLOGY

Materials:

- Prazosin hydrochloride and maltodextrin were sourced from Yarrow Chem Products, Mumbai, India.
- Chloroform, methanol, Tween 80, Span 60, and potassium dihydrogen phosphate were obtained from S.D. Fine Chem. Ltd., Mumbai, India.
- Cholesterol was acquired from Thomas Baker Chemicals Pvt. Ltd., Mumbai, India.

2.1 FORMULATION DESIGN:

Table no. 1: Composition of Prazosin HCl proniosome

SL.NO	INGREDIENTS	FORMULATIONS							
		F1	F2	F3	F4	F5	F6	F7	F8
1.	Prazosin HCl (mg)	5	5	5	5	5	5	5	5
2.	Maltodextrin (mg)	200	200	200	200	200	200	200	200
3.	Tween 80 (mg)	50	50	50	50	--	--	--	--
4.	Span 60(mg)	--	--	--	--	50	50	50	50
5.	Cholesterol (mg)	50	100	150	200	50	100	150	200

2.2 METHOD OF PREPARATION OF PRAZOSIN HCL PRONIOSOME:

Powdered proniosomes containing prazosin hydrochloride were formulated using the slurry technique. The specific composition of different proniosomal batches is outlined in Table no. 1. In summary, 60 ml of a solvent mixture (methanol and chloroform in a 2:1 v/v ratio) was used to dissolve accurately weighed quantities of lipid mixtures composed of Span 60 or Tween 80 and cholesterol in varying molar ratios (1:1, 1:2, 1:3, and 1:4), along with 5 mg of prazosin hydrochloride. The resulting solution was then transferred to a 600 ml round-bottom flask containing 200 mg of maltodextrin to create a slurry. This setup was connected to a rotary flash evaporator, where the organic solvents were removed under reduced pressure at 45 ± 2°C. Once evaporation was complete, the residue was further dried overnight in a vacuum oven at room temperature to yield a dry, free-flowing proniosomal powder. The final formulations were stored in airtight containers at 40°C for future evaluation. [11]

3. EVALUATION OF PRONIOSOMES

- **Entrapment Efficiency (EE%) Determination:** To isolate the encapsulated drug from the free drug, 1 ml of proniosomal dispersion was subjected to centrifugation at 15,000 rpm for 1 hour. The supernatant was discarded, and the resulting pellet was treated with a buffer solution to lyse the vesicles and release the entrapped drug. Prazosin hydrochloride concentration was then quantified using UV spectrophotometry at 254 nm.[12]

EE% = [Amount of entrapped Prazosin HCl /Total amount of Prazosin HCl] × 100

- **Photo microscopic analysis and scanning electron microscopy:**
  Initial observation of proniosomal vesicles was performed using an optical microscope at 10x magnification, and representative images were captured using a camera. For detailed morphological analysis of the optimized formulation, scanning electron microscopy (SEM) was utilized. A drop of the optimized proniosomal dispersion was placed onto a collodion-coated copper grid and left to settle and dry for about two minutes. Following this, a drop of uranyl acetate solution was added for contrast

enhancement and allowed to remain for one minute. Once dried, the sample was analyzed under the SEM to evaluate vesicle surface structure and morphology.[13]

- **Vesicle size analysis**: Niosomes generated from proniosome hydration, with and without agitation, were assessed for their particle size and distribution. After hydration, the resulting niosomal dispersions were analyzed under an optical microscope at 40x magnification. An eyepiece micrometer, calibrated using a stage micrometer, was employed to accurately measure the size of the vesicles.

- **Drug content analysis:** A quantity of 10 mg of the drug was placed in a standard volumetric flask and mixed with 25 mL of phosphate buffer solution (pH 6.8), allowing it to lyse for 15 minutes. The mixture was continuously stirred for two hours and then left undisturbed for five additional hours. Following filtration, the drug concentration was determined using UV spectrophotometry at 254 nm.[14]
  % drug content= practical drug content/theoretical drug content ×100

- **In-vitro drug release studies**:
  The in vitro release of prazosin hydrochloride from proniosomal formulations encapsulated in hard gelatin capsules was studied using a USP Type I dissolution apparatus (Lab India, India). Each vessel was filled with 900 mL of hydrochloric acid buffer (pH 1.2), maintained at 37.0 ± 0.5 °C and agitated at 50 rpm. A single capsule was introduced into each vessel, and 5 mL samples were withdrawn at specific time points (5, 10, 15, 20, 25, and 30 minutes). The withdrawn volume was immediately replenished with an equal volume of fresh dissolution medium at the same temperature. Drug concentration was measured spectrophotometrically at 254 nm.[15]

- **Stability studies:**
  The stability of a drug formulation refers to its capacity to retain physical, chemical, therapeutic, and toxicological integrity under defined environmental conditions. Stability testing is primarily conducted to assess how factors such as temperature, humidity, and light influence the formulation's quality over time. These evaluations are essential for establishing the product's shelf life, determining suitable retest periods, and recommending optimal storage conditions to ensure long-term efficacy and safety. A three-month stability study was conducted on the selected proniosomal formulations of prazosin hydrochloride, following ICH guidelines. The samples were stored in sterile glass beakers, sealed tightly and covered with aluminum foil to prevent light exposure. Stability evaluations were performed under two controlled conditions: 25°C with 60% relative humidity (RH) and 40°C with 75% RH, maintained consistently throughout the three-month testing period.[16]

4. RESULTS AND DISCUSSION

Hypertension remains one of the most widespread cardiovascular conditions, accounting for nearly 20–50% of global deaths linked to cardiovascular disease. Prazosin hydrochloride, a BCS Class II alpha-adrenergic blocker, is widely prescribed for managing hypertension and heart failure; however, its therapeutic potential is hindered by poor water solubility, resulting in low oral bioavailability and associated in vivo limitations.

To address these challenges, advanced drug delivery approaches have been developed to improve the absorption of poorly water-soluble drugs. Merely developing new drug molecules is not sufficient effective carrier systems are essential to enhance therapeutic outcomes. Proniosomes, a novel vesicular delivery system, present a promising strategy for increasing drug bioavailability.

This study investigates the effectiveness of proniosomal formulations containing prazosin hydrochloride for antihypertensive therapy. Proniosomes were prepared using the slurry technique with non-ionic surfactants Tween 80 and Span 60, which are widely utilized in vesicle-based systems. A total of eight formulations were developed by varying the ratios of maltodextrin, cholesterol, and surfactants. These batches were then subjected to detailed evaluation to assess their potential as effective drug delivery vehicles

4.1 Pre formulation studies:

- **Solubility tests of prazosin hydrochloride :**
  Solubility testing for prazosin hydrochloride was carried out using a range of solvents, including distilled water, phosphate buffers at pH 6.8 and 7.4, methanol, ethanol, and 0.1N hydrochloric acid (HCl). The findings are presented in Table 2. The drug showed limited solubility in distilled water, methanol, ethanol, and both phosphate buffer solutions, while demonstrating significantly better solubility in 0.1N HCl. Given its enhanced solubility in this medium, 0.1N HCl was selected as the solvent for constructing the calibration curve.

Table no.2: Solubility profile of Prazosin Hydrochloride

Solvents	Solubility mg/ml,	Inference
Distilled water	4.23 ±0.021	Slightly soluble
Phosphate buffer pH 6.8	3.20±0.032	Slightly soluble
Phosphate buffer pH 7.4	3.44±0.020	Slightly soluble
Methanol	10.10±0.071	Sparingly soluble
Ethanol	12.65±0.091	Sparingly soluble
0.1N HCl, pH 1.2	30.28±0.040	Soluble

- **Melting point determination:**
  The melting point of prazosin hydrochloride was assessed using the capillary tube method, a standard approach for evaluating the physical characteristics of solid compounds. In pharmaceutical analysis, the melting point range is commonly used as an indicator of a substance's purity. The observed melting point of prazosin hydrochloride was 278.5 °C, aligning with the United States Pharmacopeia (USP) specified range of 278–280 °C, thus confirming the purity of the drug used in the study.

4.2 Analytical method determination of Prazosin Hydrochloride:

- **λmax Determination:** The maximum absorbance wavelength (λmax) of pure prazosin hydrochloride was identified using UV spectrophotometric analysis. In 0.1N hydrochloric acid, the drug exhibited a λmax at 254 nm, which was selected as the reference wavelength for subsequent analytical procedures. The corresponding UV absorption spectrum is shown in Figure 3.

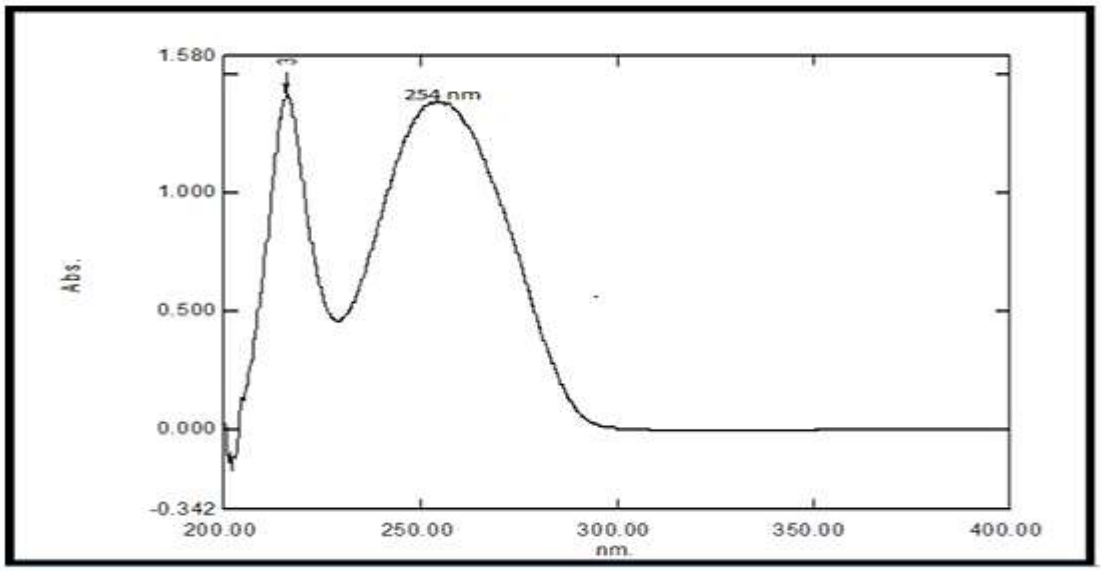

Figure 3: UV spectrum of Prazosin Hydrochloride in 0.1N HCl

- **Determination of calibration curve:** A 0.1N hydrochloric acid solution served as the blank during UV spectrophotometric analysis for constructing the calibration curve of prazosin hydrochloride at 254 nm. The drug demonstrated adherence to Beer-Lambert's law within the concentration range of 2 to 12 µg/ml. The calibration curve was generated by plotting absorbance versus concentration, as illustrated in Figure 5. Data processing and curve fitting were performed using Microsoft Excel 2010. The correlation coefficient (r^2) was calculated as 0.996, indicating strong linearity of the method in 0.1N HCl.
- **Compatibility studies using FTIR:** Figures 4–6 display the FTIR spectra of pure prazosin hydrochloride, individual polymers, and the formulated proniosomes, obtained using the KBr pellet technique. Key absorption bands identified in the prazosin hydrochloride spectrum included aromatic C–C stretching at 1454.46 cm^{-1}, aliphatic C–H stretching at 2938.70 cm^{-1}, C=N stretching at 1643.99 cm^{-1}, aromatic amine (C–N) stretching at 1221.85 cm^{-1}, and aromatic C–H bending at 727.01 cm^{-1}, confirming the drug's structural identity and purity. The spectra of both the drug-polymer mixture and proniosomal formulations retained all characteristic peaks of prazosin hydrochloride, suggesting good compatibility with the polymers. Furthermore, the chemical structure of the drug remained unchanged, as no significant shifts or loss of functional group peaks were observed. These findings confirm the absence of major interactions between the drug and excipients. A detailed summary of the FTIR results is provided in Table 3.

Table no. 3: Results of FTIR spectrum of Prazosin Hydrochloride

Functional group	Observed peaks cm^{-1}		
	Prazosin Hydrochloride	Drug and excipient mixture	Proniosomal formulation
Aliphatic C-H (s)	2938.70	2927.83	2933.72
Aromatic C-C (s)	1454.46	1414.81	1411.85
Aromatic amine C-N (s)	1221.85	1244.45	1221.59
C=N stretch	1643.99	1641.73	1643.70
Aromatic substitution (C-H) b	727.01	708.28	726.12

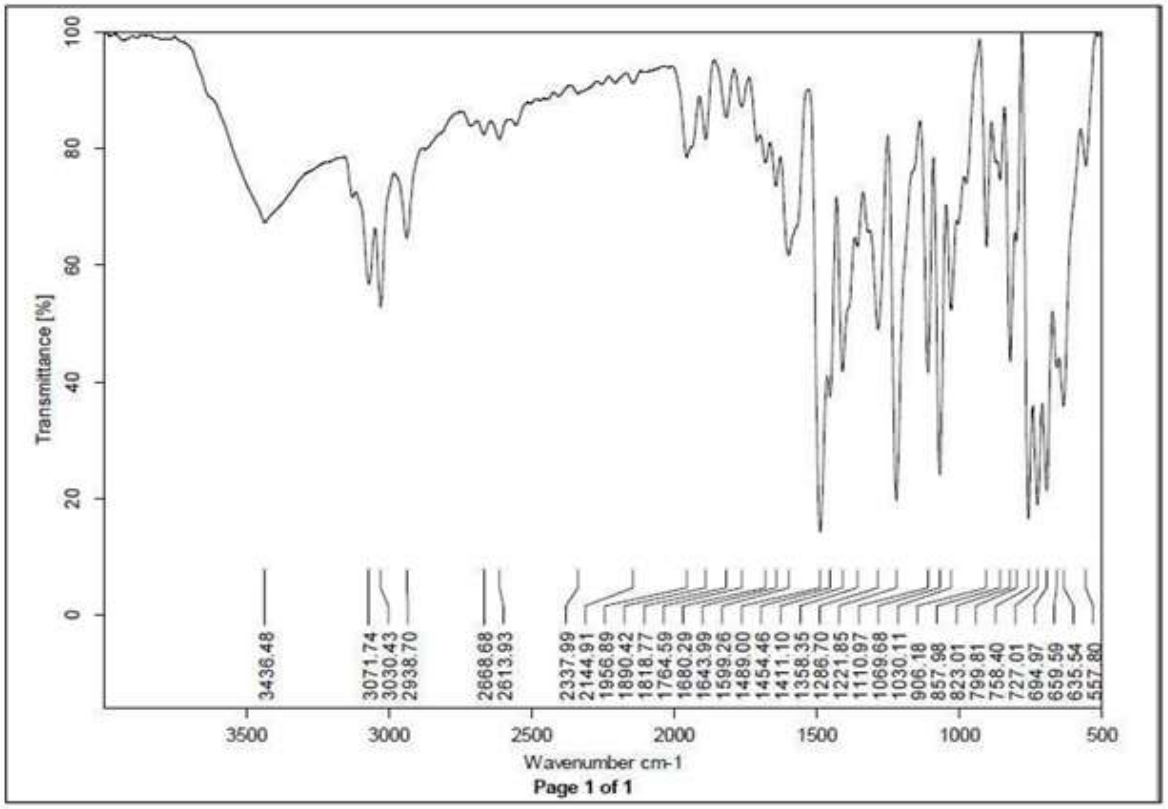

Figure 4: Infrared spectrum of Prazosin Hydrochloride

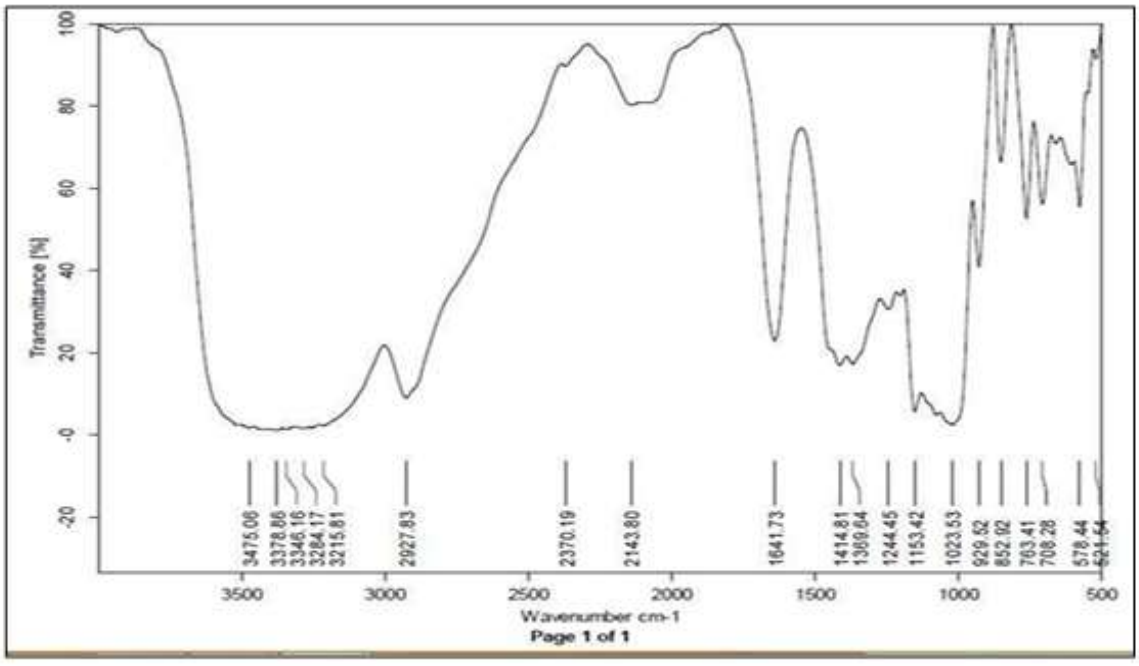

Figure 5: Infrared spectrum of drug and excipients mixture

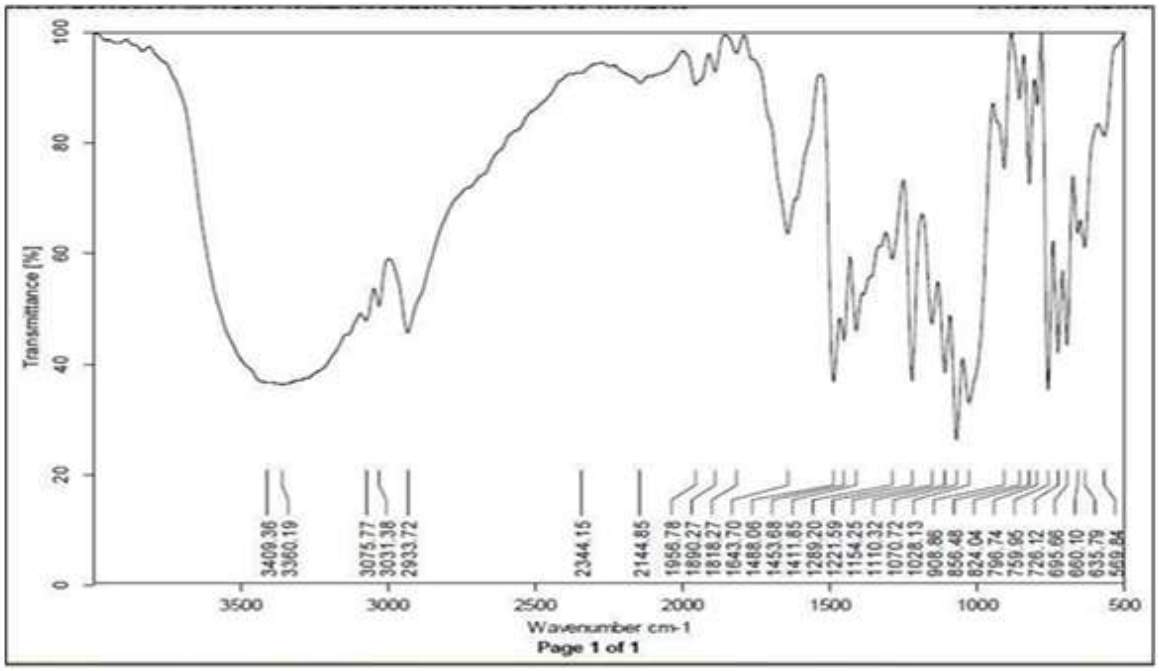

Figure 6: Infrared spectrum of optimized batch of Prazosin Hydrochloride proniosome

4.3 CHARACTERIZATION OF PRONIOSOME:

- **Entrapment Efficiency of Prazosin Hydrochloride proniosome:** The entrapment efficiency (EE%) of prazosin hydrochloride-loaded proniosomes was determined using the ultracentrifugation method. Several parameters influenced entrapment, including the type of surfactant, alkyl chain length, hydrophilic-lipophilic balance (HLB), and phase transition temperature. As indicated in Table 4, proniosomes formulated with Span surfactants exhibited higher encapsulation efficiency than those prepared using Tweens. The observed EE% values for the prazosin-loaded proniosomes ranged from $76.03 \pm 0.47\%$ to $93.44 \pm 0.21\%$. This variation is largely attributed to differences in HLB values. Lipophilic spans, having lower HLB, formed compact bilayer structures that efficiently retained the lipophilic drug. In contrast, hydrophilic tweens with higher HLB created more permeable, less stable bilayers, leading to reduced entrapment.
- Additionally, the concentration of the non-ionic surfactant played a significant role in encapsulation. Higher surfactant levels, as seen in formulations F2, F4, F6, and F8, led to improved EE% by increasing the number of niosomes and expanding the hydrophobic bilayer volume, allowing greater accommodation of the drug. Among all formulations, F4 displayed a lower entrapment value ($78.21 \pm 0.42\%$), while F8 demonstrated the highest ($94.42 \pm 0.22\%$). Span 60's elevated phase transition temperature contributed to a more rigid and stable bilayer, favoring greater drug retention. Conversely, Tween 80, with a lower phase transition temperature and liquid nature at ambient conditions, resulted in comparatively reduced entrapment efficiency.

- **Particle size analysis:** The average size of niosomal vesicles formed following hydration of proniosomes was determined using an optical microscope fitted with a calibrated ocular and stage micrometer at 40x magnification. Measurements were taken for 100 vesicles, and the results are presented in Table 4. The vesicle diameters for prazosin hydrochloride-loaded proniosomes ranged from 3.28 ± 0.43 µm to 8.92 ± 0.41 µm. Formulations containing tweens produced smaller vesicles (3.28 ± 0.43 to 6.28 ± 0.26 µm), whereas those made with spans yielded larger vesicles (5.52 ± 0.46 to 8.92 ± 0.41 µm). The increased vesicle size in span-based formulations is likely due to stronger interactions between Span 60, cholesterol, and the bilayer components. As the concentration of Span 60 was elevated, a corresponding increase in vesicle diameter was observed. Furthermore, the incorporation of the lipophilic drug into the hydrophobic bilayer region caused expansion of the vesicle structure by pushing bilayer molecules apart, further contributing to the increase in size
- **Drug content:** Drug content was analyzed using a UV spectrophotometer. Across all formulations, the drug content ranged from $95.54 \pm 0.60\%$ to $99.28 \pm 0.20\%$ w/w, indicating uniform distribution of prazosin hydrochloride within the proniosomal matrix. A detailed summary of the drug content values is provided in Table 4.

Table no.4: Drug content Entrapment Efficiency (%) and Particle size (µm) Evaluation of Prazosin Hydrochloride proniosome

Formulation	Entrapment Efficiency (%)	Particle size (µm)	Drug content (%w/w)
F1	79.47±0.63	3.28±0.43	96.24±0.29
F2	86.31± 0.90	5.40 ±0.30	99.28±0.20
F3	80.21±0.42	4.64 ±0.21	98.80±0.83
F4	84.71± 0.35	6.28±0.26	98.13±0.78
F5	89.36± 0.40	5.52±0.46	95.54±0.60
F6	91.42±0.22	6.21±0.70	98.90±0.21
F7	93.33±0.82	7.26±0.59	96.31±0.53
F8	94.42±0.22	8.92±0.41	99.14±0.60

- **Surface morphology of Proniosomes:** To validate the vesicular structure, the morphology of the proniosomal vesicles was assessed using both optical microscopy and scanning electron microscopy (SEM). As depicted in Figures 7 and 8, the vesicles exhibited a smooth, spherical appearance with no visible signs of aggregation.

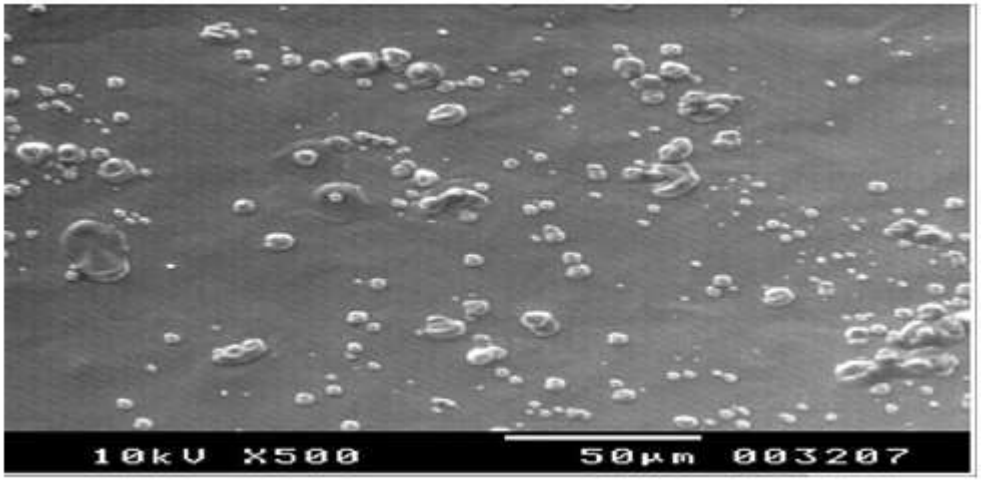

Figure7: Scanning electron microscopy of optimized batch Prazosin Hydrochloride proniosome

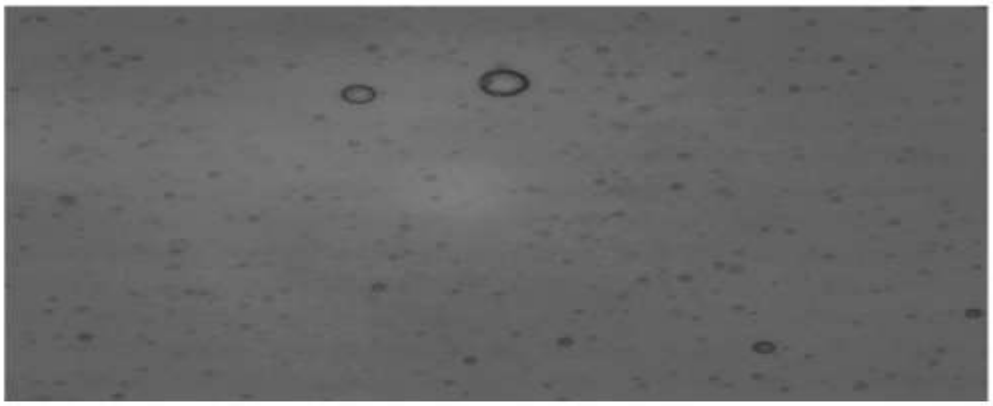

Figure 8: Optical microscopy of optimized batch of Prazosin proniosome

- **In-vitro drug release studies:** In vitro drug release studies of prazosin hydrochloride-loaded proniosomes encapsulated in hard gelatin capsules were conducted using a USP Type I dissolution apparatus (Lab India, India). Each capsule was placed in a vessel containing 900 mL of hydrochloric acid buffer (pH 1.2), maintained at 37.0 ± 0.5 ℃ and stirred at 50 rpm for a duration of 30 minutes. Among all tested formulations, batch F4—comprising Tween 80 and cholesterol in a 1:4 ratio exhibited the highest release rate, reaching 99.12 ± 0.32%. Overall, the cumulative drug release across formulations F1 to F8 ranged from 87.48 ± 0.33% to 99.12 ± 0.32% within 30 minutes. As shown in Figure 9, the proniosomal formulations demonstrated superior drug release compared to the marketed tablet. This enhancement is attributed to the lipophilic nature of prazosin hydrochloride, which favors integration into proniosomal bilayers, thereby promoting faster release. Tween-based formulations exhibited quicker release profiles than those containing spans, likely due to their hydrophilic nature facilitating the release of the lipophilic drug. The initial burst phase observed in most batches resulted from drug desorption from the vesicle surface, while the subsequent sustained release phase was controlled by diffusion through the hydrated niosomal bilayers. This rapid release profile may help achieve prompt epidermal saturation and maintain a strong concentration gradient, enhancing transdermal drug absorption. into systemic circulation.

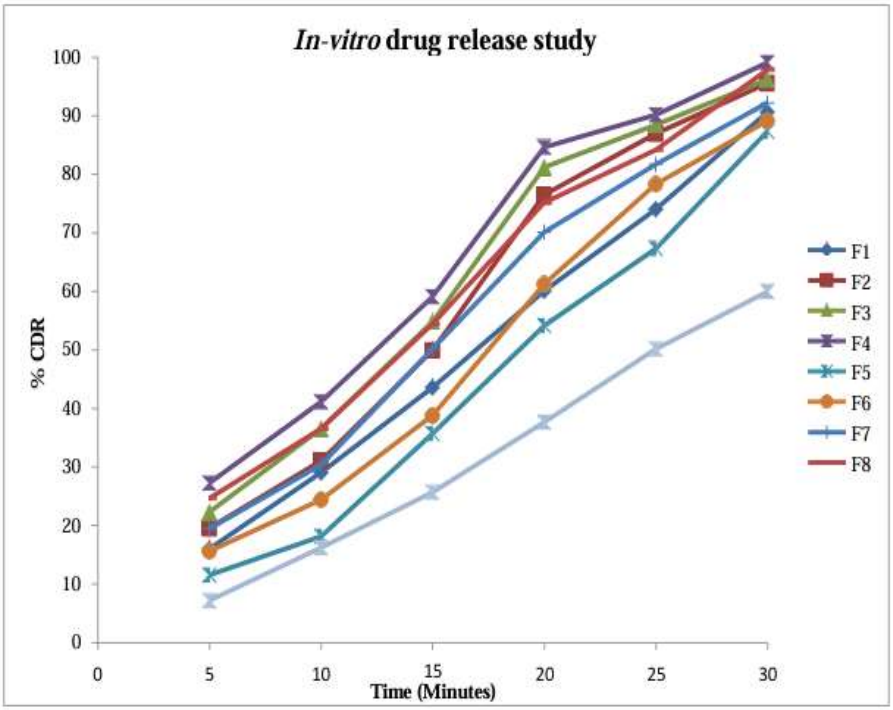

Figure 9: Comparative drug release profile of Proniosome formulation

- **Stability Studies:** The objective of stability testing is to assess the influence of environmental conditions such as temperature, humidity, and light on the integrity of a drug product over time. Proniosomal formulations were stored at 40°C/75% RH and 25°C ± 2°C/60% RH for 1, 2, and 3 months. Throughout the study period, drug content and in vitro release profiles were systematically evaluated. Among the tested formulations, batch F4 was chosen for extended analysis based on its in vitro release performance. The stability results, detailed in Table 20, revealed that proniosomes maintained under both accelerated (40°C ± 2°C/75% RH) and real-time (25°C ± 2°C/60% RH) conditions showed no noticeable variations in physical appearance, drug content, or release behaviour.

Table 6: Results of stability studies of proniosome formulation F4

Months	25°C±2°C /60% RH		40°C±2°C /75% RH	
	% Drug content	% CDR	% Drug content	% CDR
Initial	98.13±0.78	99.12±0.32	98.13±0.78	99.12±0.32
1	98.04±0.40	98.90±0.20	98.10±0.40	98.84±0.81
2	97.70±0.28	98.38±0.34	97.46±0.28	98.26±0.31
3	97.22±0.61	98.22±0.61	97.16±0.61	98.10±0.50

4 CONCLUSION

This study was designed to investigate the application of proniosomes as an innovative vesicular carrier for delivering prazosin hydrochloride. The proniosomal formulations were developed using the slurry method with non-ionic surfactants Tween 80 and Span 60 which are widely recognized for their role in vesicle formation. A total of eight formulations were prepared by altering the ratios of maltodextrin, cholesterol, and surfactants, and were systematically evaluated through various characterization techniques. The study led to several key findings, summarized as follows:

Preformulation parameters such as the solubility and melting point of the drug were thoroughly evaluated, and all results fell within acceptable parameters, confirming desirable physicochemical characteristics. Compatibility between prazosin hydrochloride and formulation excipients was established through FTIR analysis, which revealed no detectable interactions. UV spectrophotometric analysis identified the maximum absorbance (λmax) of prazosin hydrochloride at 254 nm, which was subsequently employed for further quantitative assessments. In terms of entrapment efficiency, proniosomal systems prepared using Span surfactants outperformed those made with Tweens. The drug-loaded proniosomes demonstrated high encapsulation efficiency, ranging from 76.03 ± 0.47% to 93.44 ± 0.21%, likely due to the influence of the surfactants' hydrophilic-lipophilic balance (HLB) values.The vesicle size of prazosin hydrochloride-loaded proniosomes was found to range between 3.28±0.43 µm and 8.92±0.41 µm. Vesicles prepared with Tween 80 (3.28±0.43–6.28±0.26 µm) were comparatively smaller than those formed using Span 60 (5.52±0.46–8.92±0.41 µm). All the formulations exhibited drug content values between 95.54±0.60% and 99.28±0.20% w/w. The morphological assessment revealed that the proniosomal vesicles were spherical in shape, had smooth surfaces, and were free from aggregation. A 30-minute in-vitro drug release study was conducted and compared against a marketed tablet. By the end of 30 minutes, the proniosomal formulation F4 (Tween 80: Cholesterol in 1:4 ratio) exhibited a rapid drug release of 99.12±0.32%. Overall, all proniosomal formulations (F1–F8) demonstrated superior drug release compared to the marketed formulation, with values ranging from 87.48±0.33% to 99.12±0.32%. To understand the release kinetics, the drug release profiles were evaluated using multiple mathematical models including zero order, first order, Higuchi, and Korsmeyer-Peppas. The release followed Higuchi kinetics and was governed by a Super Case II transport mechanism. Short-term stability testing was conducted on the optimized F4 formulation for a period of three months. No significant

changes were observed in the formulation's physical characteristics, drug content, or release behavior under both real-time (25°C±2°C/60% RH) and accelerated (40°C±2°C/75% RH) conditions.

These findings suggest that prazosin hydrochloride proniosomes were successfully formulated using the slurry method and may serve as a promising alternative to niosomes. Further research can be directed towards animal testing to evaluate the in vivo efficacy of the drug.

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