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# Creation and Design of a Proniosomal Transdermal Captopril Drug Delivery System

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## Abstract

***The study's objective was to create a proniosomal carrier system that would effectively transport the entrapped medication over a prolonged period of time in order to treat hypertension.Method: Proniosomes were used to encapsulate captopril in different proniosomal gel formulations made of different ratios of sorbitan fatty acid esters, cholesterol, and lecithin that were prepared using the coacervation-phase separation method in order to explore the drug's potential as a transdermal drug delivery system. Size, vesicle count, drug entrapment, drug release patterns, and vesicular stability under various storage settings were all measured in vitro for the developed systems. For four weeks, proniosomal gel stability investigations were conducted.Results: 66.7 - 78.7% of the encapsulated material was produced using the proniosome loading technique.Transmission electron microscopy was used to characterize protoniosomes. In vitro research revealed a delayed release of captopril that was entrapped. Higher drug retention was seen under cold settings.In conclusion, our research clearly shows that proniosomes have a fair amount of stability and are a viable long-term delivery strategy for captopril.***

***KEYWORDS: Transdermal delivery, in vitro release, stability studies, pioniosomes, and captopril.***

## INTRODUCTION

Functional molecules might be delivered via a carrier to the site of action and released to carry out their function in order to seek the best possible therapeutic action1. Niosomes, which are tiny lamellar structures made of non-ionic surfactant, dicetyl phosphate, and cholesterol mixed together and then hydrated in aqueous medium, are non-ionic surfactant vesicles.

Proniosomes provide a flexible vesicle drug delivery idea that may be used to administer medication transdermally. This might occur if proniosomes under occlusive circumstances transform into niosomes when they are hydrated with water from the skin after topical application.3.Proniosomes reduce niosome physical stability issues such fusion, aggregation, and leakage while offering more dosage, storage, and transit convenience4.

Interest in transdermal medicinal systems has increased due to their many benefits, which include reduced side effects, a relatively simple way to stop medication input in difficult instances, a non-invasive parental route for drug administration, and the avoidance of first pass gut and hepatic processing. 5. A common therapy for hypertension and congestive heart failure is captopril, an oral active inhibitor of angiotensin-converting enzyme (ACE). The medication is seen to be the preferred option for antihypertensive treatment because of its efficiency and little toxicity. Captopril has a 75% bioavailability, although oral absorption is decreased by 30% to 50% when food is present. A prior study found that since the oxidative product of captopril, captopril disulfide, exhibits poor intestinal absorption, the oxidation rate of captopril in dermal homogenate is much lower than that of intestinal homogenate. 7. When used initially, captopril induces hypotension, which may be dangerous for people with congestive heart failure and diuretics. Patients with myocardial infractions may have certain complications from persistent hypotension 8. Consequently, using a transdermal medication delivery method may lessen captopril's negative effects. The chemical captopril has been transported into the skin layer using niosome carriers, which are widely recognized for their potential in topical medication administration.

The aim of this investigation was to identify the variables affecting captopril encapsulation in proniosomal gel and to improve encapsulation parameters to get an appropriate delivery mechanism.

## EXPERIMENTAL

*Materials*
A present from Promed (Delhi, India) was captopril.

Hi-Media Laboratories was the supplier of dialysis tubing, cholesterol, and soy lecithin (Mumbai, India). We bought sorbitol and span 20, 40, 60, and 80 from Central Drug House (Mumbai, India).

The creation of proniosomal gel

Using the coacervation-phase separation technique 9, proxiosomal gel was created. A clean, dry, wide-mouthed glass vial with a capacity of 5.0 ml was filled with precisely weighed quantities of surfactant, lecithin, cholesterol, and medication. Additionally, 0.5 ml of alcohol was added to the vial. Following warming, all of the materials were well combined with a glass rod. To stop solvent from escaping, the open end of the glass bottle was sealed with a lid. The combination was then heated over a water bath at 60 to 70°C for about five minutes, or until the surfactant mixture was fully dissolved. After that, the aqueous phase (0.1% glycerol solution) was added and heated on a water bath until a clear solution formed. When the solution cooled, it transformed into a proteosomal gel. The resulting gel was kept for characterisation in the same glass container under dark circumstances. Table 1 lists the compositions of the formulations for poliosomal gel. Proniosomal Gel Vesicle Size Analysis Characterization: Proniosomal gel (100 mg) was hydrated by adding saline solution (0.9%) to a tiny glass vial and shaking it occasionally for ten minutes. The dispersion was examined at a 100x magnification using an optical microscope (Olympus, New Delhi). Using a calibrated ocular and stage micrometer (Erma, Tokyo) installed in the optical microscope, the diameters of 200–300 vesicles were measured.

## RESULTS AND DISCUSSION

A number of innovative delivery methods for captopril have been proposed, including beadlets, microcapsules, bioadhesive systems, floating tablets and capsules, semisolid matrix systems, microspheres, and floating tablets and capsules.

Interest in proniosomes as a topical application has increased as a means of avoiding the negative effects of oral treatment.

In order for prominoses to function as effective drug carriers, they need to be adequately loaded with an active chemical. Table 2 displays the impact of several sorbitan fatty acid esters together with their respective ratios on captopril encapsulation in proniosomal gel.

It worked well to encapsulate captopril using proniosomal preparations made with Spans 40 and 60. The fact that Spans 40 and 60 exhibit greater phase transition temperatures [Tc] 18 and are solid at room temperature may be the cause of this. Span 80 formulations had an entrapment efficiency that was 11% lower than Span 60 formulations. The head group of Spans 60 and 80 is the identical, but Span 80 contains an unsaturated alkyl chain. When a double bond is added to the paraffin chain, liposome permeability is noticeably increased. This might be the cause of the Span 80 system's decreased entrapment efficiency. 19. The size of the vesicles must be determined before applying them topically. When the dispersion was disturbed, the size decreased. The energy used in the agitation, which causes the bigger vesicles to split into smaller vesicles, is the cause of this. The range of sizes was determined to be 4.14 - 8.36 μm (with agitation) and 11.38 - 25.06 μm (without agitation).

Table 2: Captopril-Loaded Proniosomal Gel Formulations' Encapsulation Efficiency

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| S. No | Formulation Code | Vesicle Size ± SEM (µm) | | Percent Drug Loading (± SEM)* | Rate of spontaneity ($mm^3$ x 1000) |
|---|---|---|---|---|---|
| | | Without Agitation | With Agitation | | |
| 1 | AGL2 | 25.06±4.50 | 8.36±0.10 | 78.71(±1.48) | 11.19±0.52 |
| 2 | AGL5 | 18.09±1.53 | 7.59±0.11 | 77.76(±1.51) | 15.25±0.28 |
| 3 | AGL8 | 17.41±0.94 | 5.19±0.23 | 74.78(±1.72) | 14.54±1.11 |
| 4 | AGL11 | 11.38±1.70 | 6.37±0.11 | 73.78(±2.51) | 16.58±0.77 |
| 5 | AGL14 | 22.40±1.57 | 7.75±0.09 | 76.77(±1.54) | 13.59±1.17 |
| 6 | AGL17 | 19.82±2.16 | 4.14±0.18 | 66.69(±1.57) | 7.96±0.24 |

*Mean of three determinations

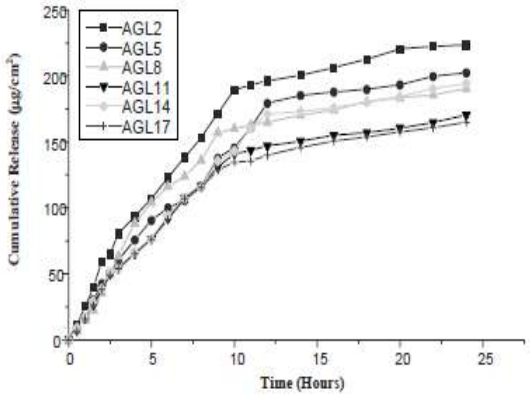


**Figure 1:** Comparison of a particular proniosomal gel formulation's in-vitro release profile

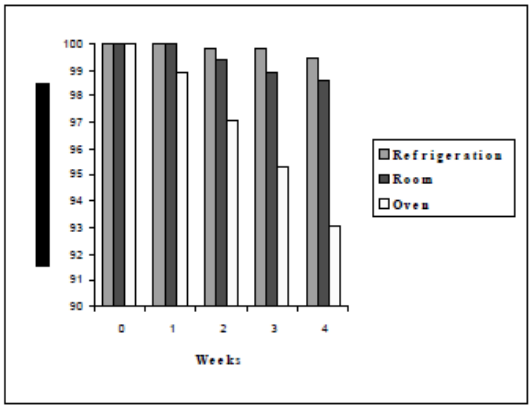


**Figure 2:** Stability study of AGL2 at different temperatures

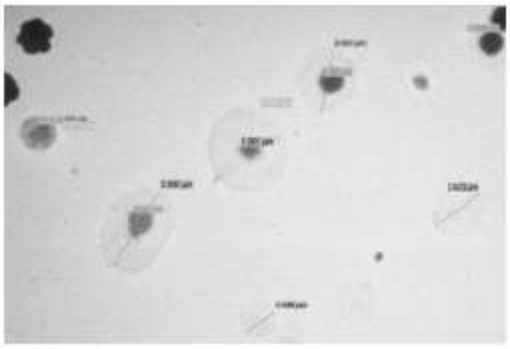

**Figure 3:** AGL2 electron micrograph

Since drug release determines the quantity of medication accessible for absorption, in vitro release studies are often conducted to forecast how a delivery system may function in an ideal scenario as well as provide some indicators of its in vivo performance. As shown in Fig. 1, the quantity of medication released from various proniosomal gel formulations was determined to be in the following order: AGL2 > AGL5 > AGL14 > AGL8 > AGL11 > AGL17. AGL2 was shown to have a regulated release characteristic lasting between 10 and 24 hours. At the tenth and twenty-fourth hours, the total release was determined to be 189.44 μg/cm2 and 223.54 μg/cm2, respectively. From the tenth to the twenty-fourth hour, the discharge rate remained steady. Consequently, throughout this time, the formulation showed zero order release.

This might be explained by the fact that, at the in vitro permeation setting of 250C, the molecules of Spans 40 and 60 are in an ordered gel state, but the formulation AGL2 demonstrated a much larger release because, at the same temperature, Span 85 is in a disordered liquid crystalline state. 21. AGL5, AGL8, AGL11, AGL14, and AGL17 were the additional formulations that demonstrated strong controlled release qualities. The drug's shelf life is ultimately determined by the quantity of medication that is kept inside the vesicles under certain circumstances. The findings demonstrated that the poliosomal gel formulation was quite stable at both ambient temperature and refrigerator temperature, since no drug leakage was seen at both settings (refer to Fig. 2). The melting of the lipid in the formulation and the surfactant (m.p.: 480C) may have resulted in a reduction in the percentage of medication retained at 450C. As a result, room temperature or refrigeration may be used to keep the proniosomal gel formulations.

## CONCLUSION

In summary, proniosomal gel has the ability to distribute captopril via regulated systemic transdermal distribution. It also has a high entrapment efficiency and employs alcohol, which has the potential to promote penetration.

The formulation process is short and does not need the use of several pharmaceutical excipients or complex steps.

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