CHAPTER V

CONCLUSIONS

Minoxidil (MN) is a well-accepted topical drug to treat scalp hair loss. The most widely used MN products are in the form of solution. Nevertheless, a more efficient topical system that can deliver the drug directly to the pilosebaceous unit should be beneficial. MN is a drug with a relatively low partition coefficient and can be classified as a lyophobic agent since the solubility of the drug is low in both water and organic solvents. Vesicular carrier systems such as liposomes and niosomes may be good candidates for MN preparations because these structures can accommodate the drug in both the lipophilic bilayer and the aqueous compartment. A previous study from this laboratory reported that MN could be formulated into niosomes with an entrapment efficiency that was higher than its solubility in water and commonly used organic solvents. However, there was no information on the stability of the resultant niosomal systems. Besides, the potential of non-ionic surfactants to cause toxicity to the mucous membrane and the skin was not studied. This present study explored further the formulations of MN in the form of niosomes prepared by the sonication method that was devoid of organic solvent. The ratios of non-ionic surfactant to cholesterol to solulan® C24 used in this present study were 67.5:27.5:5 for Span® 40, 57.5:37.5:5 for Span® 60, 67.5:27.5:5 for Brij® 52, and 47.5:47.5:5 for Brij® 76, respectively. Physical stability, chemical stability, and the potential of resultant niosomal preparations to cause irritation to the mucous membrane were investigated. The ability of the niosomal formulations to improve the stability of photosensitive drugs such as MN was also studied. In addition, in vitro drug release profiles of these formulations were monitored to gain information for further application of the systems as topical products, as well as to deduce the mechanism by which niosomal formulations protected MN from photodegradation. The results of the investigation can be concluded as follows:

1. The sonication method could be used to prepare MN niosomes from commonly available non-ionic surfactants. The method was reproducible resulting in small standard deviations in the entrapment efficiency of MN in various batches of niosomal suspensions.

2. All formulations of MN niosomes, when protected from light, were physically and chemically stable for at least three months of storage at ambient conditions.

3. All niosomal formulations could sustain the release of MN over a period of at least 12 hours. Drug release stopped within 24 hours. The highest percentage of release was obtained from Brij® 52 niosomes, followed by Brij® 76, Span® 40, and Span® 60 niosomes, respectively.

4. Photodegradation of MN in solution followed the first order kinetics, but that of MN in niosomal suspensions could not be described by the first order kinetics. This might be due to the various processes involved in the niosomal systems, including drug release from the vesicles.

5. MN stability to UV radiation was improved by its incorporation into niosomal vesicles. The ability of niosomes to protect photosensitive drugs such as MN was dependent on the properties and composition of the vesicle themselves. The more rapidly the drug was released from the system, the higher extent of the drug was degraded by UV radiation.

6. MN in niosomal formulations had less potential to cause irritation than sodium dodecyl sulfate, a standard tenside solution, and than the system simulating the commercial product (MN in 60% ethanol, 20% propylene glycol, and 20% water). Niosomes prepared from Span® had lower tendency to cause irritation than those prepared from Brij®. Cholesterol and Solulan® C24 did not show any tendency to cause irritation.

7. The potential of the system to cause irritation depended on its composition. MN itself did not show any potential to cause irritation to the mucous membrane of red blood cells.

In conclusion, the results of this present study indicate that MN niosomes could be reproducibly prepared by the sonication method. The resultant niosomal suspensions were stable for a reasonable period and had low potential to cause irritation to the mucous membrane. These results should be sufficient to justify further studies of MN niosomes in animal models and, finally, in clinical trials.