Transdermal Delivery System of Testosterone Using Solid Lipid Particles

Amal H. El-Kamel, Ibrahim A. Alsarra, Iman M. Al-Fagih

Department of Pharmaceutics, College of Pharmacy, King Saud University, P.O. Box 11495, Riyadh 11452, Saudi Arabia

Introduction

Testosterone (TES) deficiency is associated with symptoms that include impotence, fatigue and mood depression.

The conventional TES administration are problematic. Recently, transdermal drug delivery systems have been introduced as suitable alternatives to the conventional TES administration due to their potential benefits. However, the relative impermeability of the stratum corneum provides the principle resistance to percutaneous absorption.

Solid lipid microparticles (SLM), often called lipospheres, developed by Domb (1993) have been proposed as new type of fat-based encapsulation system for drug delivery of bioactive compounds. Recent investigations have indicated that improved skin targeting may become feasible by means of SLM.

For a further improvement in skin permeation, suitable enhancers and/or sonophoresis can be applied.

Objective

The main objective of the study is to formulate an improved transdermal delivery system of TES in an attempt to enhance its transdermal penetration.

Methods

Preparation of TES SLM: Emulsion melt homogenization method.

All formulations contained 0.25 or 0.5% TES. Glycerol monostearate (GM) (2.5-5%), glycerol distearate (GD) (5-10%), glycerol dibehenate (GB) (5-10%), and stearic acid (SA) (2.5-5%) were used as fatty bases.

Assay of TES: HPLC assay.

Microscopy: Scanning electron microscope (SEM).

Infrared scanning calorimetry (DSC): 30-300°C.

Particle size analysis: Optical microscope.

In vivo study: Male Wistar rats of similar age and weight were maintained on a normal diet.

DSC thermograms indicated that TES exists in amorphous form in all SLM.

Results

For 2.5% and 5% GM SLM, the particles are spherical with irregular surface.

For 5% and 10% GD SLM, they have irregular surface with no aggregation.

For 5% and 10% GB SLM, the particles have spherical shape and slightly aggregated and when GB concentration increased to 10% the surface deformed and aggregation increased.

For 2.5% and 5% SA SLM smaller particles with less aggregation was observed.

Particle size analysis shows a narrow size distribution for all formulae, where the particle size ranged from 2 to 30 µm.

Particle size distribution of SLM with high-fat content

Mean particle size slightly increases as the concentration of fat contents increased.


2. Rita Cortesi, Elisabetta Esposti, Giovanni Luca, Claudio Nastruzzi, Production of lipospheres as carriers for bioactive compounds, Biomaterials 23 (2002) 2283-2294.


References

The developed TES delivery system seemed to be promising to enhance TES penetration through the rat skin. Further studies are underway to improve TES skin permeation by testing other permeation enhancers and application of low frequency sonophoresis.

Conclusion

The enhancement factor was greatest when 1% DA used as chemical enhancer and the rat skin pretreated with high frequency US for one hour.

Acknowledgment

The authors are grateful to the Research Center, King Saud University, Women Students-Medical Studies & Sciences Sections and to King Abdulaziz City for Sciences & Technology for the financial support.

Effect of different methods of enhancement on TES flux

A synergistic effect on the skin permeation rate of TES was observed by using various enhancement methods.

When rat skin pretreated with high-frequency US, higher flux was observed in comparison with that obtained for selected formula without enhancement.

1% DA enhancer was more effective in increasing flux of TES through rat skin than 1% OA.

Upon application of US and 1% DA, greater enhancement of permeation rate of TES than each method alone was observed.

The flux of TES across excised rat skin was greatest with 10% GB SLM and lowest with 5% GB SLM. Therefore, the 10% GB SLM was chosen as the selected formula for optimizing the permeation rate of TES.

Effect of different methods of enhancement on TES flux

The flux of TES through cellophane membrane is maximum for 10% GB SLM and minimum for 5% GM SLM. However, the flux of TES when using 10% GB, 10% GD and 5% GB was similar, consequently, these three formulae are selected to be tested ex vivo.

The flux of TES from various SLM formulations through cellophan membrane

The authors are grateful to the Research Center, King Saud University, Women Students-Medical Studies & Sciences Sections and to King Abdulaziz City for Sciences & Technology for the financial support.