LIPOSOME AS A DRUG CARRIER SYSTEM FOR DIFFERENT ACTIVE SUBSTANCES

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Introduction

Liposomes have been widely used in pharmaceutical field via different routes. Liposomes are an alternative system for reducing the toxicity associated with drug [1-3].

The aim of this research work was to study the new formulation based on liposomes with different drugs which can be used a drug carrier system. In our project the liposomes were prepared by the lipid film hydration technique. In order to determine some properties of liposomes, e.g. shape, diameter and repeat distance (long spacing and water layer) the X-ray and light scattering as well as a light microscopy were applied. The X-ray scattering based on synchrotron radiation allows a high resolution structure analysis. Therefore the Small and Wide Angle X-ray Scattering (SAXS/WAXS) from the synchrotron source at the beamline B1 at HASYLAB, DESY, Hamburg was applied to determine the significant peaks of the scattering pattern.

Experimental methods

1. Preparation of liposomes

The liposomes were prepared by the lipid film hydration technique (Figure 1). The lipid films of different phospholipids i.e. Phospholipon 85G®, 90G® and 90NG® were prepared in a vial by dissolving the lipid in a 100µl of the mixture of chloroform and methanol (2:1, v/v) followed by removal of the organic solvent by a vacuum drying cabinet at 40°C for 24 h. Prior to the measurements by different techniques, the lipid films were hydrated with one of the drug solutions in sterile pure water. Various drugs were studied i.e. lidocaine base (LB), lidocaine hydrochloride LB(HCL), hydrous theophylline T(H2O), anhydrous theophylline (T), acetylsalicylic acid (ASA), and paracetamol (P). The molar ratios of drug to phospholipid were varied. Phospholipon 85G® contained phosphatidylcholine and lysophosphatidylcholine; Phospholipon 90G ® and 90NG® contained the same substances i.e. phosphatidylcholine, lysophosphatidylcholine and tocopherol but at different percentages [4].

2. Characterisation of liposomes

The liposome samples were filled in a glass capillary which was sealed with epoxide glue and radiated with X-ray from the synchrotron source at room temperature. In order to determine the form and diameter of the drop size the light microscope operating with the software Motic Images Plus (BA 300, Motic Deutschland GmbH, Germany) and static light scattering (Mastersizer-S, Malvern Instruments GmbH, Herrenberg, Germany) were applied.

Results

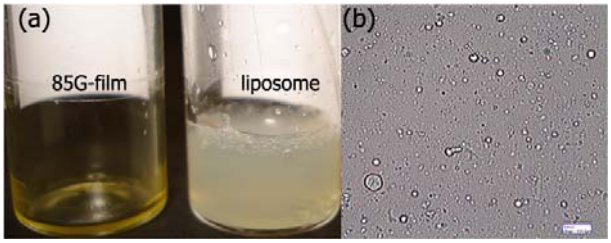

Figure 1: a) Phospholipon 85G-film (left) and liposomes after hydration of the film in the drug solution (right), b) light microscopic image of liposomes.

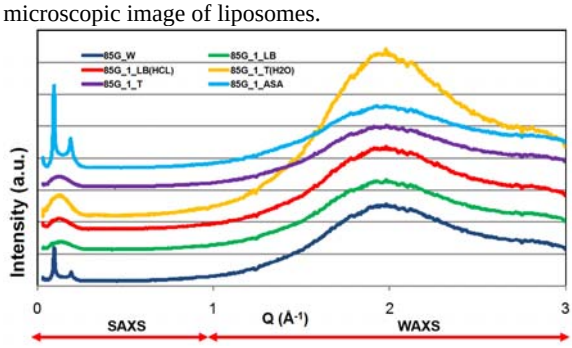

Figure 2: X-ray diffraction results (SAXS/WAXS) of liposome : Phospholipon 85G and various drugs (1:1, molar ratio at $2*10^{-5}$mol).

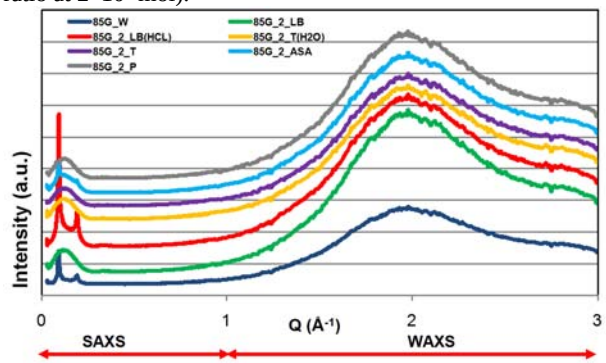

Figure 3: X-ray diffraction results (SAXS/WAXS) of liposome : Phospholipon 85G and various drugs (10:1, molar ratio at $2*10^{-5}$mol : $2*10^{-6}$mol).

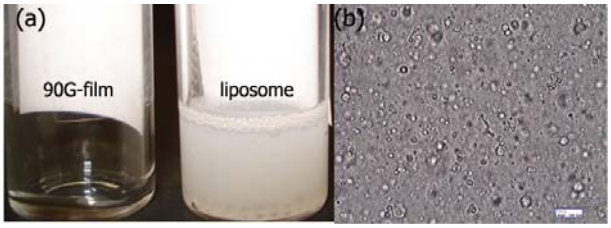

Figure 4: a) Phospholipon 90G-film (left) and liposomes after hydration of the film in the drug solution (right), b) light microscopic image of liposomes.

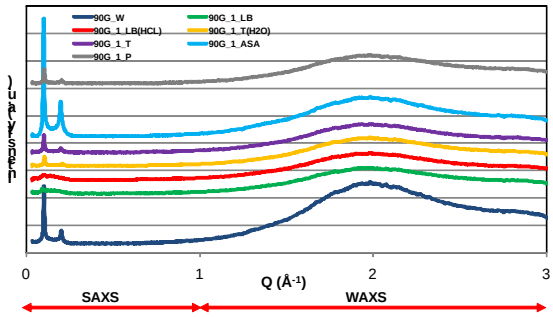

Figure 5: X-ray diffraction results (SAXS/WAXS) of liposome : Phospholipon 90G and various drugs (1:1, molar ratio at $2*10^{-5}$mol).

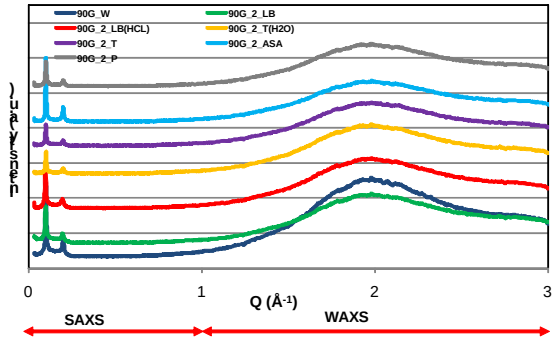

Figure 6: X-ray diffraction results (SAXS/WAXS) of liposome : Phospholipon 90G and various drugs (10:1, molar ratio at $2*10^{-5}$mol : $2*10^{-6}$mol).

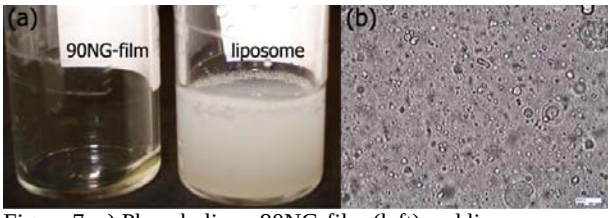

Figure 7: a) Phospholipon 90NG-film (left) and liposomes after hydration of the film in the drug solution (right), b) light microscopic image of liposomes.

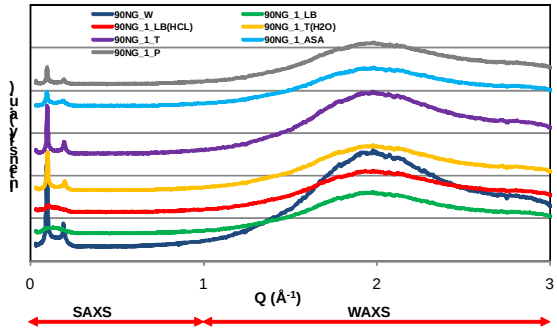

Figure 8: X-ray diffraction results (SAXS/WAXS) of liposome : Phospholipon 90NG and various drugs (1:1, molar ratio at $2*10^{-5}$mol).

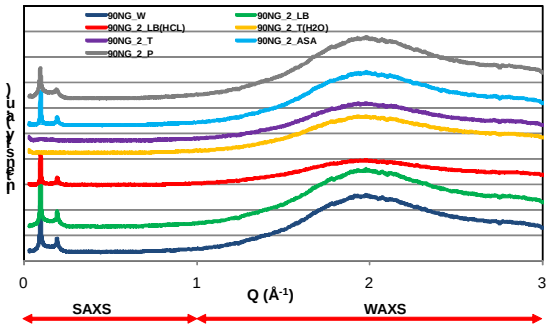

Figure 9: X-ray diffraction results (SAXS/WAXS) of liposome : Phospholipon 90NG and various drugs (10:1, molar ratio at $2*10^{-5}$mol : $2*10^{-6}$mol).

Discussion

The results show that the prepared liposomes were multilayer with the diameter of some nanometers to micrometers. The repeat distance of the lipid-layer was about 6 nm. After the incorporation of different drugs, the structure of the liposomes changed depending on the drug type. Some drugs cause the disordered structure of the liposomes and somes promoted the high-ordered structure. This can be clearly observed by SAXS and WAXS techniques. The liposomes studied in this project can be used as a drug carrier system and the active substance with different properties e.g. water solubility, pKa, polymorphism can be incorporated. However, it should be considered that the nanostructure of the liposomes may change depending on the types of the substances.

Conclusion

The structure of liposomes was changed depending on the composition of the formulations. The information about the structure of the different liposome formulations by various measuring techniques allows us to formulate a better drug carrier system and to understand the mechanism of action of different composition inside the formulation.

Acknowledgement

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References

[1] Molema, G., Meijer, D.K.F., (Eds) (2001) Drug Targeting, Wiley-VCH, Weinheim, Germany
[2] Torchilin, V.P., and Weissig, V., (Eds) (2003) Liposomes, Oxford University Press, Oxford, UK
[3] Weidenauer U., Mäder K. (Eds) (2010) Innovative Arzneiformen, Wissenschaftliche Verlagsgesellschaft GmbH, Stuttgart, Germany
[4] Phospholipid GmbH (2006/07), Product catalogue and specification of Phospholipon 85G, 90G, 90NG, Köln, Germany