Challenges in the Development and Up-scaling of Liposomes for Diagnostic Imaging

Shimon Amselem, PhD,
Chief Scientist, Delivery Technologies, IDR
Adama Agricultural Solutions Ltd., Israel

My first encounter with liposomes was 40 years ago during my M.Sc. thesis where we developed a new method for the preparation of liposomes based on French press equipment[1]. Since I was involved in many liposomal projects investigating the fusion of liposomes with viruses[2], studying membrane biophysics of phospholipid bilayers[3], encapsulation of anticancer drugs[4] antifungal agents[5] and allergens, use of liposome as diagnostic agents[6], liposomes as potent nontoxic adjuvant system[7], process optimization and upscaling of liposomal formulations[8], large scale-manufacturing of GMP liposomal products[9] and development of quality control and analytical methods for characterization and stability follow-up of liposomes and their raw materials[10]. During these four decades of liposome research I had the honor to be part of the team at the Hebrew University and Hadassah Medical School who developed the first marketed liposomal product, Doxil®, FDA approved in 1995.

In this brief lecture I will share some of the challenges we experienced in the development and upscaling of liposomal products especially during a recent project involving liposomes for diagnostic imaging and the lessons learned. Challenges to be discussed include liposome stability, leakiness of the entrapped material, equipment and manufacturing troubles, sterilization problems, analytical challenges, as well as safety issues and adverse effects during clinical trials.

---

[1] FEBS Let., 99, 210-214, 1979.
[2] Biochim. Biophys. Acta., 820, 1-10, 1985.
[3] Biochemistry, 18, 4169-4172, 1979
[4] Eur. J. Cancer Clin. Oncol., 25, 1795-1803, 1989
[5] Leukemia and Lymphoma, 9, 385-392, 1993.
[6] British J. Cancer, 64, 1125-1132 1991.
[7] Infection and Immunity, 60, 2438-2444, 1992.
[8] J. Pharmac. Sci., 79, 1045-1052, 1990
[9] J. Liposome Res., 1, 299-313, 1990.
[10] Liposome Technology, (G.Gregoriadis, ed.),Vol.1, Chapter 29, 527-616, CRC, 1993.