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Separation of liposomes from low density lipoprotein and its detection by inductively coupled plasma spectrometry

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Purpose: Native low-density lipoproteins (LDL) have been recognized as targeted drug delivery systems in cancer tissues that are upgraded level of LDL receptors. Loading of LDL techniques and its separation are considered challenges. The goal of the current study is to validate the separation between LDL and liposomes. Liposomes have been chosen to facilitate the delivery oftargeted molecules to an endogenous cholesterol carrier (LDL).

Methods: An ultracentrifugation method was developed to separate liposomes from low-density lipoprotein (LDL). Factors such as density gradient and size of liposomes were adjusted to optimize separation. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) was used for analyzing thenew cholesterol-based compounds (BCH, BCH-Da, BCH-Db and BCH-Dc) in liposomal formulations. Not only the boron compounds but also the phospholipid compositions of the liposome formulation were quantitatively analyzed.

Results: The ultracentrifugation method results show that in conjunction to time, speed and density gradient, size of the liposome also had impact on the separation using centrifugation method. In addition, reasonable limit of detection for boron (0.5 mg/ml) and phosphorous (0.09 mg/ml), respectively, was observed. ICP-MS was also utilizedfor analyzing BCH in a brain distribution study. The detection limit of boron analysis by ICP-MS is at least three orders of magnitude lower than of that of ICP-AES (1 ng B/ml). The method waslinear in the range of 500-1 ng B/ml and the linearity correlation coefficient was 1.

Conclusions: These findings show that density gradient separation methods was successful to separate of carborane-containing liposome from low density lipoprotein. Also, it shows the importance of ICP-AES as an analytical method for the analysis of element-based compounds encapsulated in phospholipid vesicles.

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