

LIPOSOMAL IMATINIB: AN EPR AND DSC STUDY

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Imatinib (Gleevec[®]) is a small molecule against BCR-ABL protein tyrosine kinase. This novel chemotherapeutic agent plays a crucial role in the therapy of chronic myeloid leukemia (CML) and gastrointestinal stromal tumors (GIST). Liposomal encapsulation is a prospective method of drug targeting altering both the antitumor activity and side effects of imatinib.

Our study aimed at designing a liposomal imatinib formulation and to investigate the molecular interactions of the lipid with imatinib. Multilamellar (MLV) and small unilamellar (SUV) vesicles were prepared from α -L-dipalmitoyl-phosphatidylcholine (DPPC), the most generally used lipid molecule, and contained various concentrations of imatinib (1-10 mM). The effect of imatinib on the lipid membrane was studied by electron paramagnetic resonance spectroscopy (EPR), and differential scanning calorimetry (DSC), at pH=5.0 (imatinib is in monocationic form) and at pH=9.0 (imatinib is neutral).

Our results indicate that imatinib interacts mainly with the DPPC-lipid headgroups and this interaction leads to a slight increase in the mobility of the polar headgroups in case of MLVs. Supporting these measurements, DSC data show evidences that pretransition temperature of imatinib-containing liposomes decreases significantly relative to control liposomes. Contrary to that imatinib causes a significant decrease in the fluidity of SUVs which is the result of a pH-dependent fusion/coalescence effect. The size distribution of liposomes was controlled by dynamic light scattering (DLS) and was found that the presence of imatinib leads to the formation of MLVs and/or LUVs.

Our results may direct attention to investigate the interactions of imatinib not only with tyrosine kinase but also with artificial/biological membranes.

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