Exploring the possibilities of formulation the rules for permeation enhancement

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In 1995, the FDA approved the first application of liposomes as lipid carriers of an active pharmaceutical ingredient (API) [1]. Since then, liposomes have been intensively studied. So far, there are more than 20 liposome formulations approved in the EU and USA, including COVID mRNA vaccines, and many others are undergoing clinical trials. Unfortunately, many APIs are hard or nearly impossible to formulate in liposomes because of their permeability and partitioning. These key properties of APIs were studied in our previous study [2]. There are few options for solving this problem, e.g. (i) a change of liposomes, (ii) adding a permeability enhancer or (iii) a small modification of the chemical structure of the API. We focused on the last option. We asked, "How much does the permeability of a small molecule change if we change its structure?". We analyzed the experimental permeability data from the MolMeDB database [3] from two experimental methods - CACO2 and PAMPA and one calculated method - COSMOPerm [4]. As a toy system, we studied the effect of structural changes on the permeability of cytarabine. We would like to present how the permeability of cytarabine changes if we systematically modify its structure.

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