

Phase separation in phosphatidylcholine membrane caused by the presence of a pyrimidine analogue of fluphenazine with high anti-multidrug-resistance activity.

Autorzy

Katarzyna Cieřlik-Boczula

Piotr Świątek

Agata Jaszczyszyn

Patrycja Zawilska

Kazimierz Gąsiorowski

Wiesław Malinka

Gottfried Köhler

Rok wydania

2014

Czasopismo

Journal of Physical Chemistry
B

Numer woluminu

118

Strony

3605-3615

DOI

10.1021/jp410882r

Kolekcja

Naukowa

Język

Angielski

Typ publikacji

Artykuł

Streszczenie

Phenothiazine compounds are known as effective inhibitors of a multidrug resistance (MDR) of tumor cells to chemotherapeutic agents. This group consists of many important substances used in human medicine such as antipsychotic drugs in the case of fluphenazine (FPh) or chlorpromazine (CPZ). Fluphenazine was on the World Health Organization (WHO) list of Essential Medicines of 2009, and its new pyrimidine analog (FPh-prm) presented in this work has been documented to have a high anti-MDR activity. In order to discover the character of alterations of the lipid bilayer structure caused by the presence of FPh-prm inside the lipid membrane, which is responsible for the essential increase of an anti-MDR activity of FPh-prm, microcalorimetric (differential scanning calorimetry), Laurdan fluorescence, ^{31}P nuclear magnetic resonance spectroscopy (NMR), and attenuated total reflectance Fourier transfer infrared spectroscopy (FTIR-ATR) were used for dipalmitoyl-*sn*-glycero-3-phosphocholine (DPPC) liposomes mixed with a different concentration of amine analogue. It was stated that the formation of domains with different content of FPh-prm/DPPC can be a reason for the membrane-related mechanism of chemoprevention associated with the inhibition of the outward transport of anticancer drugs by the glycoprotein P (Pgp) in cancer cells by the pyrimidine analog of FPh. To our best knowledge, this report is the first to show the bilayer structure of domains formed by incomplete miscibility of fluphenazine-related compounds and phospholipid molecules. Our results provide a sound basis for the design of future modifications of anti-MDR drugs by providing very effective inhibitors of the pump activity of Pgp.

Adres publiczny

<http://dx.doi.org/10.1021/jp410882r>

<https://www.acs.org/content/acs/en.html>

Plik został wygenerowany dnia 2026-08-27 23:58:03

Adres w repozytorium <https://old.chem.uni.wroc.pl/pl/repozytorium/kP5tdcZ>.