

Ionic liquids with antineoplastic activity influence the stability and physicochemical properties of lipid membrane models

Victoria Vitkova ¹*, Ognyan Petkov ¹, Velizar Georgiev ¹, Angelina Stoyanova-Ivanova ¹, Maya Guncheva ²#

¹ Institute of Solid State Physics, Bulgarian Academy of Sciences, Sofia, Bulgaria

² Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, Sofia, Bulgaria

Corresponding authors: * victoria@issp.bas.bg ; # maya.guncheva@orgchm.bas.bg

ogikrpetkov@gmail.com

Betulinic acid has been extensively studied as a natural pentacyclic triterpene with numerous pharmacological activities, including inhibition of tumour cell proliferation, as well as anti-inflammatory, antiviral, antibacterial, and neuroprotective effects, and protective activity on the cardiovascular system [1-3]. Incorporation of cations derived from charged or polar amino acids has been shown to improve its water solubility and enhance its activity and selectivity toward neoplastic cells [4]. The resulting ionic liquids exhibit cytotoxic effects against breast cancer MCF-7 cells, with notable differences among the studied salts [4]. To elucidate the mechanism of membrane damage underlying this cytotoxic activity, the present study examines the hypothesis that selectivity arises from alterations in membrane lipid organization. The mechanical and dielectric properties of model lipid membranes were investigated to quantify the effects of L-amino acid ethyl ester betulinates on membrane bending elasticity and electrical capacitance. The obtained results provide insights into the effects of structural modification of betulinic acid, through the synthesis of ionic liquids organic salts, affects the lipid matrix, with the aim of enhancing the selective cytotoxicity of the designed betulinic acid-derived pharmacophores.

Keywords:

ionic liquids, lipid membranes, thermal shape fluctuations, giant vesicles, bending elasticity, electrochemical impedance spectroscopy

References:

- [1] Zhang X, Hu J, Chen Y, Mol Med Rep., 2016, 14(5): 4489–4495
- [2] Oliveira-Costa JF, Meira CS, Neves MVGd, Dos Reis BPZC and Soares MBP, Frontiers in Pharmacology, 2022, 13, 880869
- [3] Banerjee S, Banerjee S, Bishayee A, Da Silva MN, Sukocheva OA, Tse E, Casarcia N, Bishayee A, Phytomedicine, 2024, 132, 155858.
- [4] Ossowicz-Rupniewska P, Klebeko J, Georgieva I, Apostolova S, Struk Ł, Todinova S, Tzoneva R D, Guncheva M, Pharmaceutics 2024, 16, 496.

Acknowledgements:

This study is based upon work from COST Action CA22153 EuroCurvoBioNet, supported by COST (European Cooperation in Science and Technology). The authors gratefully acknowledge financial support from the Bulgarian National Science Fund (grant No. KP-06-COST/19/22.08.2025).