the most frequently mutated gene in human cancer (about 50% of tumors express mutant p53), which results in a loss of its oncosuppressive function. The main regulator of the p53 protein is the ubiquitin ligase MDM2, which is responsible for reduced p53 levels via several mechanisms. MDM2 suppression leads to p53 activation and could trigger apoptotic death of tumor cells by increasing the expression of p53-dependent proapoptotic factors (e.g., Bax, Puma, etc.). A serious problem in the use of various chemotherapeutics, including MDM2 antagonists, currently undergoing clinical trials, is the development of acquired drug resistance. Recently, to study the mechanisms of acquired resistance of tumor cells to MDM2 inhibition using multiple *in vitro*, *in vivo* and *in silico* approaches we have demonstrated that the development of resistance to MDM2 suppression (by RG7388) in neuroblastoma model is associated with the appearance of mutations in the TP53 gene: one mutation (His193Arg) was found to destabilize the interaction of p53 with DNA[1]. Moreover, it was observed that resistant neuroblastoma cells were less sensitive to cytostatic chemotherapeutic agents (doxorubicin, cisplatin, paclitaxel), which possessed enhanced proliferation and metabolism rates compared to parental cells. In summary, these features might contribute to tumor progression. Reference: 1. Pervushin N.V. et al. (2024) Apoptosis 29(11-12), 2197-2213. The study is supported by the RSF grant (project 23-74-30006).

P-32-057
Comparative effects of propolis and polyphenolic cocktail (PFK5120) on EGFR signaling in MCF-7 hormone positive breast cancer cell line

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Breast cancer (BC) has been identified as the leading cause of cancer-related mortality among women, with an observed increase in incidence of 0.5% per year since 2004. The antioxidant, anti-inflammatory, and antineoplastic properties of polyphenols, natural secondary metabolites of plants, are well-documented. However, the potential effect of polyphenols on the EGFR signaling pathway is poorly known. Therefore, we investigated the potential effect of the combination of natural propolis and a phenolic compound (PFK5120) on the EGFR signaling pathway and HER2 protein expression. MCF-7 cells were exposed to different specific doses of propolis (6.5-13-26 ug/mL) and PFK5120 (5-10-20 ug/mL) for 48 hours in a cell culture medium. The mRNA expression levels in the RAS/MAPK pathway were analyzed by real-time PCR, and HER2 protein expression was assessed by western blotting and immunohistochemical staining. The RT-PCR analysis showed that propolis caused a significant inhibition of the gene expression in the RAS/MAPK pathway of the EGFR panel at all the doses at 48 hours. Treatment with 20 μg/mL PFK5120 resulted in a similar general inhibition of this pathway, with the exception of increased MAPK3 (FC = 6.39) and RELA (FC = 3.04) gene expression at 48 hours. However, a significant increase in HER2 protein expression was observed 48 hours after administration of 20 μg/mL PFK5120 ($p = 0.0187$). The findings were confirmed by immunohistochemical staining results. Our data suggest that further studies using standardized polyphenol capsules may be more effective as new therapeutic agents in cancer treatment. These approaches may offer a natural alternative to conventional cancer drugs, providing treatment options with minimal to no adverse effects.

P-32-058
Green light-triggered multifunctional bilosomes as an effective tool for malignant melanoma treatment

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Melanoma, as the most aggressive of all skin cancers, still poses a formidable challenge to modern oncology, mainly due to the formation of numerous metastases, including to the surrounding lymph nodes, as well as distant metastases (most commonly to the lungs and brain). Consequently, we present a novel formulation combining anionic xanthene dye of photosensitizing activity (Rose Bengal, RB) with the natural pigment from the carotenoid family (astaxanthin, AST), co-encapsulated within polyethylene glycol (PEG)-coated positively charged bilosomes, which was developed and evaluated concerning particle size, ζ-potential, and morphology. The safety and efficacy of bilosomal formulations were assessed using *in vitro* models of malignant melanoma tumor (A375 and Me45) and normal human epidermal keratinocyte (HaCaT) cells. During the study, we demonstrated enhanced uptake of the nanocarriers containing hybrid cargo by pathological cells compared to non-loaded RB and AST molecules. Moreover, double-loaded bilosomes combined with green illumination (light dose 10 J/cm^2, λ_{max} 520-560 nm) significantly reduced cellular mitochondrial activity for both melanoma cell lines tested. After phyto-photoactivation, treatment of A375 and Me45 cells resulted in a more than 70% decrease in their viability, already at a low concentration of hydrophilic photosensitizer equal to 2 μM. In conclusion, our findings provide crucial information on an integrated approach to antitumor synergy by combining novel bilosomal-origin nanophotosensitizers with advanced phyto-photodynamic therapy. Acknowledgments: This work was supported by the National Science Centre (Poland) [UMO-2023/50/E/ST4/00603] and in part by Statutory Subsidy Funds of the Department of Molecular and Cellular Biology [SUBZ.D260.24.076] at Wroclaw Medical University. The authors would also like to express gratitude for the support of the Department of Physical and Quantum Chemistry at WUST.