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## RESEARCH AREA

Bioactive natural compounds and their semi-synthetic derivatives represent a highly promising treasury of potential new drugs. Two particularly interesting naturally occurring, pharmacologically active compound groups are ecdysteroids and protoflavonoids.

Ecdysteroids are present both in flora and fauna. In mammals, they are non-toxic compounds that can exert numerous beneficial non-hormonal bioactivities, such as anabolic and adaptogenic effects. Besides, our research group has discovered the particular property of notably less polar ecdysteroid derivatives to sensitize the drug resistance of both multi-drug resistant (MDR) and non-MDR cancer cells towards various chemotherapeutics.

The pharmacological potential of protoflavonoids is also wide-ranging. They are intensively studied for their antitumor effects, which stem from their representatives' cytotoxic nature and their inhibitory effect on specific DNA damage response mechanisms (ATR-dependent signaling), through which they can enhance, e.g., the activity of cisplatin. Besides, considerable evidence has been revealed in recent years (e.g., inhibition of xanthine oxidase enzyme, antiviral activities) suggesting that the pharmacology of protoflavonoids might exceed their antitumor potential.

The focus of our research efforts is on the structural optimization of compounds of the outlined groups with therapeutic potential, according to which semi-synthetic modifications are made on the molecules, which may result in the improvement of their chemical-physical parameters, the enhancement of their biological effects and/or the reduction of their potential disadvantageous side effects.

## TECHNIQUES AVAILABLE IN THE LAB

Versatile organic synthetic techniques and drug functionalization methods that enhance the *in vivo* efficacy of the compounds (e.g., the preparation of self-assembled nanoparticles of bioactive agents) can be studied in our laboratory. An extensive array of instrumental chromatographic techniques is available for

the qualitative analysis and purification of products: high performance liquid chromatography (HPLC), supercritical fluid chromatography (SFC), flash chromatography, rotation planar chromatography, and centrifugal partition chromatography (CPC). In addition to the above, we provide an opportunity to learn about methods used for the structure elucidation of molecules (mass spectrometry, nuclear magnetic resonance spectroscopy).

## SELECTED PUBLICATIONS

**Vágvölgyi, M.**, Bélteky, P., Bogdán, D., Nové, M., Spengler, G., Latif, A.D., Zupkó, I., Gáti, T., Tóth, G., Kónya, Z., Hunyadi, A. (2020) Squalenoylated Nanoparticle Pro-Drugs of Adjuvant Antitumor 11 $\alpha$ -Hydroxyecdysteroid 2,3-Acetonides Act as Cytoprotective Agents Against Doxorubicin and Paclitaxel. **Front Pharmacol** **11**: 552088.

**Vágvölgyi, M.**, Girst, G., Kúsz, N., Ötvös, S.B., Fülöp, F., Hohmann, J., Servais, J-Y., Seguin-Devaux, C., Chang, F-R., Chen, M.S., Chang, L-K., Hunyadi, A. (2019) Less Cytotoxic Protoflavones as Antiviral Agents: Protoapigenone 1'-O-isopropyl ether Shows Improved Selectivity Against the Epstein-Barr Virus Lytic Cycle. **Int J Mol Sci** **20**: 6269.

Fumagalli, G., Giorgi, G., **Vágvölgyi, M.**, Colombo, E., Christodoulou, M.S., Collico, V., Prosperi, D., Dosio, F., Hunyadi, A., Montopoli, M., Hyeraci, M., Silvani, A., Lesma, G., Dalla Via, L., Passarella, D. (2018) Heteronanoparticles by Self-Assembly of Ecdysteroid and Doxorubicin Conjugates To Overcome Cancer Resistance. **ACS Med Chem Lett** **9**: 468-471.

**Vágvölgyi, M.**, Martins, A., Kulmány, A., Zupkó, I., Gáti, T., Simon, A., Tóth, G., Hunyadi, A. (2018) Nitrogen-containing ecdysteroid derivatives vs. multi-drug resistance in cancer: Preparation and antitumor activity of oximes, oxime ethers and a lactam. **Eur J Med Chem** **144**: 730-739.

**Vágvölgyi, M.**, Girst, G., Kuo, C-Y., Wang, H-C., Fülöp, F., Hunyadi, A. (2018) Synthesis of Nontoxic Protoflavone Derivatives through Selective ContinuousFlow Hydrogenation of the Flavonoid B-Ring. **Chempluschem** **83**: 72-76.