Enzymatic Production of Bioactive Pentacyclic Triterpenes:

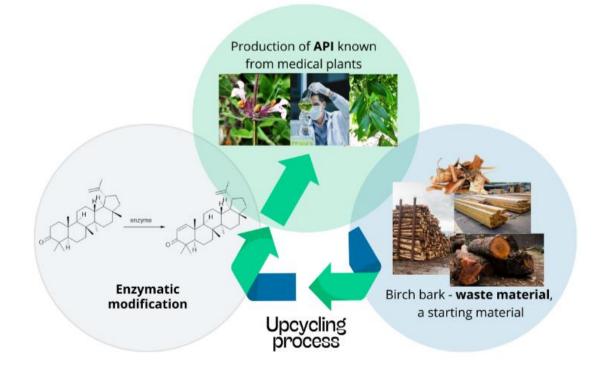
A Case Study of Upcycling

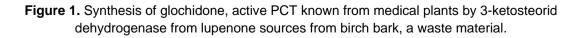
A. M. Wojtkiewicz¹, G. Oleksy¹, M. A. Malinowska²

¹Jerzy Haber Institute of Catalysis and Surface Chemistry, PAS, Niezapominajek 8, Krakow 30-239, Poland

² Cracow University of Technology, Warszawa 24, Krakow 31-155, Poland agnieszka.wojtkiewicz@ikifp.edu.pl

Recently we proved that 3-ketosteroid dehydrogenase from *Sterolibacterium denitrificans*, known as AcmB2 conducts an efficient and regioselective oxidative dehydrogenation of lupenone to glochidone [1]. The lupenone precursor – lupeol, a common natural compound derived from birch bark, is available in quantities of up to 20 g per kg of dry matter. While glochidone, also extractable from medicinal plants, occurs in significantly lower amounts, ranging from 11.4 to 83 mg/kg, representing the plant production 24 to 181 times lower. Furthermore, the extraction of glochidone from natural sources on a scale measured in milligrams does not suffice to meet the commercial demand for this biologically active compound. Addressing this challenge, enzymatic synthesis offers a solution, enabling the production of glochidone on a scale measured in grams, thereby exemplifying, in addition, an effective upcycling process.





Pentacyclic triterpenes (PCTs), natural compounds present in tree bark or leaves due to their diverse biological properties, are the subject of intensive research regarding their applications in pharmacy, food industry, and cosmetics. Documented properties of PCTs are anticancer, anti-inflammatory, antiviral, and antioxidant activities [2]. In some cases PCTs are even proposed as a beneficial alternative for steroidal chemotherapeutic or rheumatoid arthritis treatment [3], [4]. Among other PCTs, glochidone, due to the presence of the C1-C2 double bond, remains a more potent active agent with therapeutic properties [5].

In our work we evaluated glochidone's cosmetic properties unveiling its significant rejuvenating potential, particularly its robust sirtuin induction activity, making it an attractive candidate for cosmetic formulations aimed at enhancing skin health [1]. Our study provides valuable insights into enzymatic synthesis and the biochemical properties of AcmB2, offering promising avenues for the development of bioactive compounds in the pharmaceutical and cosmetic industries.

References

[1] A. M. Wojtkiewicz, G. Oleksy, M. A. Malinowska, and T. Janeczko, "Enzymatic synthesis of a skin active ingredient - glochidone by 3-ketoste - roid dehydrogenase from Sterolibacterium denitrificans," *J. Steroid Biochem. Mol. Biol.*, vol. 241, no. February, p. 106513, 2024, doi: 10.1016/j.jsbmb.2024.106513.

[2] P. Darshani, S. Sen Sarma, A. K. Srivastava, R. Baishya, and D. Kumar, *Anti-viral triterpenes: a review*, vol. 21, no. 6. Springer Netherlands, 2022. doi: 10.1007/s11101-022-09808-1.

[3] M. K. Shanmugam, A. H. Nguyen, A. P. Kumar, B. K. H. Tan, and G. Sethi, "Targeted inhibition of tumor proliferation, survival, and metastasis by pentacyclic triterpenoids: Potential role in prevention and therapy of cancer," *Cancer Lett.*, vol. 320, no. 2, pp. 158–170, 2012, doi: 10.1016/j.canlet.2012.02.037.

[4] L. Pinheiro, "Triterpenes as Potential Drug Candidates for Rheumatoid Arthritis Treatment," 2023. [5] H. Chen *et al.*, "Glochidiol, a natural triterpenoid, exerts its anti-cancer effects by targeting the colchicine binding site of tubulin," *Invest. New Drugs*, pp. 578–586, 2020, doi: 10.1007/s10637-020-01013-1.

Acknowledgments

This research has been financially supported by the National Science Centre Poland under the MINIATURA grant 2018/02/X/ST4/01963 (AcmB2), ICSC Statutory fund and ICSC development grant. We sincerely thank Tomasz Więcaszek (NATCHEM Company) for providing lupeol and lupenone.