

GLUCURONIDATION OF DIOSGENIN: THE STRATEGY FOR ENHANCING ANTIMICROBIAL ACTIVITY

Daria Grzywacz^a, Grzegorz Detlaff^a, Małgorzata Paduszyńska^b, Beata Liberek^a

^a Faculty of Chemistry, University of Gdańsk, Wita Stwosza 63, 80-308 Gdańsk, Poland
daria.grzywacz@ug.edu.pl

^b Faculty of Pharmacy, Medical University of Gdańsk, Hallera 107, 80-416 Gdańsk, Poland

Diosgenin, a steroidal sapogenin recognized as a natural precursor to numerous pharmacologically significant compounds [1-3], continues to reveal its potential. *In vivo*, it undergoes metabolic transformations, including glucuronidation.

This study presents the synthesis and structural characterization of diosgenyl glucuronides, covering both the α and β anomers (Fig.). While the β anomer is a naturally occurring metabolite, the α anomer has not yet been synthesized or isolated. Through a precisely designed synthetic strategy, both anomers were obtained, and their structures were confirmed using X-ray crystallography.

Subsequent investigations were aimed to enhance the biological properties of the synthesized compounds. To achieve this, the carboxyl group was modified through conjugation with L- and D-alanine. The obtained derivatives were subjected to microbiological assays, which demonstrated diverse antimicrobial activity. Moreover, selected compounds were subjected to an in-depth evaluation of their effects on *Staphylococcus aureus* biofilm, a structure that represents a significant challenge in contemporary medicine. Notably, certain derivatives exhibited biofilm-disrupting activity, which is rare among structurally related compounds.

The research findings indicate a potential correlation between molecular structure and biological activity, offering valuable insights for further exploration of steroidal glucuronides as prospective antimicrobial agents.

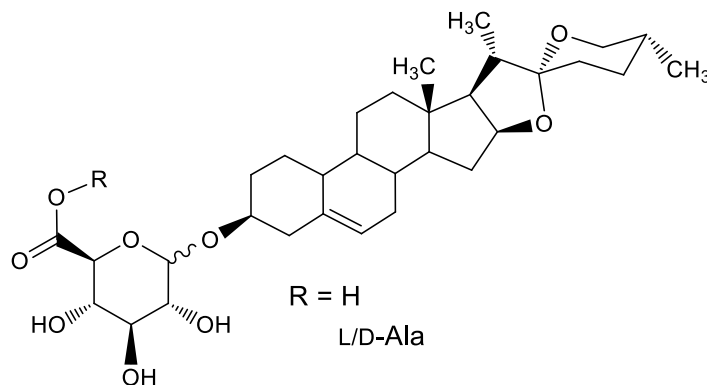


Figure 1. Chemical structure of diosgenyl glucuronides and their derivatives.

References:

1. P. Semwal, S. Painuli, T. Abu-Izneid, A. Rauf, A. Sharma, S.D. Daştan, M. Kumar, M.M. Alshehri, Y. Taheri, R. Das, S. Mitra, T.B. Emran, J. Sharifi-Rad, D. Calina, W.C. Cho, *Oxid. Med. Cell Longev.* **2022**, 29, 1035441.
2. D. Parama, M. Boruah, K. Yachna, V. Rana, K. Banik, C. Harsha, K. K. Thakur, U. Dutta, A. Arya, X. Mao, K. S. Ahn, A. B. Kunnumakkara, *Life Sciences*, **2020**, 260, 118182.
3. D. Grzywacz, B. Liberek, H. Myszka, *Molecules*, **2020**, 25, 5433.