

**ATRANORIN IS A NOVEL POTENTIAL CANDIDATE DRUG FOR TREATING
MYELOYDYSPLASTIC SYNDROME**

J.A. Rizayev¹, K.N. Semyonov², D.K. Kholmuradova²

¹*Samarkand State Medical University 18 Amir Temur Street, Samarkand, 140100,
Uzbekistan*

²*Scientific and Practical Center for Immunology, Allergology and Human Genomics
under Samarkand State Medical University*

Lichens are producers of a large number of specific secondary metabolites, most of which are not found in other living organisms. Currently, more than 800 secondary metabolites of lichens are known 1. The majority of aromatic lichen metabolites (about 500 compounds) are formed during the acetate-polymalonate biosynthetic pathway, which occurs with the participation of polyketide synthase (PKS) enzymes, which are very similar to fatty acid synthases in the organisation and mechanism of biosynthesis. In this work, a comprehensive study of the biocompatibility, cytotoxicity and genotoxicity of atranorin, a secondary aromatic metabolite of a number of lichens, was carried out. Atranorin belongs to the β -orsinol type depsides and is often the main metabolite in many lichen families Cladoniaceae, Parmeliaceae, Streocaulaceae and others. The compound was characterised using a complex of physicochemical methods of analysis: UV, IR, NMR spectroscopy, mass spectroscopy, elemental analysis.

The biocompatibility study included the study of haemocompatibility, antiradical activity, cytotoxicity against the ECV340 and HEK293 cell lines, as well as genotoxicity using the pBR322 plasmid and the DNA comet method. It has been shown that atranorin does not cause haemolysis, exhibits weak pro-aggregant activity, forms a stable complex with HSA ($K_b = 7.6 \cdot 10^4 \text{ M}^{-1}$) and DNA ($K_b = 2.88 \cdot 10^4 \text{ M}^{-1}$), and has pronounced antiradical properties in model reactions with radicals DPPH and ABTS, and is also non-cytotoxic (to non-tumour cell lines ECV340 and HEK293) and does not exhibit genotoxicity. Atranorin has previously been shown to be an AKT kinase inhibitor. The present study found that the consequence of this is a decrease in AKT-dependent expression of PD-L1 and TIM-3. In addition, molecular modelling of atranorin-AKT complexes showed stable interaction of the atranorin molecule with proteins, with the greatest binding strength at the allosteric site of AKT3 inhibition.