EFFECTS OF *FERULA TADSHIKORUM* RESIN EXTRACT ON CELL VOLUME REGULATION IN RAT THYMOCYTES AND MEMBRANE INTEGRITY OF HUMAN ERYTHROCYTES

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ABSTRACT. The study presents data on the ethanol extract of *Ferula tadshikorum* resin. It was found that the extract inhibits the cell volume regulation system in thymocyte cells and induces the formation of pores with a radius of ~3.3 nm in the erythrocyte membrane. The extract decreases the resistance of cells to osmotic and colloid-osmotic stress, with lytic effects occurring at concentrations <10 μg/mL, while sublytic effects are observed even at 1 μg/mL.
KEY WORDS. *Ferula tadshikorum*, *RVD*, erythrocyte, thymocyte

Plants of the genus *Ferula* belong to the family *Apiaceae* and include approximately 200 species widely distributed in the Mediterranean region and Central Asia. *Ferula tadshikorum* is a member of this genus and is considered an endemic species of Central Asia. Plants of the genus *Ferula* contain a range of biologically active compounds, such as coumarins, sesquiterpenes, and sulfur derivatives, and are used for their anti-inflammatory, antibacterial, antiviral, anticancer, and antiulcer properties. To date, the biological activity of extracts from *Ferula tadshikorum* has been scarcely studied. In this work, we investigated the effects of *Ferula tadshikorum* resin extract on the cell volume regulation system of rat thymocytes and the integrity of human erythrocytes.

In our initial studies, rat thymocytes maintained a stable volume in isotonic Ringer's solution for 20 minutes. When exposed to a hypotonic medium, the cells initially swelled and then partially recovered their volume within 15 minutes (regulatory volume decrease, *RVD* = 75.1±5%, *n*=5). Addition of *Ferula* extract at 0.125 μg/mL had no significant effect, but increasing concentrations led to a dose-dependent inhibition of *RVD*, with complete blockage at 2.5 μg/mL. Hill equation approximation yielded a half-maximal effect (C_{50}) of 0.7±0.1 μg/mL and a Hill coefficient of 1.7±0.4, indicating that the extract strongly inhibits cell volume regulation in a dose-dependent manner.

During our studies, we determined that the concentration of *Ferula tadshikorum* resin extract required to induce half-maximal hemolysis (C_{50}) was 7.8±2.4 μg/mL. The dry weight of the extract was measured as 7.2±0.9 mg/mL, which was used to calculate the concentration necessary to achieve complete hemolysis in experiments involving

polyethylene glycol. The extract was found to induce the formation of pores with a radius of approximately 3.3 nm in the erythrocyte membrane. Importantly, at low sublytic concentrations that do not cause hemolysis, the extract reduced the resistance of erythrocytes to osmotic stress and to colloid-osmotic stress induced by the channel-forming agent nystatin. The observation that lytic effects occur at concentrations above 10 μg/mL, while sublytic effects are evident at 1 μg/mL, underscores the extremely high biological activity of the bioactive compounds present in the resin extract of *Ferula tadshikorum*. These findings highlight the potent effect of the extract on human erythrocytes and on cell membrane integrity, emphasizing the presence of bioactive molecules in the resin extract of *Ferula tadshikorum* that require identification in further studies.

CONCLUSION. The ethanol extract of *Ferula tadshikorum* resin exhibits potent biological activity, significantly affecting both rat thymocyte volume regulation and human erythrocyte membrane integrity. It dose-dependently inhibits regulatory volume decrease in thymocytes and induces pore formation in erythrocyte membranes, thereby reducing cell resistance to osmotic and nystatin-induced colloid-osmotic stress, highlighting the strong activity of its bioactive compounds. These findings suggest that *Ferula tadshikorum* resin contains highly active biomolecules with potential physiological and pharmacological relevance, warranting further identification and investigation.

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