

PLENARY PRESENTATIONS

DI TERPENOID ALKALOIDS: FROM CHEMICAL AND TECHNOLOGICAL RESEARCH TO PHARMACOLOGICAL STUDIES AND PHARMACEUTICAL DEVELOPMENT

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Diterpenoid alkaloids (DAs) represent a large class of natural compounds characterized by complex polycyclic structures, high biological activity, and considerable pharmacological potential. Long-term studies conducted at the Institute of Plant Chemistry of the Academy of Sciences of the Republic of Uzbekistan have resulted in the isolation and identification of more than 200 diterpenoid alkaloids from plants of the genera *Aconitum*, *Delphinium*, and *Consolida*. A significant proportion of these compounds belong to new natural products of the C20-diterpene, C19-norditerpene, and C18-bisnorditerpene series. The most widespread and biologically significant compounds are alkaloids of the aconitine type, which exhibit pronounced pharmacological activity.

In this field, researchers of the ICPS AS RUz have developed a number of original medicinal preparations, whose efficacy has been confirmed by long-term clinical use (Allapinin), clinical trials (Antiaritmin, dihydroatisine hydrochloride, and others). Chemical modifications have also been performed, and promising molecular platforms have been developed for investigating the reactivity of DAs and for obtaining novel compounds based on them for the treatment of cardiovascular, neurological, and oncological diseases. The biological activity of DAs is associated with their ability to interact with voltage-gated sodium, potassium, and calcium channels of cell membranes, as well as to modulate nerve impulse conduction and myocardial contractile function. Owing to these properties, diterpenoid alkaloids are considered promising molecular platforms for the development of medicinal agents for the treatment of cardiovascular, neurological, and oncological diseases. To date, their anti-inflammatory, local anesthetic, analgesic, antispasmodic, muscle-relaxant, neurotoxin-antidotal, and ganglion-blocking activities have been investigated.

The technology for obtaining DAs involves the isolation of individual compounds from plants of the genera *Aconitum*, *Delphinium*, and *Consolida* using modern integrated approaches, including the selection of appropriate extraction solvents, gel filtration, ultrafiltration, supercritical fluid extraction, high-performance liquid chromatography (HPLC), and other methods, taking into account the basicity, polarity, and solubility of the target compounds. Structural elucidation of the isolated substances is performed using spectroscopic methods and X-ray crystallographic analysis.

An important area of modern natural products chemistry is the investigation of the relationship between the structure and biological activity of diterpenoid alkaloids. It has been established that the nature and spatial arrangement of functional groups substantially influence the pharmacological properties of these compounds. Accordingly, methods for the targeted chemical modification of natural molecules are being actively developed to obtain novel derivatives with enhanced selectivity, improved bioavailability, and reduced toxicity. The results obtained to date demonstrate the high potential of diterpenoid alkaloids as a source of novel medicinal agents.