

## PRECLINICAL RESEARCH OF OTOPROTECTIVE DRUGS

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**Background.** Drug treatment of Sensorineural Hearing Loss (SHL) is characterized by: administration of preparations from various pharmacological groups (nootropics, antioxidants, corticosteroids, etc.), combined prescription of drugs. The mentioned aspects indicate the need to use combined products in SHL pharmacotherapy.

**Objectives.** Determination of harmlessness and preclinical pharmacological efficacy in SHL of the combined product containing as active principle active principles – taxifolin, glycine (CAF-01).

**Material and method.** Acute toxicity and subchronic toxicity was performed on 72 mice and 54 male and female white rats by peroral and intraperitoneal administration with determination of physiological, hematological, biochemical and morpho-histological indices. Modeling of SHL induced by administration of gentamicine i/m and the determination of otoprotective effects was performed on 18 white rats with evaluation of Preyer's reflex, impedancemetry and otoacoustic emission (OAE). The research was carried out in collaboration with the Laboratory of Biochemistry and the Laboratory of Tissue Engineering and Cell Culture.

**Results.** The researched product shows reduced acute toxicity, being classified according to the Acute Toxic Class Method in toxicity class 5 with the average lethal dose (LD50) > 5000 mg/kg - practically non-toxic. In the context of subchronic toxicity, we determined that CAF-01 does not possess cumulative properties. There was a statistically significant increase ( $p < 0.01$ ) in the content of SH-groups of proteins and serum albumins. CAF-01 improves the balance between the pro- and antioxidant systems, the importance of dysfunctions in the respective systems for the etiology of SHL is known. The improvement of the Preyer reflex and the OEA parameters ( $p < 0.01$ ) was found, which indicates the improvement of the function of the inner ear of the animals that received the studied preparation. CAF-01 inhibits POL (lipid peroxidation) hyperactivation and increases antioxidant activity by restoring glutathione, antioxidant enzyme activity (catalase, glutathione peroxidase and superoxide dismutase). Through the respective mechanisms, as well as through the elimination of the spasm of the arterioles and capillaries of the vascular stria from the membranous labyrinth, the beneficial otoprotective action on the sensorineural components of the organ of Corti, the auditory nerve, is distinctly outlined.

**Conclusions.** Estimating the effectiveness of drug treatment presents an innovative and forward-looking element in hearing recovery in patients with hearing loss. An important direction for the treatment of auricular diseases is the development and use in medical practice of combined medicinal preparations, which contain synthetic and natural substances. The researched combined medicinal product shows a high degree of harmlessness, does not lead to the development of toxic processes and at the same time has an otoprotective effect.

**Keywords:** sensorineural hearing loss, combined drugs, harmlessness, pharmacotherapy.