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Особливості структури заморожених кріозахисних розчинів

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Peculiarities of the Structure of Frozen Cryoprotective Solutions

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The transformation of cryoprotective solutions being cooled into a stable amorphous state at the minimum possible concentration of the cryoprotective substance is a rather urgent task of modern cryobiology. At the same time, it has been established that at the cooling rates of 0.5...20 K/min, which are usually used in cryobiology, the concentrations of liquid fractions that completely vitrify are above 45wt% for aqueous solutions of PEG-1500, above 55wt% for aqueous DMSO solutions, and above 60wt% for aqueous glycerol solutions. Therefore, much attention is traditionally devoted to studying the processes of crystallization and vitrification of solutions near these concentrations. For this purpose, differential scanning volumetric tensodilatometry was used in the work. On the basis of the obtained dilatograms V(T), diagrams of the state of the specified solutions, including the region of existence of the cluster phase, were constructed. With their help, an analysis of the structures of solid-phase compositions created at T < Tg was carried out. It is shown that at concentrations lower than those noted, they contain ice crystals, particles of the cluster phase, clathrates from hydrated molecules of the cryoprotective substance. At the same time, cluster crystallization takes place in hydrated clathrates near Tg due to the conformational mobility of clathrate fragments. The formation of ice nanocrystals in such clathrates without breaking hydrogen bonds between water molecules and the cryoprotective substance sharply reduces the stability of amorphous fractions. This process can be active during temperature fluctuations in the cryo-storage even at temperatures below Tg. It is shown that the number of hydrated clathrates in the amorphous matrix depends significantly on the initial concentration of the solution and the speed of its cooling. In addition, the heterogeneous structure of the solid-phase matrix, which occurs in cryoprotective solutions below Tg, leads to its mechanical degradation during cooling and heating and appropriate damage to biological objects. This process is caused by the difference in the coefficients of thermal expansion of the fractions included in it (thermoelastic stress of the second kind).

The obtained results make it possible to analyze options for increasing the stability of amorphous fractions, which is necessary to improve the long-term preservation of cryopreserved biological objects.

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Паклітаксел індукує аксональну дегенерацію та змінює чутливість до низьких температур у дорослих щурів

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Paclitaxel Induces Axonal Degeneration and Alters Cold Temperature Sensitivity in Adult Rats

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Paclitaxel induced peripheral neuropathy (PIPN) is a severe adverse effect observed in most cancer patients receiving paclitaxel. Although highly effective in blocking tumor progression, a major dose-limiting side effect of paclitaxel can persist for up to two years after completing treatment, greatly affecting both the course of chemotherapy and patients' quality of life. The main neuropathic pain symptoms – cold and tactile allodynia, numbness and paresthesia can develop in most of the paclitaxel-treated subjects. In this study, axonal degeneration has been observed in sections of dorsal roots as well as caudal nerves in a rat model of PIPN. In adult rats, we have observed a dose-dependent large-fiber sensory neuropathy with no deleterious effects on overall health. The predominantly sensory nature of the neuropathy was revealed by the histological results. In animals receiving two doses of 18 mg/kg or 30mg/kg respectively, examination of the L4 dorsal root and ventral caudal nerve collected 2 weeks after paclitaxel administration revealed reductions in axon caliber and density and degenerated myelin profiles. Dark axonal profiles indicating Wallerian degeneration were apparent. Because Schwann cells myelinate both motor and sensory fibers, the results suggest that the severe pathology we observed is due to sensory neuronal or axonal damage rather than a primary lesion of Schwann cells. The performance of paclitaxel-treated rats in behavioral tests was consistent with histopathological changes. Cold allodynia was induced using two intravenous doses of 18 mg/kg paclitaxel within one week. Cold sensation studies after paclitaxel treatment reveals deficits preferentially in the structure and function of large sensory fibers. A statistically significant increase in the pain response in the acetone evaporation test was found in the hind paws of the adult rats 14 days after paclitaxel application. Our findings demonstrate a dose-dependent neurotoxic effect of paclitaxel under *in vivo* conditions. We show that paclitaxel administered intravenously twice weekly 3 days apart in adult rats produces a strong, sensory neuropathy without apparent adverse effects on the general health of the rat. As the mechanisms of PIPN remain unclear, there are currently no therapeutic options available to prevent and treat this disease. In the future, however, we believe that this work can help clarify important features of the functioning of cold receptors, respectively the formation of cold sensitivity in the body, as well.