Features of the biological action of substances of high dilution and ultra-low doses in conditions in vivo and in vitro

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Modern stage development biomedical research characterized by increased attention to the experimental and clinical aspects of the biological action of substances in high dilutions and ultra-low doses [1, 2]. A compelling reason for this interest, of course, is their ability to exert an effect similar to that of pharmacological agents in the usual dosage, but without their inherent disadvantages. Moreover, the establishment of a modifying effect in the combined use of drugs in conventional quantities and in ultra-low doses (biopathy) opens up fundamentally new possibilities in their therapeutic use [3]. So, for example, the anticonvulsant effect of phenozepam and the neuroleptic effect of haloperidol with preliminary or simultaneous administration of drugs in conventional and ultra-low doses are significantly enhanced [4, 5]. Thus,

Determination of the degree of manifestation of the biological effect when exposed to substances of high dilutions and ultra-low doses is based on studies of the dose-effect relationship using experimental models or test objects. The latter is due to the fact that not all substances have biological activity, taken at different concentrations, including at high dilutions (ultra-low doses) [6]. A bibliometric analysis of publications showing the results of dose-effect relationships at high dilutions and various experimental models was carried out as a result of a search in MEDLINE and HOMBREX systems from 1940 to the present [7]. Found 107 published research results, of which 69% had results comparable to baseline. 10% presented various effects and 21% showed no effect. The large number of described models and the limitation of the scope of this publication does not allow a complete analysis of the different nature of the dose-effect relationships at high dilutions and ultra-low doses obtained on experimental models under conditionsin vivo and in vitro.

As one of the typical examples of such studies, we can cite the results of experiments with the effect of the anticancer drug cisplatin on the proliferative activity of cells, which were carried out under conditionsin vivo and in vitro, and with the same dilutions in both series [eight]. In the first experimental series, rats received cisplatin with drinking water at concentrations of 10^{-eight} (10 pg / ml) and 10^{-16} (10 ag / ml), and there were 140 pg and 140 ag of the drug per animal, respectively. The study of the effect of cisplatin in the second series was carried out under conditionsin vitro on cells of culture

human lung carcinoma line A549... Cisplatin was added to the culture medium at three concentrations - 1 μg / ml, 10 pg / ml, and 10 ag / ml. The results of the two experimental series turned out to be opposite: cystpastin stimulated the growth of healthy rat cells, but inhibited the growth of tumor cells in culture, and the nature of the dose-effect dependencies under conditionsin vitro and in vivo wasunequal.

Previously, as a result of numerous studies, it was proved that under conditions in vitro dose-effect curve in the study of a series of highdilutions or ultra-low doses has a polymodal character, consisting of maxima of the biological response, alternating with a minimum or no effect. As a characteristic type of such dependence, one can cite the results of studies that were obtained in independent laboratories in France, Canada, Israel and Italy under the leadership of J. Benveniste on a model of human polymorphonuclear basophils under conditionsin vitro [nine]. It should be noted that similar polymodal dose-effect curves were obtained in many experiments under conditionsin vitro and published in monographs and journals from the end of the 19th century. Thus, we can conclude that the polymodal nature of the dose-effect relationship is typical of the biological action of high dilutions (ultralow doses) substances under conditionsin vitro.

A fundamentally different nature takes place in studies of biological effects at the level of the whole organism, when a biphasic rather than polymodal nature of dose-effect relationships is observed, as was demonstrated in the cisplatin biological effect publication cited as an example [6]. This effect is based on the phenomenon of hormesis, which is an exclusively two-phase effect of substances of high dilutions or ultra-low doses, when low concentrations (doses) cause a stimulating effect on biological processes, while higher ones act in the opposite way, inhibiting these processes [10]. The concept of hormesis is based on the well-known principle formulated by R. Arndt and H. Schulz (Arndt-Schulze law): weak effects increase the physiological activity of the body, strong ones inhibit, and the very strong paralyze. It can be assumed that one of the reasons for such differences in the action of high dilutions (ultralow doses) in studies on biological models under conditionsin vitro and in vivo consists in the features of the regulation system in the whole organism, which inthe latter case is absent [11, 12].

The performed analysis convincingly shows the fundamental differences in the biological action of substances in high dilutions and ultra-low doses in studies on models under conditions in vitro and at the level of the whole organism. Togetherhowever, one cannot but believe that other experiments on new biological models will provide new data that can either confirm or change the stated point of view.

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