Immunomodulating properties of the antimicrobial preparation composed of incapsulated rifampicin and interferon inducer

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Background. Antibiotic drugs occupy the leading position among preparations for treatment of infectious diseases. However, the results of antibiotic therapy indicate its inadequate efficacy and side effects particularly immunosuppression in patients. It is known, that therapeutic properties of drugs may be improved with regard to prolonged pharmacological effect and decreased toxicity by incorporating an active agent into the nano- or microparticles. Such advancement may also be obtained by designing composition preparations that contain synergetic agents, apart from antibiotic, or agents reducing the severity of side effects. By present the evidence has been accumulated about successful use of human recombinant cytokines (IFN-α, IFN-γ, TNF-α) and their inducers in immunotherapy (Sukhanov D.S. et al., 2010). It was shown that interferon inducers based on yeast double-stranded RNA (dsRNA) demonstrated a wide range of immunomodulating activity and increased the efficacy of phagocytosis and destruction of mycobacteria by macrophages (Masycheva V.I. et al., 2004). These data suggest the possibility to improve the therapeutic properties of an antibiotic drug by incorporating it in microcapsules and combining with dsRNA. Therefore, the goal of this work was to study immunomodulating activity of the composition containing encapsulated antibiotic rifampicin and dsRNA and the dynamics of rifampicin accumulation in phagocytic cells.

Materials and Methods. The composition preparation containing rifampicin encapsulated in polysaccharide capsules with dsRNA as well as reference substances (rifampicin, dsRNA) was orally administered to ICR mice in doses of 5 and 50 mg/kg. Rifampicin accumulation in peritoneal macrophages was analyzed 1 and 3 h. after administration by spectrophotometry. To evaluate the immunomodulating activity of rifampicin preparations we determined the level of macrophage functional activity and IFN-α concentration in blood. Macrophage activity was evaluated by HCT-test (Rook G.A.W. et al., 1985). IFN-α concentration in mice blood serum was measured by Mouse IFN Alpha ELISA Kit (PBL Biomedical Laboratories). To evaluate the direct effect of rifampicin preparations on macrophage activity we used the short-term peritoneal cell culture.

Results. The study revealed that antibiotic accumulation in mice peritoneal exudate cells significantly increased with administering the composition of encapsulated rifampicin and dsRNA compared to rifampicin (12,9 times higher, 3 h after administration). The evident increase of IFN-α in blood (by 67% after administration in dose of 5 mg/kg and by 44% -in dose of 50 mg/kg, 3 h after administration) was observed in composition- administered group whereas in the control group was not. The composition of rifampicin and dsRNA (in dose of 5 mg/kg) as well as dsRNA increased the oxidation-reduction activity of phagocytizing macrophages which was confirmed by quantitative increase of HCT-positive cells (by 39% and by 59% correspondingly, 24 h after administration). Both rifampicin and the composition of rifampicin and dsRNA possessed the ability to increase the metabolic activity of macrophages in vitro, though the stimulating effect of the composition appeared at 100-fold lower doses as compared with rifampicin, and the level of stimulating increased by 38-40% at equivalent doses.

Conclusions. Rifampicin encapsulated in polysaccharide capsules with dsRNA excels by its ability to intensively accumulate in macrophages and stimulate the metabolic activity of phagocytizing cells which is important in terms of strengthening their antibacterial activity. Incorporating dsRNA into the composition contributes to the ability to induce endogenous interferon which is significant for modulating immunosuppressive effects of the antibiotic.

Keywords incapsulated rifampicin; double-stranded RNA; dynamic of accumulation; oxidation-reduction activity; interferon alpha production; peritoneal macrophages; mice