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Differential effect of iodine bioorganic molecular complex on host defense in balb/c and c57bl/6 mice - Tamara Bukeyeva – Kazakh National University

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Abstract

Long involvement with the utilization of different iodine arrangements has demonstrated that while having articulated antibacterial and antiviral properties, wide-range antimicrobial movement, and lacking mutagenic and teratogenic impacts, they are harmful when acquainted with the human body, which altogether limits the extent of their clinical application. The quest for elective approaches to take care of the issue of high harmfulness of inorganic iodine mixes has prompted the improvement of iodine-containing natural buildings. Iodine is described by a high bioactivity and applies wide antimicrobial range with no recorder confirmations of opposition advancement to iodine in microscopic organisms and infections. The new enemy of irresistible medication (FS-1) containing sub-atomic iodine has been as of late made.

They are active ingredients of mixtures that in aqueous solutions consist of molecular iodine, bio-organic ligands, and potassium and lithium halo genides. In these drugs molecular iodine is in such an active form that after oral administration it minimizes toxic effects in humans. Previously it was shown that the active complex (AC) of the drugs contains molecular iodine that is located inside α-helix of dextrin and is coordinated by lithium halides and polypeptides (LiI5-α-dextrin polypeptide). In these types of complexes the electronic structure of the I2 molecule is different from the electronic structure of I2 in complexes with organic ligands, or in its free state. Interestingly, in the AC the molecular iodine exhibits acceptor properties with respect to polypeptides, and donor properties with respect to lithium halide. α-dextrins ensure the presence in the studied mixtures of the three active centers located within the α-dextrin helix: molecular iodine coordinated lithium halo genides and polypeptides, triiodide, and lithium halo genides. Using UV spectroscopy, the interaction of α-dextrin-LiCl(I)-I2-polypeptid with the AGA nucleotide triplet was investigated. Comparison of the quantum chemical calculations carried out for electronic transitions obtained for the structure that models the interaction of α-dextrin-LiCl(I)-I2-polypeptid with the nucleotide triplet indicates that the DNA nucleotides can displace polypeptide and form stable complexes with molecular iodine and lithium halo genides.

In such structures, molecular iodine binds both the nucleotide triplet and lithium halogenides. We have shown that the presence of molecular iodine is vital for activity of compounds that inhibit the active site of HIV-1 integrase. Iodine prevents the active site of integrase from the formation of a complex with HIV DNA and inhibits the active complex of integrase and viral DNA, becoming the center of another nucleoprotein complex, and binding together the active site of integrase and viral DNA.

The manifestation of the phagocytic response is a significant indicator of the body reactivity state and level of its immune activity. The coordination compound of iodine with alpha-dextrin and polypeptides was synthesized at the Scientific Center for Anti-Infectious Drugs JSC, the effect of which on the phagocytic activity of granulocytes and monocytes in BALB/c and C57BL/6 mice was studied. Phagocytosis is considered as one of the major host defense function, which is a fundamental component of the innate immune response.

Host defense to intracellular infections caused by pathogens such as mycobacteria, salmonella, and leishmania involves both innate and adaptive cell-mediated immune responses. It is believed that the innate immunity provides the initial resistance in the first two to three weeks after infection before the adaptive type 1 cell-mediated immunity fully develops. The major cellular components involved in innate immunity include neutrophils, macrophages, and NK cells, whereas lymphocytes and macrophages are the major effector cells in cell-mediated immunity against intracellular infection. Innate immune components serve as a linker to cell-mediated immunity in part by releasing soluble signals such as interleukin 12 (IL-12). Cell-mediated immunity plays an essential role in conferring the ultimate protection against intracellular infection (2, 16, 18). Compelling evidence by us and others indicates that type 1 cytokines, including IL-12, gamma interferon (IFN-γ), and tumor necrosis factor alpha (TNF-α) play a critical role in the development of type 1 cell immunity against intracellular infections. Materials and methods:

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The animals of each line were divided into 3 groups of 10 mice, including 5 females and 5 males. Two doses of the drug were used in the study: 1/20 of maximum tolerated dose (MTD) is 125 mg/kg and 250 mg/kg (1/10 MTD) of animal weight. Blood was collected on day 14 after the administration of the drug. The analysis was performed by flow cytometry.

Flow cytometry (FCM) is an instrumental tool for rapid detection and characterization of microbial cells based on their light scatter and fluorescence properties. FCM allows analysis of complex populations according to user-defined cell characteristics, with typical analysis rates approaching 10 000 cells s−1. Information about cell number, size, macromolecular content, and genetic identity can be determined through use of various labels, stains, and probes. Although FCM was developed originally for analysis of relatively large mammalian cells, it is finding increased use by microbiologists, including food microbiologists. The recent advent of smaller, less expensive yet versatile FCM instruments is expected to facilitate even greater use of FCM in food microbiology in applications, including monitoring of food fermentations, physiological characterization of microbes exposed to various food processing-related stressors, and rapid detection of pathogens in foods.

Findings:

It was shown that a new complex of iodine with bioorganic molecules upon repeated oral administration for 14 days in the examined doses did not affect the phagocytosis in BALB/c mice. The findings indicated that a new complex of iodine with bioorganic molecules at a dose of 250 mg/kg increased the phagocytic activity of both granulocytes and monocytes in C57BL/6 mice.

Conclusion & Significance:

One of the explanations for the differential effect of a new complex of iodine with bioorganic molecules on different lines of mice may be based on the genetic characteristics of these animals. Macrophages of BALB/c mice are known to be of M-2 type, which inhibits inducible NO synthesis and stimulates cell division. Macrophages of C57BL/6 mice are of M-1 type, which produces NO and inhibit cell division, and increases the cytostatic or cytotoxic activity of phagocytes. We can therefore conclude that a new complex of iodine with bioorganic molecules enhances the cellular factors of the natural resistance in the prototype mouse strains Th1 (C57BL/6), but not Th2 (BALB/c). This, in turn, fits into the single mechanism of action of the studied complex, namely, the activation of phagocytic cells through the induction of IFN-γ production and the ability of the complex to switch T cells to the Th1-type response path.

Recent Publications:

1. Hirayama D., Iida T., Nakase H. (2018) The Phagocytic Function of Macrophage-Enforcing Innate Immunity and Tissue Homeostasis. Int. J. Mol. Sci. 19:92.

2. Mills C.D. (2015) Anatomy of a discovery: M1 and M2 macrophages. Front. Immunol. 6:212. doi: 10.3389/fimmu.2015.00212.

3. Martinez F.O., Gordon S. (2014) The M1 and M2 paradigm of macrophage activation: time for reassessment. F1000Prime Reports 2014, 6:13 (doi:10.12703/P6-13).

4. Shu-Hui Su, Hsiun-ing Chen and Chauying J. Jen (2001) C57BL/6 and BALB/c Bronchoalveolar Macrophages Respond Differently to Exercise. J Immunol, 2001, 167 (9) 5084-5091; DOI: https://doi.org/10.4049/jimmunol.167.9.5084.

Biography:

In 2004 she graduated from Kazakh National University. Al-Farabi, Faculty of Biology, Department of Human and Animal Physiology and Biophysics with a Master of Biology. The total scientific experience is more than 16 years. The main research areas are in the field of cell and molecular biology. She is an experienced specialist in conducting cultural work with tumor cell lines, hematopoietic stem cells, and the isolation and cultivation of immunocompetent cells.