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A brief review: Potential pharmacological activity of dipotassium trioxohydroxytetrafluorotriborate, $K_2[B_3O_3F_4OH]$

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Statement of the Problem: Dehydration products of organoboronic acids and their derivatives such as trimethylboroxine, triphenylboroxine and dipotassium-trioxohydroxy tetrafluoro triborate $K_2[B_3O_3F_4OH]$ make up a broader class of compounds called boroxines. Recently, the halogenated boroxine $K_2[B_3O_3F_4OH]$ was listed as inhibitor of different enzymes and it has been suggested as potential drug in the prevention and/or treatment of benign or malignant changes of the epidermis visible in the form of, for example, nevus or skin cancer as well as other types of cancers. In the recent studies it was investigated the kinetic parameters and inhibition mechanism of $K_2[B_3O_3F_4OH]$ on enzymes catalase, peroxidase and human carbonic anhydrases. It was shown that its mM concentration could significantly reduce catalase activity and that $K_2[B_3O_3F_4OH]$ is a potent inhibitor of some human carbonic anhydrases. It was hypothesized that the local application of $K_2[B_3O_3F_4OH]$ -containing cream or by its intra-tumor injection could significantly reduce enzymes activity and produce beneficial effects in tumor tissue alone. **Methodology & Theoretical Orientation:** The catalase-mediated conversion of hydrogen peroxide, was studied in the absence and in the presence of $K_2[B_3O_3F_4OH]$. Manometric method was applied to monitor the enzyme reaction kinetics. The inhibitory actions of $K_2[B_3O_3F_4OH]$ were demonstrated only in the presence of elevated concentrations. The kinetics conformed to the Michaelis–Menten model and Lineweaver–Burk plot showed non-competitive inhibition. The horseradish peroxidase kinetics was studied by spectrophotometric and electrochemical methods. *In vitro* and *in vivo* effects of $K_2[B_3O_3F_4OH]$ were investigated with 4T1 mammary adenocarcinoma, B16F10 melanoma and squamous cell carcinoma SCCVII cells. *In vitro* investigation undoubtedly showed that it affect the growth of cancer cells and that the proliferation of cells depends on the concentration.

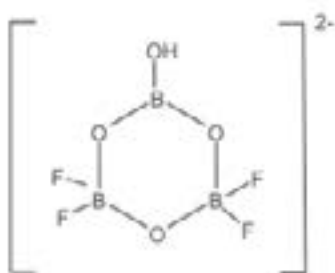


Figure. 1. Dipotassium trioxohydroxytetrafluorotriborate ion $[B_3O_3F_4OH]^{2-}$.

Recent Publications

1. Herenda S, Ostojic J, Hasković E, Hasković D, Milos M; Galic, B
2. (2018) Electrochemical Investigation of the Influence of $K_2[B_3O_3F_4OH]$ on the Activity of Immobilized Superoxide Dismutase, International Journal of Electrochemical Science. 13: 3279-3287.

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3. Ostojic J, Herenda S, Besic Z, Miloš M, Galic B. (2017) Advantages of an Electrochemical Method Compared to the Spectrophotometric Kinetic Study of Peroxidase Inhibition by Boroxine Derivative. *Molecules*. 22: 1120-1129.
4. Ivankovic S Stojkovic R Maksimovic M, Galic B, Milos M. (2016) Impact of calcium ion on cytotoxic effect of the boroxine derivative, $K_2[B_3O_3F_4OH]$. *Journal of enzyme inhibition and medicinal chemistry*. 31: 70-74.
5. Ivankovic S, Stojkovic R, Galic Z, Galic B, Ostojic J, Marasovic M, Milos M (2015) *In vitro* and *in vivo* antitumor activity of the halogenatedboroxinedipotassiumtrioxohydroxytetrafluorotriborate ($K_2[B_3O_3F_4OH]$). *Journal of enzyme inhibition and medicinal chemistry*. 30: 354-359.
6. Islamovic S, Galic B, Milos M (2014) A study of the inhibition of catalase by dipotassium trioxohydroxytetrafluorotriborate $K_2[B_3O_3F_4OH]$. // *Journal of enzyme inhibition and medicinal chemistry*. 29: 744-748.

Biography

Mladen Milos teaches biochemistry courses in the fields of natural sciences, chemistry, biochemistry and medical chemistry. By developing the program and introducing new subjects in undergraduate and postgraduate studies, he contributed to the improvement of the teaching process at the Faculty of Chemistry in Split. His basic and applied scientific research is in the field of biochemistry, research of mechanisms of control of living cells and intercellular communication and research of the biological activity of natural organic compounds isolated from Mediterranean aromatic herbs as well as synthetic compounds.

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