



## STUDY THE PROCESS OF INHIBITION OF INDAPAMIDE NITROSATION BY DIHYDROXYFUMARIC ACID - DNA CO-POLYMER

**M. Gonta<sup>1</sup>, Gh. Duca<sup>2</sup>, E. Sîrbu<sup>1</sup>**

<sup>1</sup> *Moldova State University, Moldova*

<sup>2</sup> *Institute of Chemistry of the Academy of Sciences of Moldova, Moldova*

A large number of drugs containing nitroso groups such as secondary amines, tertiary amines, amides could form N - Nitroso compounds (NNC) by the interaction of this target groups with nitrite ion. The stomach provides a suitable environment with low pH level that favors the interaction of amines functional group with nitrite ions. The NNC formed in the process of nitrosation of drugs can lead to development and evolution of colorectal cancer. Therefore, there is currently a considerable interest in diminishing or avoiding the potential toxicity of orally administered drugs containing secondary amines functional group [1].

**The main purpose of this paper** is to study the process of nitrosation of indapamide (IDA) by spectrophotometric method, to obtain functionalized antioxidants co-polymers and their use in the inhibition of this process of nitrosation. In order to achieve this purpose, the following objectives have been established: to study the nitrosating process of indapamide by the spectrophotometric method; NNC formation process depending on various parameters such as pH, concentration of NO<sup>2-</sup> and the concentration of indapamide. To obtain the functionalized antioxidants co-polymers and their use in the inhibition of nitrosation process of indapamide with nitrite ions.

**In experimental studies**, nitrosation process of indapamide was conducted in step change pH range in the model solutions: 1.6, 2.6, 3.0, 3.6 and 4.0. It was found that the rate of indapamide nitrosation depends on the pH, and by increasing pH, there is a reduction in the speed of the sodium diclofenac nitrosation process. Moreover, it was established that the concentration of nitrosating agents, which are formed in the process of interaction of nitrite ions and the nitrosated substrate, depends by a maximum molar ratio ([NO<sup>2-</sup>]/[IDA], 1:1). In this interaction nitrosonium cation participate as nitrosating agent, which was formed in an acid environment. We also investigated the formation of natural functionalized co-polymer, DNA- dihydroxyfumaric acid (DNA-DFH<sub>4</sub>) according to their mass ratio. It was found that the increase of percentage of antioxidant activity (AA, %) is in correlation with the concentration of antioxidant in the complex. Inhibitory activity of the nitrosation process was achieved in the presence of IDA, IDA - DFH<sub>4</sub> complex, which was higher compared to the model system IDA -DFH<sub>4</sub>, in the same conditions. Finally, the composition of IDA -DFH<sub>4</sub> can be used in the formulation of pharmaceutical products containing IDA in order to decrease the concentration of NNC formed *in vivo*.

### Reference:

1. Jun Liu, Xiao-yuan Wen, Jian-feng Lu, Juan Kan, Chang-hai Jin. Free radical mediated grafting of chitosan with fumaric and ferulic acids: Structures and antioxidant activity. *În: International Journal of Biological Macromolecules*, 65, (2014), p. 97–106.
2. Mohammad R. Kasaai, Joseph Arul, Intrinsic Viscosity–Molecular Weight Relationship for Chitosan, Gerrald Charald. *În: Carbohydrate Polymers*, 83, (2011), 905–913.