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Fund “Nauka” Project № 14001 Resume – Competition-Based Session 2014:

“New polymeric pharmaceutical forms with potential antitumor activity”

Project leader: Assoc. prof. Rumyana Tsoleva Cherkezova, PhD

The main research goal of this project is to synthesize new polymeric anticancer prodrugs. Poly (oxyethylene H-phosphonate) was used as a polymer carrier; the drug that is known for its therapeutic benefit in treating cancer is paclitaxel, which usefulness is limited due to its toxic side effects. Organic synthesis was performed and resulted in high-molecular weight compounds based on phosphorus-containing monomers. Synthesized polymeric products were characterized using the NMR, IRS and DSC methods. Polymeric pharmaceutical forms (also called conjugates) were developed based on the low-molecular weight drug paclitaxel immobilized onto the polymer carrier. In addition to NMR, IRS and DSC, the obtained polymer conjugates were also characterized by a biological evaluation. It included an in vitro study of the polymer conjugate and the results revealed that polymeric pharmaceutical drug forms showed cytotoxicity comparable to that of paclitaxel to a human lung cell line. Taking into consideration the strict requirements for pharmaceutical forms, an in vivo experimental animal study was also carried out.

The key conclusions that can be drawn from the scientific research are: **firstly**, establishment of strong interactions between paclitaxel and the polymer carrier that determine drug dispersion in the polymer matrix, and **secondly**, the biological evaluation shows that the polymer conjugate prevents the toxic effect connected with weight loss.

Therefore, the therapeutic options presented in the project are noteworthy for the fact that the multiagent therapy is preferred to monotherapy in treatment and prophylaxis of illnesses such as cancer. It is fully justified to expect even more complex polymers that will be a new and considerably larger addition to the approaches used up to date in cancer activities. Results arising from numerous studies (improved water solubility of lipophilic drugs and significantly reduced side toxic effects) give good reasons for the future development of polymeric pharmaceutical forms with a view to improving the treatment quality and efficiency for millions of patients.

Results are published in the following articles:

1. Mitova V, Hristova T, Cherkezova R,Koseva N,Yusa S, Troev K. Polyphosphoester-based paclitaxel complexes. *J.Appl. Polym. Sci.*2015; 132 (45): 42772.
2. Hristova T, Cherkezova R, Koseva N, Mitova V, Troev K. Polymeric pharmaceutical forms–the forms of the future. ScriptaScientificaPharmaceutica. 2015; 2(2): 20-24.

3. Hirota K, Hristova T, Mitova V, Koda T, Fushimi M, Kuniya M, Makino K, Tirada H, Cherkezova R, Yusa S, Koseva N, Troev K. Polyphosphoester-based paclitaxel complexes. Biological evaluation. Anticancer Res. 2016; 36(4): 1613-20.

Results are presented through the following contributions:

1. Cherkezova R, Hristova T, Yusa S, Troev K. Immobilization of paclitaxel onto poly(hydroxyoxyethylene phosphate). 25-th Jubilee Annual Assembly of IMAB, 14-17 May 2015, Varna, Bulgaria – poster.
2. Hristova T, Cherkezova R, Troev K, Hirota K, Tirada H,. Polyphosphoesters Based - Paclitaxel Complexes. Biological Evaluations. 25-th Jubilee Annual Assembly of IMAB, 14-17 May 2015, Varna, Bulgaria – poster.
3. Mitova V, Hristova T, Hirota K, Koda T, Fushimi M, Kuniya M, Makino K, Tirada H, Cherkezova R, Koseva N, Troev K. Polyphosphoesters based complexes of paclitaxel. Challenges in Science and Technology of Polymer Materials, 19-23 May 2015, Bansko, Bulgaria – poster.
4. Hristova T, Cherkezova R, Yusa S, Mitova M, Troev K. Poly(hydroxyoxyethylene phosphate)s – promising polymer carriers. Forth Scientific Session of the Medical College of Varna, 8 October 2015, Varna, Bulgaria – poster.