

***In vivo* toxicology of fullerene C₆₀ in low aggregation state**

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It is well known that the biological properties of fullerene C₆₀ depend on aggregation state [1]. Earlier *in vivo* experiments we showed by morphological analysis that the single intraperitoneal (i.p.) injection of fullerene C₆₀ in low aggregation state [as complex of C₆₀ with polyvinylpyrrolidone (C₆₀/PVP complex)] did not cause any visible injuries of parenchymatous organs [2]. Therefore the main goal of this work was the more detailed study of toxicological parameters of C₆₀/PVP complex, namely the LD₅₀ values and its influence on internal organs after prolonged i.p. injection (30 days). C₆₀/PVP complex, containing 0.5 % of C₆₀ and PVP pharmaceutical grade m.m. 12000, was used.

At the first stage of the study we determined the acute toxicity (LD₅₀ values) of C₆₀/PVP complex and the vehicle (PVP) after single i.p. injections into mice and Wistar rats (Rappolovo). Both compounds were injected as aqueous solutions concentration of 20, 25, 30 and 40 % (maximal possible concentration). The determined LD₅₀ values were: for mice 11.2±0.8 g/kg for C₆₀/PVP complex and 9.7±0.8 g/kg for PVP alone. Accordingly for rats these values were 7.9±1.0 g/kg and 6.8±0.7 g/kg.

Chronic toxicity studies were done on Wistar rats (180-200 g). Every animal was i.p. injected every day within 30 days. Both compounds were used in doses 350 and 700 mg/kg, 1/20 and 1/10 of LD₅₀, respectively, as aqueous solutions. The following activities were determined: integral activity, influence on central nervous system, urinary bladder and haematological parameters (leukocytes, platelets and erythrocytes). On 15 and 30 days of the experiment the morphological analysis of some internal organs (spleen, liver, and kidney) was made.

The most important result of our investigation is that pristine fullerene C₆₀ in low aggregation state (as C₆₀/PVP complex) is not only nontoxic, but reduces the toxic manifestation of high doses of PVP. These data indicate that the C₆₀/PVP complex can be used for medical purposes.

- [1] Piotrovsky L.B., Dumpis M.A., Litasova E.V., Eropkin M.Yu., Eropkina E.M. and Kiselev O.I. *Fullerenes, Nanotubes and Carbon Nanostructures* **19**(1), 147 (2011).
- [2] Popov V.A., Tyunin M.A., Zaitseva O.B., Karaev R.H., Sirotinkin N.V. Dumpis M.A., Piotrovsky L.B., *Fullerenes, Nanotubes and Carbon Nanostructures* **16**(5), 693 (2008).