

Toxicity, Metabolism And Excretion Of [60]Fullerene In Rats

Najla Gharbi,¹ Monique Pressac,²
Michelle Hadchouel,³ Henri Szwarc,⁴
Rene Victor Bensasson⁵ And Fathi
Moussa^{1*}

¹ Faculté De Pharmacie, Université Paris Xi,
Rue J-B Clement-F92296 Chatenay-Malabry,
France

² Faculté De Pharmacie, Université Paris V,
Rue De L'observatoire-F75006, Paris, France

³ Inserm, Unité 347, Chu Kremelin-Bicetre, Rue
Du Gal Leclerc-F94265 Kremelin-Bicêtre,
France

⁴ UMR 8000 Du Cnrs, Batiment 490, Université
Paris Sud, 91405 Orsay, France

⁵ ESA 8041 CNRS, Muséum National D'histoire
Naturelle, 63 Rue Buffon-F75005 Paris

Over the last decade, it has been shown that some fullerene derivatives exhibit considerable biological activity; however, only few additional studies concerning fullerene toxicity have been performed. Most of these studies suggest that C₆₀ accumulates in the liver and remains apparently unchanged with no acute toxic effects in general. Therefore, use of C₆₀ derivatives that could be cleaved back to the parent C₆₀ *in vivo* would likely lead to long-term fullerene accumulation (1), which is a negative factor for potential biomedical applications.

We report here the *in vivo* behavior and potential metabolism of C₆₀ in rats, after intraperitoneal injection of a single large dose (0.5 g/kg) of an aqueous suspension of micronized C₆₀. Our results show that: i) most of the C₆₀ crystals (< 2 µm) accumulate in the liver and spleen within 2 to 4 days as revealed by light and electronic microscopy as well as by HPLC determination; ii) there is no acute toxicity; 3) C₆₀ reacts with vitamin A and its ester forms in rat livers as previously observed in mouse livers (2); 4) C₆₀ is slowly but significantly eliminated (up to 7 mg per

week) through the bile ducts as demonstrated by HPLC analysis of feces extracts. The mechanism of elimination is now under investigation in our laboratory.;

Acknowledgement. This work was performed under European contract "Evaluation of the biological properties of fullerenes and new fullerene derivatives" (ERB FMRX-CT98-0192)

(1) Bullard-Dillard, R et al. Bioorganic Chemistry, 1996, 24 (4), 376-385.

(2) Moussa, F et al. New J Chem, 1998, 32, 989-992.

* Corresponding author: Tel. 01 46 83 54 72,
Fax. 01 46 83 53 06, Email:
fathi.moussa@cep.u-psud.f