In vivo testing of a bone-selective fullerene: preliminary safety and efficacy testing

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It has been demostrated that, when properly derivatized, a fullerene molecule can help ensure the delivery of any drug to a specific site in the body. Hydrophilic bisphosphonate groups are known to possess high affinity for the main bone mineral hydroxyapatite (HAP). Thus, functionalization of C_{60} with bisphosphonate groups should lead to bone-vectored, water-soluble fullerene derivatives [1].

A facile synthesis for derivatizing fullerene molecules with bisphosphonate groups based on the Bingel reaction has been explored. Five different bisadduct isomers of C_{60} with tetraisopropyl methylenediphosphonate, $CH_2(PO_3iPr_2)_2$, have been synthesized, separated and characterized. Hydrolysis of the $CH_2(PO_3iPr_2)_2$ isomers generates water-soluble diphosphonic acids, $CH_2(PO_3H_2)_2$, which have been used to perform *in vitro* studies in which mineralized bone tissue was be selectively targeted.

These *in vitro* experiments successfully demonstrated that the addition of a bisphosphonate to C_{60} may lead to a drug delivery system targeted to bone. To determine the safety and the efficacy of the compound, a rat model of osteoporosis was employed for *in vivo* experiments. This study demonstrated that the compound is safe in the rat model: no significant behavior changes occurred, weight gains were normal, and no significant pathology was noted in either the kidney or liver of the animals. The compound resulted in positive changes in the bone architecture of the treated ovariectomized animals. To improve our results, more testing is under way in which higher doses of the compound are given to the animals.

[1] A.Mirakyan and L.J. Wilson, *J. Chem. Soc*., *Perkin Trans.* **2**, 1173-1176 (2002).