Dose effect activity of ferrocifen-loaded lipid nanocapsules on a 9L-glioma model

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Résumé en anglais	Ferrociphenol (Fc-diOH) is a new molecule belonging to the fast-growing family of organometallic anti-cancer drugs. In a previous study, we showed promising in vivo results obtained after the intratumoural subcutaneous administration of the new drug-carrier system Fc-diOH-LNCs on a 9L-glioma model. To further increase the dose of this lipophilic entity, we have created a series of prodrugs of Fc-diOH. The phenol groups were protected by either an acetyl (Fc-diAc) or by the long fatty-acid chain of a palmitate (Fc-diPal). LNCs loaded with Fc-diOH prodrugs have to be activated in situ by enzymatic hydrolysis. We show here that the protection of diphenol groups with palmitoyl results in the loss of Fc-diOH in vitro activity, probably due to a lack of in situ hydrolysis. On the contrary, protection with an acetate group does not affect the strong, in vitro, antiproliferative effect of ferrocifen-loaded-LNCs neither the reduction of tumour volume observed on an ectopic model, confirming that acetate is easily cleaved by cell hydrolases. Moreover, the cytostatic activity of Fc-diOH-LNCs is confirmed on an orthotopic glioma model since the difference in survival time between the infusion of 0.36 mg/rat Fc-diOH-LNCs and blank LNCs is statistically significant. By using LNCs or Labrafac to carry the drug, a dose-effect ranging from 0.005 to 2.5mg of Fc-diOH per animal can be evidenced.

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