Supplementary materials

Enhancement of iodinin solubility by encapsulation into cyclodextrin nanoparticles

Anthony Prandina\textsuperscript{a,b}, Lars Herfindal\textsuperscript{c}, Sylvie Radix\textsuperscript{a}, Pål Rongved\textsuperscript{b}, Stein O. Doskeland\textsuperscript{d}, Marc Le Borgne\textsuperscript{e}, and Florent Perret\textsuperscript{e}

\textsuperscript{a}Université de Lyon, Université Claude Bernard Lyon 1, Faculté de Pharmacie - ISPB, EA 4446 Bioactive Molecules and Medicinal Chemistry, SFR Santé Lyon-Est CNRS UMS3453 -INSERM US7, 8 avenue Rockefeller, F-69373, Lyon cedex 8, France; \textsuperscript{b}Department of Pharmaceutical Chemistry, School of Pharmacy, University of Oslo, PO Box 1068 Blindern, N0316 Oslo, Norway; \textsuperscript{c}Centre for Pharmacy, Department of Clinical Science, University of Bergen, Jonas Lies vei 87, N-5009 Bergen, Norway; \textsuperscript{d}Department of Biomedicine, University of Bergen, Jonas Lies vei 91, N-5009 Bergen, Norway; \textsuperscript{e}Université de Lyon, Université Claude Bernard Lyon 1, Institut de Chimie et Biochimie Moléculaires et Supramoléculaires, UMR 5246 CNRS - CPE Lyon - INSA, 43 Boulevard du 11 Novembre 1918, F-69622 Villeurbanne cedex, France.

Dynamic light scattering measures were performed using a Zetasizer Nano ZSP instrument from Malvern Instruments, UK.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure.png}
\caption{Dynamic light scattering experiments spectra and mean diameter of iodinin loaded C\textsubscript{4}H\textsubscript{9} amphiphilic CDs.}
\end{figure}
Figure S2. Dynamic light scattering experiments spectra and mean diameter of iodinin loaded C₆H₁₃ amphiphilic CDs.

Figure S3. Dynamic light scattering experiments spectra and mean diameter of iodinin loaded C₅H₁₇ amphiphilic CDs.
Figure S4. Dynamic light scattering experiments spectra and mean diameter of iodinin loaded C₄F₉ amphiphilic CDs.

Figure S5. Dynamic light scattering experiments spectra and mean diameter of iodinin loaded C₆F₁₃ amphiphilic CDs.
**Zeta Potential Analysis:** Zeta potentials of empty and loaded nanoparticle dispersions were measured by Malvern Zetasizer Nano-ZS (Malvern Instruments, UK) at 25°C, in triplicate to assess the surface charge. Zeta potential of nanoparticles were directly measured on suspension of nanoparticles in water pH 7.4.

|            | Loaded / Empty |
|------------|----------------|
| C₄H₉       | -20.2 mV ± 3.5 / -16.4 mV ± 4.0 |
| C₆H₁₃      | -29.6 mV ± 5.1 / -25.1 mV ± 5.5 |
| C₆H₁₇      | -43.3 mV ± 6.2 / -38.0 mV ± 5.2 |
| C₄F₉       | -26.6 mV ± 4.2 / -21,9 mV ± 5.6 |
| C₆F₁₃      | -32.5 mV ± 5.0 / -28.0 mV ± 6.8 |

No significant changes were observed for zeta potential values. For both empty and iodinin-loaded nanoparticles, they were in the same range with a little increase with the chain length. No differences were observed between loaded and empty ones. It is worth noticing that even if the amphiphilic cyclodextrins are not charged, the zeta potentials are negative at this pH, meaning that these suspensions are stable, avoiding aggregations. Recent results in DLS showed indeed that these suspensions were stable after 6 months (same sizes...). We found that the iodinin-loaded nanospheres using C₄H₉ and C₆F₁₃ were the most potent formulations (highest cell death on AML cell line IPC-81), with zeta potentials of -20.2 mV and -32.5 mV, respectively. With the formulations using C₆H₁₃ and C₄F₉ (with similar zeta potentials), cytotoxicity results were lower (Figure 5). Cytotoxicity and zeta potential were not correlated in this study.

![Zeta Potential Distribution](image)

**Figure S6.** Zeta potential distribution of iodinin-loaded C₄H₉ amphiphilic CDs.
**Figure S7.** Zeta potential distribution of iodinin-loaded C₆H₁₃ amphiphilic CDs.

**Figure S8.** Zeta potential distribution of iodinin-loaded C₈H₁₇ amphiphilic CDs.
Figure S9. Zeta potential distribution of iodinin-loaded C₄F₉ amphiphilic CDs.

Figure S10. Zeta potential distribution of iodinin-loaded C₆F₁₃ amphiphilic CDs.