RAMAN AND SERS MICROSPECTROSCOPIC STUDY OF ANTICANCER DRUG DOXORUBICIN IONICALLY BOUND TO SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES

Igor Chourpa*, Laurence Douziech-Eyrolles, Eric Sarazin, Lazare Ngaboni Okassa, Martin Soucé, Simone Cohen-Jonathan and Pierre Dubois

Laboratoire de Chimie Analytique, UFR de Pharmacie, 31 av. Monge, 37200 Tours, France; E-Mail: chourpa@univ-tours.fr

Keywords: *nanovectors, magnetical targeting, anticancer drug*

Abstract: This contribution reports on qualitative/quantitative spectroscopic characterization of novel nanovectors developed in our group for magnetic targeting of the anticancer drug doxorubicin. The study is based on Raman and surface-enhanced Raman scattering (SERS) microspectroscopy data, combined with those of spectrofluorimetry and UV-visible spectrophotometry.

In recent years, nanoparticle-based vectors have been extensively studied as specific vectors for oligonucleotide complexes, DNA, proteins and drugs. Depending on the type of specificity desired, drug vectorization can be achieved via different technologies, including magnetic targeting proposed about twenty years ago [1]. For this purpose, the drug molecule should be attached to magnetic nanoparticles. Furthermore, the particles should be incorporated into pharmaceutical polymers to provide them with specific biocompatibility and biodegradability. With respect to their therapeutical potential, the vectors need to be stable during storage until use, they should have prolonged blood circulation time after i.v. administration and then provide appropriate drug charge/release ratios [2].

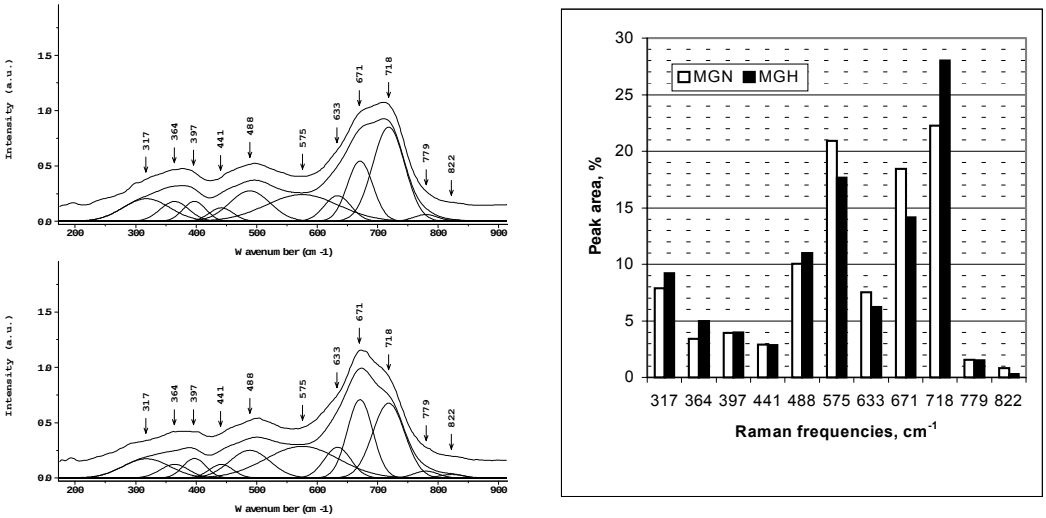

Figure 1. Raman spectra (left) of FF of different oxidation state and their fitting with Gaussian profiles enabling a semi-quantitative estimation (right) of the magnetite (MGN)/maghemite (MGH) content.

In this communication, we present our data on the spectroscopic characterization of novel magnetic nanovectors being developed in our group as carriers of anticancer drugs. These vectors are based on ferrofluids (FF), aqueous suspensions of superparamagnetic nanoparticles of iron oxides. It is very important to know the molecular composition of FF particles, since it is determinant for both their magnetic and surface properties. Raman microspectroscopy data prove that the major components of FF nanoparticles are magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3). Characteristic Raman features of the two iron oxides (Fig. 1) have been exploited to obtain a semi-

quantitative estimation of the magnetite/maghemite content in different FF preparations. The results obtained were in correlation with the expected oxidation state.

As the next step of the vector preparation, the FF were charged with the anticancer agent doxorubicin (DOX), ionically bound to the FF nanoparticle surface in the form of a DOX-Fe^{2+} complex. Drug incorporation efficiency, stability and release kinetics were measured by UV-visible spectroscopy and microspectrofluorimetry.

The molecular state of the drug, before and after release from vectors was another important factor in qualitative evaluation, achieved by surface-enhanced Raman scattering (SERS) microspectrometry. SERS data (Fig.2) indicate the existence of two different DOX-Fe^{2+} complex species, depending on ion/drug molar ratio. Complex I represents a monomeric ferric iron complex whereas complex II is consistent with a more or less aggregrated oligomeric ion-anthracycline system. Interaction of these two complexes with various biological molecules is actually studied in our group.

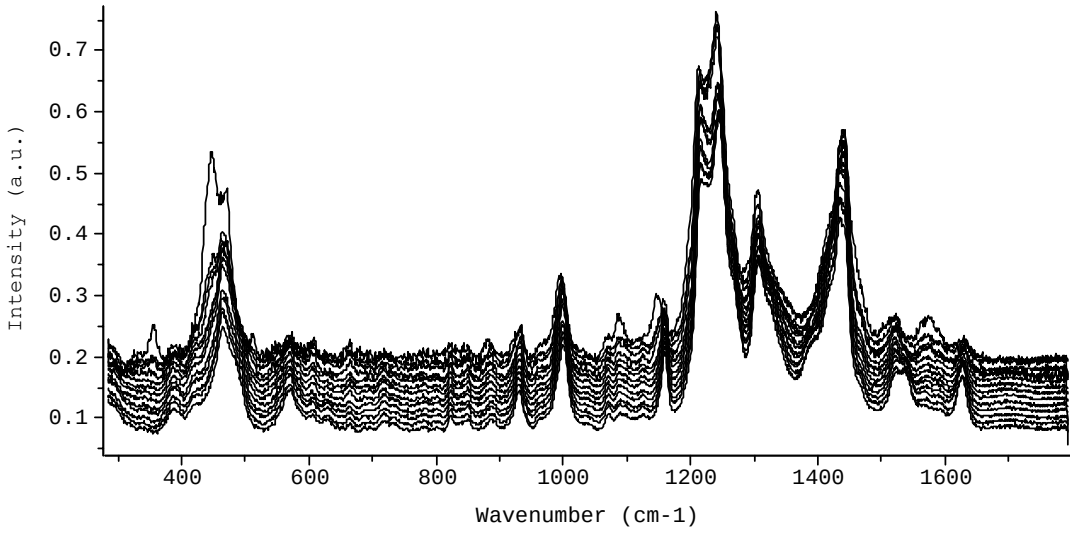

Figure 2. SERS spectra of free DOX (top) and of the DOX : Fe^{2+} complex at ion/drug molar ratios varied from 0.1 to 3 (from top to bottom).

SERS experiments are being continued to provide further insight into DOX/Fe^{2+} and DOX/Fe^{2+}/FF molecular interactions upon various experimental conditions (pH, concentration, molar ratio, etc.).

References:

1. Widder KJ; Senyel AE; Scarpelli GD *Magnetic microspheres: a model system of site specific drug delivery in vivo.* Proc Soc Exp Biol Med 1978, 158(2):141-6
2. Lübbe AS, Alexiou C, Bergemann C, *Clinical applications of magnetic drug targeting,* The Journal of Surgical Research, Volume 95, Issue 2, February 2001, Pages 200-206.