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INTRODUCTION

The efficiency and safety of targeted alpha therapy (TAT) has been shown in a large number of pre-clinical studies and has been successfully applied to clinical trials. Among the different potential alpha-emitters, Astatine 211 (At-211) is considered to be one of the most promising candidates for targeted alpha therapy. So far, At-211 has being used in two clinical trials in the US [1] and Sweden. It is also the subject of a wide research program in Nantes (France). A clinical trial of prostate cancer is notably planed in the near future.

Very few data on the chemistry of Astatine are available. On the one hand, Astatine is a rare element and it has only short half-life radioactive isotopes. On the other hand, it is an "invisible" element: the amount of At–211 produced allows working at ultra trace concentrations (typically 10^{-11} to 10^{-15} M) and no spectroscopic techniques can be used to estimate astatine characteristics at the molecular level. As a result, Astatine chemistry is not well understood. These two major points restrain the development of efficient labelling protocols and the utilization of At–211 for TAT [2].

By analogy with labelling protocols already established with iodide, the studies are focused on formation of astatine-carbon bounds. While some approaches provide "suitable" in vivo stability to move into clinical studies, additional studies still need to be conducted to develop improved labelling approaches and particularly for systemically administration [2].

DESCRIPTION OF THE ACTUAL WORK

Based on these considerations, a research program has started in Nantes in 2005 to explore the basic properties of At using a multi-disciplinary chemical approach. The objective is to contribute to the development of efficient labelling protocols applicable in nuclear medicine. The particularity of the project is the elaboration of a combined experimental and theoretical approach to study astatine behaviour in order to access both at macroscopic and molecular level data [3-5].

The theoretical approach is based on quasi-relativistic quantum chemistry calculations. The experimental approach considers that a given astatine species is characterized by its distribution coefficient experimentally determined in liquid-liquid or solid-liquid biphasic systems. The change in speciation arising from a change in experimental conditions is observed by a change in the distribution coefficient.

The existence of an astatine species is validated when the thermodynamics parameters obtained by both approaches are in agreement.

RESULTS

The methodology enabled us to define a reliable Pourbaix diagram (Eh/pH diagram) of astatine in non-complexing aqueous medium. We showed the existence of two stable metallic forms of Astatine, *i.e.* At^+ and AtO^+ [1,3]. This highlighted the metallic character of At by comparison with others halogens, as it was already proposed in the 60's [6].

However, no ligand has been so far designed for TAT using AtO^+ species. Only few data are available regarding to its reactivity [7] (what are the atoms interacting with AtO^+? What is the nature of the bonds formed?). Our recent results on the reactivity of AtO^+ for model organic and inorganic ligands demonstrate the potentiality to form both coordination and covalent bonds. These significant progress findings offer new perspectives for TAT compared to conventional labelling protocols using the "halogen character" of At.

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