Anticancer activity of metal complexes: synthesis and characterization methods

Cancer is one of the biggest global health threat nowadays. Although many types of cancer can be cured if detected early and treated effectively, it is still the leading cause of death worldwide (~10 million deaths in 2020). The idea of treating cancer with metal-containing compounds is not new, since they were also used in the ancient Egypt (gold salts) and in the ancient China (arsenic containing drugs). The latter one in the form of As_2O_3 was used against leukaemia in the 18^{th} and 19^{th} centuries. Metal complexes were in the spotlight again in the 1960s, when the discovery of the anticancer activity of cisplatin started a revolution in cancer treatment. It is so powerful agent that half of the patients are receiving platinum drugs in mono- or in combination therapy.

However, several problems occur during the treatment: i) the severe side effects can lead to poor patient compliance; ii) the presence of untreatable tumours; iii) the appearance of (multi)drug resistance during treatment; iv) secondary malignancies related to the DNA damage caused by chemotherapeutics; v) environmental risk of platinum compounds. There is a need for the development of novel chemotherapeutic agents, which will be better alternatives considering the abovementioned problems.

Complexes of ruthenium are the closest for the clinical approval. In 2021 a Ru(III) complex named BOLD-100 got orphan drug designation status from FDA for the treatment of gastric and pancreatic cancer, while the Ru(II)-containing TLD1433 has an ongoing phase II clinical trial against bladder cancer. The organometallic half-sandwich Ru (and Rh) complexes also has promising cytotoxic and/or antimetastatic activity *in vitro* and *in vivo* on several cancer cells. In this presentation the different directions in the development of these complexes will be introduced as well as the effects of structural modifications on the behaviour in solution and in solid state of these complexes. The characterization of the solution chemistry (solution stability, stoichiometry, chloride affinity, interaction with serum proteins and DNA, etc.) was investigated by the combination of various techniques, such as pH potentiometry, UV-visible and NMR spectroscopy, spectrofluorimetry, ultrafiltration. As most of the metal complexes are undergoing structural change, their speciation has a crucial role in their mechanism of action. It is an important task to find the relationship between their structure and their solution behaviour, since all of these have a crucial effect on the pharmacokinetics and on their biological activity.