Proton transfer reactions in 5-Halouracils investigated with XUV HH radiation

Pierre Çarçabal[1], Valérie Blanchet[2], Dominique Descamps[2], Yann Mairesse[2], Stéphane Petit[2], Francesca Calegari[3], Mattea Castrovilli[3], Mauro Nisoli[3], Andrea Trabattoni[3], Lorenzo Avaldi[4], Paola Bolognesi[4], Patrick O'Keeffe[4] and Raluca Cireasa[1]

[1] *Institut des Sciences Moléculaires d'Orsay, Université Paris Sud, Orsay, France*
[2] *Centre Lasers Intenses et Applications, Université de Bordeaux, Talence, France*
[3] *Department of Physics, Politecnico di Milano, CNR-IFN, I-20133 Milan, Italy*
[4] *Istituto di Struttura della Materia, 00016, Monterotondo Scalo, Italy*

In the last decade, the high harmonic generation (HHG) has emerged as a new photon source capable to provide structural and dynamical information, including (sub)-femtosecond arrangements of nuclei and electrons. Currently, the HH radiation is also used for investigating more complex molecules of interest for chemistry and biology.

5-Halouracils (5-HaloU) belong to a particular class of biomolecules called radiosensitisers that enable the use of the radiation damage for therapeutic purposes. When utilised in combined chemo- and radio-therapy treatments to replace Thymine in the DNA of the tumour cells, these molecules enhance the lethal effects of the UV, X-ray, proton and γ radiation on these cells.

To study the dynamics underlying the radiosensitivity of 5-HaloU, we have employed ultra-short XUV pulses produced by HHG. The XUV attosecond pulse train duration were either 1.5 fs (POLITECNICO campaign) or 10 fs (CELIA campaigns) and their associated energy domain spectra corresponded to a modulated quasi-continuous spectrum or to a frequency comb where the harmonics were separated by 6 eV, respectively. Broad band radiation at 800 nm was used as probe. The ensuing dynamics was detected by recording mass spectra as a function of the pump-probe delay. The 5-Fluorouracil (5FU) and 5-Bromourcail (5BrU) mass spectra indicate that the parent ionisation is followed by complex dynamics involving among others processes, proton or hydrogen transfer. An ultrafast decay of about 40 fs was observed for the transient signal of m/z=43 ($HNCO^+$) produced in the dissociative ionisation of 5FU. The complementary rising behaviour on the same timescale was observed for m/z=44 ($HNCOH^+$) fragment, which can only appear if the complete fragmentation is preceded by an H/H^+ transfer via tautomerisation. Similar behaviours, although slower, were measured for m/z=31 (FC^+) (~80 fs), and m/z=32 (FCH^+) and for the equivalent BrU fragments. These dynamics may be associated with H or H^+ transfer processes where the difference in timescale is determined by the initial and final sites of the transfer and, in particular, to the involvement of the halogen atom. In addition, we speculate that the H^+ transient rising signal may also reveal the H/H^+ transfer process leading to the isomerisation.

Since 5-FU is structurally related to the DNA bases and it is routinely used in radiotherapy treatments, the present work provides new insights in the XUV induced structural changes (tautomerisation and isomerisation) that may be responsible for DNA mispairing and mutagenesis, but also for the DNA break occurring when these molecules are embedded in the DNA of the tumour cells.