Free radicals and anticancer drugs

Heterocyclic nitrogen compounds are basic building blocks of life on earth. They can be found in DNA, and the color of our eyes, hair and even our height depend on their combination. In the course of the development of science we have learnt how to exploit them for our needs, e.g in medicine – popular anxiety-reducing drug, lorazepam or morphine – opiate based powerful painkiller are bases on heterocyclic nitrogen compounds. DNA consists of four heterocyclic compounds – nucleic based, which are built from only four elements: hydrogen, nitrogen, carbon and oxygen, but there is possibility to swap oxygen for sulfur. On the basis of this swap, we obtain sulfur analogs of nucleic bases, so called thiobases, which are subject of my research.

The second aspect of my project is radical chemistry. Free radicals, which you probably heard of, are believed to be responsible for ageing and certain diseases. Despite the fact that their reputation in mass media is poor, free radicals are essential for our organisms. They are responsible for killing bacteria or transfer of signals between cells in our body. Problem arises when there is imbalance in fragile equilibrium of oxidative and reductive species which can lead to significant overproduction of free radicals. We call this imbalance oxidative stress, which manifests itself by organisms inability to neutralize excess of radicals, leading to cell damage and disturbance in their normal activity.

In hereby project I am going to investigate how aforementioned thiobases react with free radicals and what are the products of this reactions. My interests is mostly due to their biological activity, because sulfur analogs of nuclear bases are in use as an immunosuppressive (reducing immune system activity after organ transplantation) and anticancer drugs. One of compounds, investigated in this research, mercaptopurine in 1950s became groundbreaking medicine for children with acute lymphoblastic leukemia, drastically improving survival rates. Since in most cancer tissue there is overproduction of free radicals it is crucial to assess how given drug reacts with them.

Generating high concentration of free radicals is not trivial. Therefore in my research I use quite unique technique, called pulse radiolysis, which can be found in only few places in Europe (including two in Poland). Pulse radiolysis technique is based on linear electron accelerator – device which is able to accelerate electrons to extremely high speed (and therefore high energy). This energetic electron beam hits aqueous solution of investigated compound, splitting water molecules and forming free radicals. Generated radicals react with dissolved compounds, forming (often colorful) products, which appear and decay on unimaginably short timescales – often ten million times shorter that eye blink. By shining short pulses of light into the solution I am able to observe chemical reactions and deduce what are the products.

I hope my research will contribute to better understanding of transformations which anticancer agents (including thiobases) undergo in human body. Perhaps in the future it would lead to more effective and less harmful treatment strategies.