From several years, there is observed an increasinginterest in extracts obtained from natural sources due to their potential antioxidant properties. Recentstudies are dedicated to post-industrial waste extracts of *Oenothera sp* seeds used in global oil production. It is well established that these secondary products are rich in polyphenols content which besides their antioxidant properties reveal potential antitumor activity in particular cancer cells. Moreover, both extracts and their individual components, including penta-*O*-galoilo-β-D-glucose (PGG), increase cancer cells sensitivity to standard therapeutics in pro-oxidative manner. One of the antitumor compounds, which is currently under clinical trial on the cells of malignant pleural mesothelioma (MPM) is an arginine deiminase in the form of pegylation (commonly referred to as ADI-PEG20), responsible for L-arginine degradation. Its antitumor activity is critical in case of cancer cells whose growth and viability are highly dependent on the presence of this particular amino acid. Given that L-arginine is a precursor for nitric oxide synthesis and that the relative reduction of this amino acid promotes superoxide anion production we attempted to investigate the mechanism of action of ADI and studied evening primrose extract (EPE) in directing MPM cells death. Previous studies have shown that the increased generation of free radicals promotes protein modifications, including enzymatic proteins, potentially affecting their activity. Hence, our research will be directed towards modification of thymidylate synthase which is involved in the synthesis of deoxyribonucleic acid (DNA) critical for cells growth.

We aim to analyze the pro-oxidative effect of both EPE and ADI in human-derived MPM cells with parallel determination of changes in the protein nitration status including thymidylate synthase modification. The study employs analysis of particular reactive oxygen species using fluorescent dyes as well as determination of the protein nitration status including thymidylate synthase modification as a reflection of prevailing in EPE/ADI-treated MPM cells oxidative stress. To confirm the hypothesis and the influence of EPE/ADI on *de novo* thymidine synthesis pathway there will be assessed the targeted pyrimidine nucleotides level (dTMP, dUMP) in high resolution metabolome profiling studies using microLC-MS technique.

The obtained results will provide knowledge about the mechanism of pro-oxidative action both the extract and the arginine deiminase in cells of malignant pleural mesothelioma. For the first time we will document the potential impact of a polyphenols-rich extract of evening primrose in increasing activity of arginine deiminase therapeutic. We believe that these results will allow us to consider using *O. paradoxa* extracts synergistically with ADI chemotherapeutic in suppressing malignant pleural mesothelioma tumor growth. In clear and definitive way we will demonstrate benefit from the use of novel anti-cancer therapy using the pioneering drug and widely occurring natural waste source of *Oenothera paradoxa*.