The aim of proposal is to obtain composite catalyst based on chemical compounds which are similar to heme structure and will be able to mimic drug metabolism in laboratory environment. The catalyst will consist of porphyrazine (macrocyclic compound belonging to porphyrinoids like heme or chlorophyll) attached by chemical bonds or electron interactions to multi-walled cabon nanotubes or modified graphene oxide sheets.

Many drug substances are metabolized in the liver. Various studies provided in research centers worldwide assess the effect of drug metabolites appearing after microsomal cytochrome P450 enzymes action. These enzymes are responsible for catalyzing various reactions of xenobiotics which are foreign substances to the human body. It is a substantial issue for drug safety and efficacy due to the fact that enzymatic reactions may lead to novel compounds of increased or decreased potency or even toxic for the body. For this reason before the introduction of new drug to the market it is necessary to study its metabolic pathway. Nowadays, there are several studies on animal models proceeded by an in vitro tests with the use of microsomal extracts. However, there are few examples of action of drug metabolites in which they appear only in clinical trials. These studies are also expensive and can lead to real threat for trial volunteers. The other flaws are as follows: (i) metabolites are isolated in insufficient amount for providing further studies and (ii) the obtained amount of metabolites limits their characterization.

Biomimetics is a complementary method to toxicological studies. It stands for mimicking the structures, reactions and mechanisms natural occurring. Biomimetics play also a role in drug studies. Due to the fact that heme is a prosthetic group in cytochrome P450 enzymes responsible for catalyzing reactions the compounds utilized in biomimetic studies have to possess similar structure.

Heme belongs to porphyrinoids which possess fused pyrrolyl or indollyl ring with metal cation inside. Porphyrinoids consist of several group of compounds including porphyrins (i.e. heme), chlorins, phhalocyanines and porphyrazines which differentiate by way of rings connection. The last two ones are synthetic dyes with various applications in industry or medicine, especially in oncology. Porphyrazines were the least verified in biomimetic studies. They are composed of four pyrrolyl rings fused together by nitrogen bridges. They may possess metal cation entity inside macrocyclic core which implicates properties of compound. Utilizing porphyrazines in biomimicking studies requires presence of transition metal cations (d block metals) inside the core.

In the proposed research project, the obtained porphyrazines will possess transition metal cations inside macrocyclic core like iron(II), cobalt(II) or manganese(II). All synthesized macrocycles will be fully characterized with various analytical techniques like mass spectrometry (ES MS, MALDI) or nuclear magnetic resonance spectroscopy (NMR) to structure identification and confirmation. There will be also provided additional studies to assess properties of obtained porphyrazines including cyclic and differential pulse voltammetry or Mössbauer spectroscopy.

Selected porphyrazines will be attached to multi-walled carbon nanotubes and graphene oxide sheets after proper preparation. Obtained systems will be characterized with advanced microscopic techniques like transmission electron microscopy and atomic force microscopy. The attachment of synthesized porphyrazines on nanostructures will increase their catalytic properties due to unique electrochemical properties of carbon nanotubes or graphene and will provide the opportunity to reuse the catalyst.

The last part of the proposed research project embraces biomimetic studies on novel porphyrazines and their catalytical systems to assess catalytic properties in various oxidation reactions using reference compounds, like diphenylisobenzofurane or common drugs i.e. diclofenac. These studies will allow to optimize reagents and conditions of biomimetic reactions which further will be adopted for additional measurements. The obtained products will be characterized by various techniques, including ES MS, UV-Vis, NMR and FT-IR.

The most promising porphyrazines and their systems will be utilized further in biomimetic studies on kynurenic acid and its derivatives. Kynurenic acid is a metabolite of tryptophan. It is responsible for various functions in central nervous system. Many studies indicate that it is a novel promising drug candidate for CNS deseases. For this reason further metabolic studies are worth to be considerd. Metabolites obtained in planned biomimetic reactions will be identified, characterized and transferred for further pharmacological and toxicological studies.