Depression and neurodegenerative disorders such as Parkinson's and Alzheimer's diseases are a growing health, social and economic problem. Their cause, among others, is disturbance in the functioning of monoamine oxidase (MAO), a flavine-containing enzyme catalysing the oxidative deamination of a number of biogenic amines such as serotonin, dopamine, adrenaline and noradrenaline. On the basis of substrate selectivity and inhibitor sensitivity, two forms of MAO (MAO-A and MAO-B) were distinguished. Monoamine oxidase inhibitors (MAOIs) used in a treatment of central nervous system (CNS) disorders are a cause of severe side effects which are caused by lack of affinity and selectivity towards one of the MAO isoforms. Therefore identification of novel and selective MAO inhibitors lacking serious side effects is of great interest of scientists.

From beginning of history, people used herbs for therapeutic properties. Plants itself were a source of new active ingredients but also a source of lead structures for the development of new synthetic drugs. Recent studies showed that herbal natural products can be an important source of new MAO inhibitors.

Viscum album L. (Santalaceae), commonly known as European mistletoe, is a hemiparasitic, evergreen shrub growing on deciduous and coniferous trees. The biologically active constituents of mistletoe depends on the species of the host tree and harvest season but typically include lectins, viscotoxins, flavonoids, phenolic acids, terpenoids, lignans, fatty acids, sterols, diarylheptanoids, phenylpropanoid glycosides, alkaloids and polysaccharides. Nowadays, mistletoe preparations are used in two main therapeutic areas, cardiovascular disorders and in oncology. However, in folk medicine *Viscum album* L. was used in a treatment of central nervous system disorders system such as epilepsy, hysteria, insomnia, nervous excitability, neuralgia, headache, dizziness and fatigue. It was also recommended to use mistletoe in combination with other herbs such as skullcaps and valerian. Several studies have showed recently that complementary treatment with mistletoe preparations seem to improve quality of life of cancer patients. Emotional and functional well-being in general as well as improvements in regard to fatigue, sleep, depression and anxiety were reported. Nevertheless, the mistletoe preparations are not applied for neurological diseases in modern medicine, which is due to lack of research studies on the topic. To the best of our knowledge, mistletoe extracts and its selected compounds have never been studied for their inhibition of MAO-A and MAO-B enzymes.

The aim of our project is to support thesis that mistletoe can be a source of new compounds that act as MAO inhibitors. Once, we confirm thesis that crude extracts from mistletoe herb and its fractions exhibit potent activity on MAO-A and MAO-B enzymes, selcted compounds will be detailed analysed for structure elucidation and tested *in vitro* with fluorometric methods to investigate kinetic characteristics and mechanism for the MAO enzymes' inhibition. An innovative part of our research is use of *Galleria mellonella* as model organism to study selected compounds *in vivo*. It is more often that invertebrates are used as models for drug discovery research. It is also in line with the 3Rs, an international principle of experiments using mammals, which goal is the use of alternative animals (replacement), pain relief (refinement), and reduction of the number of animals used (reduction). We believe that administration of selected compounds to larvae of *Galleria mellonella* will lead to inhibition of MAO-A and MAO-B enzymes and thus to an increase in serotonin and dopamine levels.

Project could lead to novel pharmaceutical preparations containing either standardized mistletoe extracts or extracts enriched in specific bioactive compounds, which could be used as a complementary therapy in a treatment of depression and neurodegenerative disorders such as Parkinson's and Alzheimer's diseases. Furthermore, project could lead to the detection of new compounds that could be used directly as active substances in innovative drugs or could become a lead structures for design, synthesis and development of new innovative drugs with either improved therapeutic activity or reduced toxicity.