

Candidiasis is the most common infectious fungal disease in the world. It is caused by fungi of the genus *Candida*. The greatest number of candidiasis cases, i.e. more than 50 percent, is caused by *Candida albicans*, which is a serious problem for humans, especially those susceptible to infections. The currently used antifungal drugs represent four classes: polyenes, azoles, echinocandins, and 5-Flucytosine. A serious barrier in the development of new drugs is the great similarity of fungal and human cells, which makes it difficult to find a biological target of drug action that would only occur in fungi. Unfortunately, firstly, the knowledge of the pathological activity of *Candida* fungi is still insufficient; secondly, the incidence of candidiasis continues to increase, and thirdly, yeasts are becoming more resistant to the drugs used. Hence, there is a great need to develop new effective antifungal drugs.

In response to this need, together with a group of scientists, we have tested several new molecules for their antifungal properties in recent years. These were newly synthesized metallacarboranes, i.e. molecules made of boron, carbon, hydrogen, and metal atoms (cobalt, iron, or nickel) with a characteristic "cage" structure. A feature of metallacarboranes that we paid special attention to is their abiotic nature. This means that these molecules are "invisible" to the cells of organisms, including fungi, and thus, it is possible that they can "bypass" the metabolic pathways that determine the phenomenon of drug resistance. It turned out that the metallacarboranes tested by us potently inhibit the growth of the fungus *Candida albicans*. It is particularly important that, among these microorganisms, there were those that were isolated from patients suffering from mycosis and were found resistant to the action of standard antifungal drugs. The results of these studies were published last year in the prestigious American *Journal of Medicinal Chemistry* and are the starting point for the research project presented in the proposal to NCN.

In fact, there is a group of available molecules with high antifungal potential, but the knowledge of their mechanism of action in the fungal cell is still insufficient. Therefore, together with a group of experienced researchers, we have designed studies aimed at finding the cellular target of antifungal metallacarboranes. During the implementation of this project, we will study the impact of these molecules at both the cellular and molecular levels. The first step will be the analysis of *Candida albicans* cells using advanced microscopic methods to find out whether metallacarboranes affect the morphology and physical properties of fungal cells. We will then test whether the molecules are able to influence cellular processes that enable *Candida albicans* to cause infection. In addition, we will examine how the molecules affect the transcription process, i.e. which genes of the fungus are involved in the cell's response to the presence of "foreign" molecules. In the final stages of the research, we will try to find a protein that may be able to interact with metallacarboranes.

The prospective results of the project will, firstly, provide researchers from around the world with knowledge about the biological activity of metallacarboranes and their cellular targets, and secondly, they will open further research paths contributing to the future use of metallacarboranes as innovative antifungal drugs.