The era of chemotherapy began in the last century (1909), with the introduction of antisyphilitic drug – salvarsan by Paul Ehrlich. Despite the successes already achieved, there is still a need to continue research on cancer therapy. Cancer diseases are becoming each year an increasing problem in developed countries. In the USA in 2010, about 2.5 million deaths were recorded, of which 23% were caused by cancer (it is the second cause of death after cardiovascular diseases). Bray and colleagues presented the prognosis for cancer incidence in 2008–2030. In 2008, cancer was diagnosed in 12.7 million people, while in 2030 cancer detection is expected to reach 22.2 million people. In summary, the incidence of cancer is expected to increase even by 75% during this period. Such a large increase in the number of cases, and the lack of fully effective treatments, causes further development of, inter alia, chemotherapy to be highly desirable. One of the options considered is the research on drug transporting systems. The concept of creating "magic sphere" capable of depositing and releasing the chemotherapeutic agent at the target site, was proposed by Paul Ehrlich, the Nobel Prize winner in Physiology and Medicine in 1908. This hypothesis has been further developed by Helmut Ringsdorf, who proposed separation of the following components within the structure of a conjugate: hydrophilic region, transporting region and the linker region (Figure 1). All of these components play their respective roles. The hydrophilic region modifies the physicochemical properties of the conjugate, in particular its solubility, region providing tropic properties is responsible for the transport and accumulation in target tissues. Linker region enables anchoring therapeutic substances. In the current macromolecular project, hydroxyethyl cellulose is the carrier. Hydroxyethyl groups in this polymer constitute the hydrophilic region. An integral part of MTX, the glutamic acid residue plays the role of the linker region.

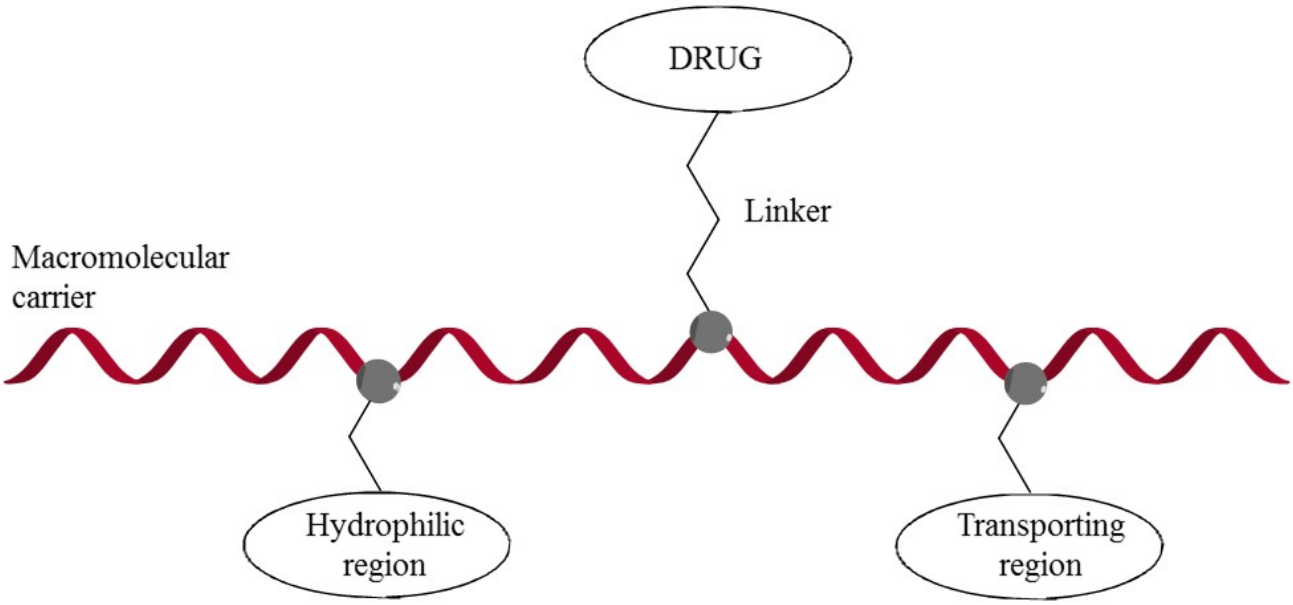

Figure 1. Drug-carrier conjugate model according to the Ringsdorf hypothesis.

In recent years, the geometry of the molecules has been considered an important factor in the effectiveness of drug delivery. Elongated or filamentous nanoparticles demonstrate clear advantages in terms of surface to volume ratio and elimination from the body. Cellulose derivatives are elongated glucose polymers, and their geometry makes them a promising carrier of therapeutic substances. The hydroxyl groups present in the number of three per each molecule allow easy attachment of fluorescent dyes, transporting elements and the therapeutic substance to the surface of the polymer.

The present project will optimize the method for the development of HEC polymers and their conjugates with methotrexate of established physicochemical parameters, such as the hydrodynamic volume, zeta potential and molecular weight. In subsequent stages of the project, conjugates will be subject to a thorough physicochemical and biological analysis. As part of physicochemical tests, basic information will be provided concerning: the degree of carrier substitution with the drug, hydrodynamic volume and zeta potential of the conjugate, rheological properties and stability of the conjugates in both the mineral buffers that and human plasma. The culmination of the project will be analyzing the activity of the conjugates obtained in the antiproliferative tests in vitro and antitumor activity in the murine model of mammary carcinoma 4T1, wherein the preparations will be administered intravenously at a considerable distance from the tumor (or alternatively into the tumor mass). Biological experiments will be completed by determining the biodistribution for the most active preparation.