Abstract

Colon cancer is one of the most common cancer in human population. The greatest chance to achieve remission we can obtain using radical surgical procedures and chemotherapy and radiotherapy – it depends on the localization of the tumor. Actually our schedules of chemotherapy are based mainly on fluorouracil. Very important problems are disadventages caused by oncological treatment and that is why in my doctoral thesis I focus on searching for natural substances. Challenge for future medicine is searching for new drugs which can effectively inhibit the progression of cancer disease but don't discrupt the function of normal tissues. The results of published medical research reveal a potential anticancer activity of fungal extracts. They have enormous terapeutic effect against many cancer diseases using different mechanisms. For the most part the supression of the cancer disease is associated with stimulating apoptosis and damaging DNA of cancer cells.

In my research I focused on the influence of the fungal extracts: *H. annosum and P. fulgens* over the proliferation of the DLD-1 colorectal cancer cells and skin fibroblasts CRL-1474. In *in vitro* studies I observed the supression of the proliferation and viability of the cancer cells DLD-1 and fibroblasts CRL-1474 after the exposition of *P. fulgens* extract which was confirmed in MTT test and H3- tymidine incorporation test. *H. annosum* extract significantly decreases the proliferation and viability of the cancer cells, but has no significant influence over the proliferation and viability of the fibroblasts.

In animal studies I used the most effective extract – *H. annosum*. In the population of mice I inducted cancer disease by subcutaneus implanting cancer DLD-1cells type. The mice were given the fungal exctract, referential drug- 5- fluorouracil or were treated with combination of these two drugs. At this stage of my research I analyzed the size of the cancer tumor after the exposition to these drugs and I also evaluated parametres of apoptosis: caspase 8, p53 protein and survivin. In 35th day of study the greatest volume of tumor was confirmed in control group. In the population treated with 5- fluorouracil the volume of the tumor was 3,3-fold smaller in comparison with control group; in the population treated with fungal extract (lowest concetration) was 2,2- fold smaller in comparison with control group.

The assessment of apoptosis was performed using ELISA method. On the basis of the results of my study I observed increasing concentration of caspase 8 and p53 protein after the exposition to 5- fluorouracil and *H. anosum* extract. The highest level of caspase 8 was confirmed in the population receiving the fungal extract in lowest concentration. The highest

level of p53 protein was observed after the exposition of 5- fluorouracil with *H.annosum* ectract in a dose of 2mg/kg m.c. Decreasing concentration of survivin, one of the inhibitors of apoptosis I observed in the population of mice receiving *H.annosum* extract. Interaction between HA extract and 5- fluorouracil was observed in the field of examined parameters of apoptosis depending on the dose of *H.annosum* extract.

On the basis of my results the following conclusions have been drawn:

1. The *Pycnoporellus fulgens* extract is also highly cytotoxic to healthy cells

2. Decrease of the growth of the colorectal cancer cells and insignificant decrease of viability of healthy fibroblasts suggest positive efficiency of *Heterobasidion annosum* extract.

3. Decrease volume of the cancer tumor in the population of mice depending on the dose of HA extract and interactions with 5- fluorouracil indicate the positive cooperation with this chemotherapeutic agent.

4. Interference in the process of apoptosis in the field of action of survivin, p53 protein and caspase 8 suggest new mechanism of action of *Hetreobasion annosum* extract and its interaction with 5- fluorouracil.

5. Heterobasiodion annosum extract possess high potential of anticancer activity against colon cancer cells.