International Conference on Natural Products and Physiologically Active Substances (ICNPAS-2004)
September 12-17, 2004, Novosibirsk, Russia
Poster Presentation

The Influence of Betulonic Acid and Its Amides on Blood and Bone Marrow Values in Postcytostatic Period

[1]E.B. Volkova, [1]N.A. Zhtukova, [1]I.V. Sorokina, [1]T.G. Tolstikova, [1]N.I. Petrenko, [1]N.V. Uzenkova, [1]E.E. Shults, [2]S.V. Poszdnjakova, [2]O.R. Grek

[1]Novosibirsk N.N.Vorozhtsov Institute of Organic Chemistry
630090, Lavrentyev Av 9, Novosibirsk, Russia. Phon. (3832) 30-36-63
e-mail: lfi@ngs.ru
[2] Novosibirsk State Academy of Medicine. 630091, Red Av. 52, Novosibirsk, Russia.

Hemotoxicity and myelodepression are the most frequently and rapidly developed complications in patients during antitumor polychemotherapy. Decreasing leucocyte number in blood and bone marrow, coursed by cytostatics, leeds to diminish the effective dose or to rejection of the treatment. To develop new agents, decreasing side effects of cytostatic polychemotherapy, a new amides of betulonic acid with β-alanine moiety were obtained. Recently, these compounds were found to possess an antioxidant properties (Sorokina I.V. et al., 2003). The aim of this research is to study the influence of betulonic acid (BA) and its two amides - [3-oxo-20(29)-lupen-28-oyl]-3-amino-propionic acid (BA-2β) and methyl ether of [3-oxo-20(29)-lupen-28-oyl]-3-amino-propionic acid (EBA-2β) on rats blood and bone marrow values in the model of experimental polychemotherapy.

The complex of cytostatic drugs (cyclophosphamide, vincristine, doxorubicin, prednisolone) were injected parenteraly into Wistar rats just once at dosage 1/5 of LD_{50}. BA and its derivatives were administrated oraly during 14 days after cytostatic drugs injection at dosage 50 mg/kg. The control animals were received a water. A cell composition of blood was investigated at 5-th, 9-th and 15-th days after cytostatics injection. A bone marrow slides were analyzed at 15 day.

It was found a reliable leucopenia in blood of experimental animals (50-55% as to normal) at 5-th day of postcytostatic period. Under the BA-2β the leucocytes level was not reliable decreased (up to 62%). A recovery of leucocytes pool of animals, treated with BA-2β and EBA-2β (up to 70 and 85% correspondigly), was observed at 9-th day. Whereas in control and group, treated with BA, the leucopenia was still maintained (57-59% as to normal). The number of circulating leucocytes at 15-th day of postcytostatic period was not reliable different from normal in all experimental groups. Leukogram of bone marrow was full correlated with the same of the blood.

It is concluded, that during postcytostatic period amides of betulonic acid with β-alanine moiety recovery leucocyte level in blood more rapidly, than betulonic acid. So these derivatives of BA may be interested of developers as potential hemoprotective drugs.