Chemiluminescent analysis of the antioxidant and immunomodulation effects of several psychotropic drugs on peritoneal macrophages

Hadjimitova V,1 Traykov T,1 Bakalova R,2 Petrova V,3 Lambev I,3 Ishikawa M,2 Baba Y2
1. Department of Medical Physics and Biophysics and 3. Department of Pharmacology, Medical University, 2 Zdrave Str., Sofia 1431, Bulgaria
2. Single-Molecule Bioanalysis Laboratory, AIST-Shikoku, Takamatsu, Japan

The ability of peritoneal macrophages to produce superoxide radicals and to induce luminal-dependent chemiluminescence was used to test the antioxidant and immunomodulating effects of several psychotropic drugs – three-cycled antidepressants (imipramine – IMI, amitriptyline – AMI), phenothiazines (chlorpromazine – CPZ), and thioxanthenes (chlorprothixene – CPX). The induction of luminol-dependent chemiluminescence was carried out by activation of protein-kinase C- or calmodulin-dependent “oxidative burst” of macrophages, using phorbol-12-myristate-13-acetate (PMA) and calcium ionophore A23187, respectively. The viability of macrophages was determined by detection of ATP-bioluminescence as a result of luciferase-catalyzed luciferin + ATP reaction.

It was observed that the neuroleptics (CPZ, CPX), in concentrations higher 1 µmol/l (corresponding to clinically relevant doses), decreased markedly the chemiluminescent index of PMA- or A23187-activated macrophages in a dose-dependent manner. The inhibitory effect of CPZ on the PMA-/A23187-induced cell chemiluminescence was higher than the ability of the drug to decrease KO2-induced chemiluminescence in a pure chemical system, as a result of its scavenger activity against superoxide radicals only. Presumably, the inhibitory effect of CPZ on the PMA-/A23187-induced macrophage chemiluminescence was also a result of its immunomodulating activity.

In contrast, the antidepressants (IMI, AMI) manifested a weak effect on the luminal-dependent chemiluminescence of the macrophages and did not express any effect on KO2-induced chemiluminescence.

It was observed also that the suppression of the macrophage chemiluminescence by all investigated drugs was not a result of their cytotoxicity. Moreover, it was established that all drugs enhanced dose-dependently the macrophage ATP-bioluminescence, which is an indirect evidence for an immunomodulation.