Effects of N,N'-benzilidenoaniline (bzan), 1,1'-bis(diphenylphosphine)ethylene (dppe) and cyclopalladated complex [Pd(bzan)(NCS)(dppe)] on the NO and H_2O_2 production by murine peritoneal macrophages

Alessandra Stevanato[1,2]*, Antonio Eduardo Mauro[2], Iracilda Zeppone Carlos[3]

[1] Chemistry Department of the Federal Technological University of Parana (UTFPR) – Londrina / PR, Brazil, [2] Chemistry Institute - Department of General and Inorganic Chemistry – UNESP – Araraquara / SP, Brazil, [3] Faculty of Pharmaceutical Sciences - Department of Clinical Analyses – UNESP – Araraquara / SP, Brazil.

The interest in uses and application of inorganic chemistry in medicine continues to expand. Cisplatin is probably the best know example of a small metal-containing drug. In early analog development of platinum compounds, complexes with "windows of reactivity" similar to platinum may find similar uses. It is well documented that Pd(II) analogs are too kinetically reactive to be of usc as drugs[1], mainly of those derived from N-donor ligands. Actually, there is a clear tendency to investigate the biological activity between inorganic complexes with DNA and RNA. However, at this moment, few studies dealing with the stimulation of macrophages mediated by these complexes. Macrophages constitute one the major components of immunologic system besides, and they are the first cell to be activated in host defense mechanisms. Nitric oxide (NO) and hydrogen peroxide (H_2O_2) are some of the microbicidal and tumoricidal substances released by macrophages in the immune response. As a part of our ongoing studies on cyclometallated palladium(II) complexes, we described in this work the synthesis, spectroscopic characterization of the compounds [Pd(bzan)(NCS)(dppp)] (X = SCN (**1**), NCO (**2**); bzan = *N*,*N*-benzylideneaniline; dppe = 1,1'-*bis*(diphenylphosphine)ethylene as well their antitumor activity. The compound [Pd(bzan)(NCS)(dppe)] was synthesized from the reaction of the precursor $[Pd(bzan)(\mu\text{-}NCS)]_2$ and dppe, in a methanol:acetone mixture 2:1. Evaluate cytotoxic and/or immunological activity of organopalladated compound [Pd(bzan)(NCS)(dppe)] (**1**) and their ligands bzan (**2**) and dppe (**3**), as well the investigation of their induced immune response in peritoneal macrophages mice in comparison with cisplatin (*cis*-DDP) (**4**) used as standard substance. Cytotoxic index (IC_{50}) of the [Pd(bzan)(NCS)(dppe)] (**1**), bzan (**2**), dppe ligands (**3**) and cisplatin (**4**) showed IC_{50} (mol L^{-1}) of 22,01 ± 3,38; 401,55 ± 2,02; 148,79 ± 3,27 and 49,79 ± 1,58. These data indicated that (**1**) showed a higher cytotoxicity *in vitro* than cisplatin and the ligands, whereas the ligands showed a lower cytotoxicity *in vitro* than cisplatin on peritoneal macrophages. The compounds bzan, dppe and [Pd(bzan)(NCS)(dppe)] inhibits NO. The complex [Pd(bzan)(NCS)(dppe)] appears to stimulate the H_2O_2 production more than cisplatin and ligands, whose H_2O_2 production is lower than the positive control LPS (lipopolyssacaride). These data suggested that palladium complex and the ligands may possess anti-inflammatory properties. Others tests will be carried out in order to confirm the anti-tumor potential of the compound (**1**) compared with the ligands (bzan and dppe) and the standard substance cisplatin (**4**).

1 Farrell, N. Coord.Chem. Reviews. 2002, 232, 1.

UTFPR – Londrina, fapesp, CNPq and CAPES.