THE INFLUENCE OF CENTRAL HEAVY METAL IN WATER-SOLUBLE CHLOROPHYLL DERIVATIVES ON THE PHOTODYNAMIC EFFECT *in vitro*

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Chlorophylls and their semi-synthetic water-soluble metalloderivatives belong to a very interesting group of photosensitizing compounds because of their advantageous spectral characteristic, very low toxicity and short retention times in the organism. Insertion of heavy central metal into the tetrapyrrole structure results in increased triplet states formation and, in consequence, intensifies their photocytotoxic potential.

The effect of central metal in chlorophyllide (Chlide) (a phytol-free chlorophyll derivative) structure was examined among the naturally occuring Mg-Chlide and their semi-natural metallosubstituted derivatives: Zn-Chlide and Pt-Chlide. All tested compounds exhibited no cytotoxicity in the dark and were stable under experimental conditions. *In vitro* photodynamic activity was evaluated using murine Cloudman S91 melanoma cells irradiated with wavelengths > 600 nm. Results were assessed after 48 h using a MTT assay.

Both Zn(II) and Pt(II) substituted structures showed increased photodynamic effect in comparison with Mg-Chlide, however Pt-Chlide was found to be the most effective derivative. The insertion of platinium ion enhanced *in vitro* photosensitizing efficiency five times in comparison to the natural Mg-Chlide. What is most important, this substantial photocytotoxicity was obtained already for very low light doses (8.7 J × cm^{-2}) and very low concentrations (40 nM) of the chlorophyllides. It is a good approximation of the conditions during therapy *in vivo*, because drug level achievable in the organism is the same order of magnitude. Similarly, light doses which can penetrate deeply into tumor tissue are comparable.

Our results showed that metallosubstituted chlorophyllides reveal highly advantagenous photophysical and biological characteristic, promising for further research in anticancer PDT applications.