## Binding of Cu(II) and Cd(II) ions with DNA from Spirulina Platensis

## Eteri Gelagutashvili<sup>a</sup>, David Djoxadze<sup>b</sup>, Liguri Mosulishvili<sup>a</sup>

- <sup>a</sup> E.L. Andronikashvili Institute of Physics, Georgian Acad. Sci., 6 Tamarashvili str., Tbilisi, 0177, Georgia
- E-mail: gel@www.iphac.ge, gelaguta@yahoo.com
- <sup>b</sup> Tbilisi State University, 1 Chavchavadze str., Tbilisi, 0137, Georgia

The action mechanism of antitumor and antibiotic pharmaceuticals often involves the formation of complexes with DNA. Some of these DNA-binding drugs exert their effects only in the presence of a metal cation [1]. The binding of Zn-finger proteins to DNA was shown to be affected by cadmium and other metals in two major ways [2]. Cd(II), as well as Cu(II) has been shown to change the binding characteristics of the SP1 transcription factor of Zn-finger to DNA[3]. Inhibition of DNA reparative ability is an important mechanism of Cd(II) genotoxicity [4].

Although presently the search for innovative treatment technologies focuses attention on the metal binding capacities of various microorganisms and their components, the mechanism of metal ions interaction with them is essentially unknown. Blue-green algae S.platensis has antiviral and anticancer effects and high sorption capacity for cadmium [5], but interaction of heavy and toxic metal ions with DNA from *S. platensis* is not defined.

The energetics of Cu(II) and Cd(II) ions binding to DNA isolated from blue-green algae S. platensis was determined from their binding isotherms by equilibrium dialysis and Atomic-absorption spectroscopy. Binding constants were determined from the Scatchard plots (fig.1). For Cu(II)-DNA stoichiometric binding constant K=1.56 x10<sup>5</sup> M<sup>-1</sup>. In the case of Cu(II)-DNA and Cd(II)-DNA from *S. platensis* two energetically different sites of their binding on DNA were observed. Micro constants  $k_1$ ,  $k_2$  and corresponding numbers of binding sites  $n_1$ ,  $n_2$  for Cu(II), were determined. It was shown, that for Cu(II) ions  $k_1 > k_2$  i.e. the association of Cu(II) ions with DNA can be described by the model with two patterns of binding, one of them corresponding to the strong binding, the other corresponding to the weak one. The same nature of binding was obtained for Pb(II)-DNA complexes [6,7].

At a low proportion of occupied sites corresponding up to one copper molecule bound per 10 phosphorus, and one cadmium bound per 25 DNA phosphorus. At saturation corresponding to one site per two bases for both metal ions (n). The same value of n was obtained in [8,9], where the interaction of Mn(II) and Mg(II) with DNA was studied. When investigating the interaction of Mn(II) ions with DNA bases of different origin Zimmer[9] showed that the conformation of DNA plays a major role in the number of binding sites.

For Cd(II) -DNA complexes a positive slope was observed, indicative of positive cooperativity of Cd(II) binding to DNA. When the proportion of bound cadmium(II) ions per DNA phosphorus fell in the range between 1:25 and 1:2, an approximate linear relationship with negative slope was obtained. The best fit slope for the descending portion of the binding curve revealed stoichiometric binding constant  $K=1.44 \times 10^5 \text{ M}^{-1}$ .

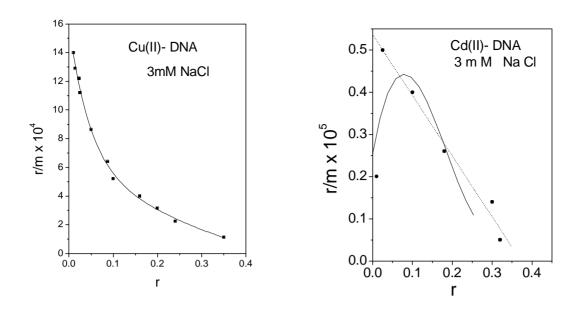


Fig.1 Binding isotherms of Cu(II) -DNA and Cd(II)-DNA complexes.

(The dependence r/m vs r, where r- is the concentration of bound metal ions, m-is the concentration of free metal ions).

## References

- B. A.Chabrer, C. J.Allegra, C.A.Curt and P. Calabresi. Chemotherapy of Neoplastic Diseases. (1996). In Hardman J.G., Limbird L.E., Molinof P.B. and Ruddon R.W. (eds), Goodman and Gilman's The Pharmacological Basis of Therapeutics, 9<sup>th</sup> Edn. McGraw-Hill, New York, NY, pp.1233-1287.
- 2. B.Sarkar. Nutrition (1995), 11(5Suppl), 646.
- 3. H.J. Thiesen, C.Bach. Biochem. Biophys .Res. Commun. (1991), 176(2), 551.
- 4. A.Hartwig. Toxicol Lett. (1998), 102-103,235.
- 5. N. Rangsayatorn, E.S. Upathum, M. Kruatrachue, P. Pokethitiyok, G.R. Lanza. *Environ. Pollut.*, (2002), 119, 45.
- 6. E.S. Gelagutashvili, A.N. Rcheulishvili, L.M. Mosulishvili. *Biophysics*,(2001), 46(6),957.
- 7. E.S. Gelagutashvili, A.N. Rcheulishvili, L.M. Mosulishvili. Proceeding of Georgian Academy of Sciences, Chem. Series, (2003), 29(1-2), 57.
- 8. J. Granot, D.R. Kearns. Biopolymers. (1982),21,203.
- 9. G. Luck, Ch. Zimmer . Eur. J. Biochem. (1972), 29, 528.