Antioxidant Activity of a Ni (II)-2-deoxy-D-glucose Complex Compound

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In this paper, we describe the synthesis of a new Ni(II)-2-deoxy-D-glucose complex compound. The compound was investigated by elemental analysis, UV-Vis spectroscopy, FTIR spectroscopy, molar electrical conductivity measurements, magnetic measurements as well as thermal analysis. Based on these results we have formulated the complex compound as binuclear species: Na[Ni₂(L)₅(L-H)₄Cl]. The antioxidant activity was also investigated.

Keywords: Ni(II), 2-deoxy-D-glucose, complex compound, antioxidant activity, biological activity

Nickel is known to be a non-toxic metal, an essential element for several species of animals. Bacteria use nickel to make enzymes (urease, hydrogenase, methyl CoM reductase, acetyl CoA synthetase, CO dehydrogenase) necessary for maintaining their functions. Though many researchers suspect that nickel in small quantities is necessary for human health, yet it has not been demonstrated [1-3]. People having low levels of nickel in their bodies are known to have liver and kidney diseases. In addition, a high level of nickel in the human body generates heart disease, thyroid disease and cancer affecting hormones and cell membranes even though it is not known exactly how. Nickel is widely distributed in the environment, and can be found in air, water and soil. Natural sources of atmospheric nickel include dusts from volcanic emissions and the weathering of rocks and soils. The level of nickel in ambient air is small (about 6 - 20 mg.m⁻³), but levels up to 150 mg Ni.m⁻³ could be present in air contaminated by anthropogenic sources [4,5]. Most food (dark chocolate, hazelnuts, dry fruits and vegetables) contains below 0.5 mg Ni.kg⁻¹ wet weight. Like many environmental agents, the toxic effect of Ni is related to the way it gets into an organism. Ni can enter body via inhalation, ingestion and dermal absorption, but the route by which Ni enters cells is determined by its chemical form. A number of nickel-binding proteins (like histidine, α1-antitrypsin and prealbumin) were described in the literature [6].

Contact with Ni compounds can cause a variety of adverse effects on human health, such as nickel allergy and skin dermatitis, lung fibrosis, cardiovascular and kidney diseases and cancer of the lung and nasal sinus. The 2-deoxy-D-glucose ligand belongs to saccharides class and was tested as an antiviral therapeutic and especially as an anticancer agent used for various types of cancer such as breast cancer [7,8]. The existence of saccharides in a variety of macromolecules such as nucleic acids offers multiple binding sites for the metals. Formation of Ni(II)-carbohydrates complex compounds was identified in human kidneys [9].

We report in this paper the synthesis, characterization and antioxidant activity of a new complex compound of Ni (II) with 2-deoxy-D-glucose. This study could be very useful for examining and mimeting the behaviour of one of the saccharide compounds (2-deoxy-D-glucose) in the presence of a metallic ion (nickel) found in human body fluids.

Experimental part
Materials and methods
All reagents and solvents were supplied by Sigma Aldrich. Metallic sodium (12 mmol) was slowly added to a solution of 2-deoxy-D-glucose (6 mmol, 100 mL). After 45 min of stirring, to the reaction mixture was added drop wise an aqueous solution of NiCl₂.6H₂O (2 mmol, 100 mL). The reaction mixture was kept at 60°C for 12 h. The precipitate of Ni (II) with 2-deoxy-D-glucose was isolated by filtration and purified by stirring four times in a 9:1 methanol-water, followed by washing two times with methanol. Finally, the precipitate was dried under vacuum. The yield of Ni(II) complex was 60 %, based on the nickel content. Anal Na[Ni₂(L)₅(L-H)₄Cl]. (NaC₅₈H₁₁₄O₅₄Ni₂Cl) Found (%): C, 37.75; H, 6.37; Na, 1.25; Cl, 1.95; Ni 6.37. Calculated for Na[Ni₂(L)₅(L-H)₄Cl] (%): C, 37.63; H, 6.21, Na, 1.24; Cl, 1.91; Ni, 6.34. The experimental values are in good agreement with the calculated values.

Elemental analysis
The nickel content of the complex compound was identified by atomic absorption spectroscopy with a SAA1 instrument. The C and H values were determined using a Carbo Erba Model 1108 CHNSO elemental analyser. The sodium content and chlorine contents were measured by Flame Emission Photometry method and by gravimetric method, respectively.

The UV-Vis spectra investigations were achieved using a JASCO V560 spectrophotometer with solid sample accessory, in the domain 200-800 nm, with a speed of 200 nm.min⁻¹. The FTIR spectra were performed on KBr pellets with a Bruker Tensor 27 spectrometer in the 4000-400 cm⁻¹ domain.

The thermal decomposition of the compound was recorded with a Netzsch 449C STA Jupiter. Samples were placed in open alumina crucible and heated with 10°C min⁻¹ from the room temperature to 800°C, under the flow of 20 mL min⁻¹ dried Ar.

The molar electrical conductivity was obtained in 10⁻⁴M DMF solutions, at 25°C, with OK 102/1 Radelkis®
Conductometer, 0.1 – 0.5 S, Δ_m obtained for was 70Ω cm/mol attributed to 1:1 electrolyte type.

The magnetic measurements were done using Faraday method, at room temperature.

The antioxidant activities of the 2-deoxy-D-glucose ligand and Na[Ni2(L)5(L-H)4Cl] complex compound were investigated in comparison with a chemiluminescent generating system formed by luminol 10⁻⁴ M and H₂O₂ in lampon solution buffer of TRIS-HCl with pH = 8.4 and the final volume was 1 mL. The chemiluminescent signal was registered after 5 seconds of mixing the system reactants. The obtained results were expressed as relative values of the luminosity intensity taking into consideration the figures of the standards.

The antioxidant activity was measured by chemiluminescence method, luminol/H₂O₂ system using Chemiluminometer - TurnerBioSystem (USA) [10]. Results were expressed as activity percents (S%).

Results and discussion

**UV-Vis spectroscopy**

The electronic reflectance spectrum of Na[Ni2(L)5(L-H)4Cl] solid sample presents three distinct bands: at 650 nm assigned to 3A₂g → 3T₁g (F) transition, at 470 nm assigned to 3A₂g → 3T₁g (P) and at 320 nm probably attributed to a charge transfer (CTML) band from nickel to 2-deoxy-D-glucose ligand. According to literature data these transitions are assigned to nickel (II) in octahedral geometry [11].

**FTIR spectroscopy**

Figure 2 shows the FTIR spectra of 2-deoxy-D-glucose ligand and Na[Ni2(L),(L-H),Cl] complex compound.

The comparison between the FTIR spectra of the complex compound and the ligand revealed that all the spectral bands are shifted or merged upon complexation. This feature is characteristic to transition metal-saccharide complexes synthesized starting from the saccharides sodium salts [12].

The ν₁(H₂O) groups from 3500-3200 cm⁻¹ region become a broad band at ~ 3400 cm⁻¹ with a shoulder at ~ 3250 cm⁻¹. This region is difficult to discuss due to the overlapping with the OH vibration of water molecules.

The peak observed in the 2-deoxy-D-glucose spectrum at 2860 cm⁻¹ assigned to asymmetric C-H stretching vibration was found at 2800 cm⁻¹ in complex compound spectra.

The stretching vibrations from 2-deoxy-D-glucose spectrum assigned to C-O and C-C presented in the region 1140-990 cm⁻¹ were merged at ~ 1050 cm⁻¹ upon complex formation. The bands attributed to C-O, C-C, O-CH and C-CH presented in the regions 1600–1650 cm⁻¹, 1350–1450 cm⁻¹ and 1000–1100 cm⁻¹ in complex spectra were merged and shifted in comparison with those of free ligand spectra, indicating the existence of some interactions between nickel and 2-deoxy-D-glucose. In the region 400-1000 cm⁻¹ are the bands corresponding to Ni(II)-O vibrations.

Therefore, the FTIR spectra support the complex formation indicating the binding of 2-deoxy-D-glucose units to the nickel ions. In addition, using FTIR spectroscopy was investigated the stability of Na[Ni2(L),(L-H),Cl] by dissolution and mixing in water for 24 h. The FTIR spectra of the complex compound measured before and after this procedure did not show modifications of the spectral bands (fig. 2b). This hydrolytic behaviour was indicated by our previous studies on the saccharide complexes [10].

**Magnetic measurements**

In order to obtain more information about the coordination geometry of complex compound, the magnetic susceptibility was measured. The value corresponds to a calculated magnetic moment of 2.51 BM. This value of the magnetic moment is suitable for Ni (II) with octahedral symmetry [12].

**Thermal analysis**

The compound Na[Ni2(L),(L-H),Cl] presents a good stability up to 125°C when first decomposition process begins. The thermal analysis for the complex compound
presents three decomposition steps 125-190°C, 190-250°C and 250-475°C. A fourth mass loss in the interval 475-800°C, is attributed to the oxidation of the carbonaceous mass, previously formed in the decomposition process (fig.3).

The first two decomposition processes are partially overlapped:
- 125-190°C, with a mass loss of 11.79%, accompanied by an endothermic effect on DSC curve, and
- 190-250°C with a mass loss of 32.51%, accompanied by an endothermic effect on DSC curve.

The third decomposition step (-18.47%) takes place in the interval 250-475°C and corresponds to the degradation and partial oxidation of the ligand, being associated with an exothermic effect.

The last decomposition process appears as a continuous mass loss and is attributed to the slow oxidation of the carbonaceous residue. The corresponding mass loss on TG curve is 11.13%. The process is associated with a broad exothermic effect.

The residual mass, 23.96%, probably consists of NiO, Na₂NiO₂ and carbonaceous mass.

The proposed structural formula of the synthesized complex based on all results of physico-chemical measurements is presented in figure 4.

**Antioxidant activity investigation**

In figure 5 is presented the antioxidant activity for the ligand and the corresponding Na[Ni₂(LL)(L-H)Cl] complex compound versus time. Two concentrations of the ligand and the complex were tested (10⁻³ M and 10⁻⁵ M).
At the lowest concentration tested (10^{-5}M) the Na[Ni_2(L)_5(L-H)_4Cl] (b - •) has an antioxidant activity with 33% higher than that of the ligand (a - ▲) (fig. 5a), whereas for 10^{-3}M the ligand and complex variation curves are similar (fig. 5b), having almost the same values of the antioxidant activities. However, figure 5c shows the existence of a slightly higher antioxidant activity of the ligand. At 10^{-5}M concentrations the tested samples have higher antioxidant activities than for 10^{-3}M concentrations.

The antioxidant activities (%S) were calculated using the following formula:

\[
\% S = \frac{I_o - I_p}{I_o} \times 100
\]

where:

\(I_o\) – the signal intensity of the standard read after 5 s;
\(I_p\) – the signal intensity of the samples read after 5 s.

The antioxidant activity values calculated were presented in table 1.

**Conclusions**

A new complex of Ni (II) with 2-deoxy-D-glucose ligand having the following formula Na[Ni_2(L)_5(L-H)_4Cl] was obtained. The FTIR spectroscopy, UV-Vis spectroscopy, molar electrical conductivity and magnetic measurements sustain the formation of the complex compound. The Na[Ni_2(L)_5(L-H)_4Cl] complex has a good antioxidant activity.

### Table 1

<table>
<thead>
<tr>
<th>Compound/ Concentration (M)</th>
<th>(I_p)</th>
<th>%S</th>
</tr>
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<tbody>
<tr>
<td>Na[Ni_2(L)_5(L-H)_4Cl] complex / 10^{-5}</td>
<td>6005</td>
<td>49.45</td>
</tr>
<tr>
<td>2-deoxy-D-glucose / 10^{-5}</td>
<td>4212</td>
<td>64.54</td>
</tr>
<tr>
<td>Na[Ni_2(L)_5(L-H)_4Cl] complex / 10^{-3}</td>
<td>2501</td>
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<tr>
<td>2-deoxy-D-glucose / 10^{-3}</td>
<td>2525</td>
<td>78.74</td>
</tr>
</tbody>
</table>

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**References**

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