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INFLUENCE OF GLYCINE AND ARGININE LIGANDS ON SOME OF PHYSICOCHEMICAL PROPERTIES OF MAGNESIUM ASPARTATE

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INTRODUCTION

Magnesium aspartate, which belongs to average chelates, is a good supplement and because of this it is commonly used in magnesium therapy (CLASSEN 2002, SPATLING et al. 2000, WINK et al. 2001, DURLACH, SARIS 2000). Aspartic acid creates the complex with Mg and is essential for magnesium transport through membrane and blood vessel barriers into blood and tissue. The change of properties of magnesium salts desired by medical therapists in order to improve both Mg absorption and transport can be obtained by introducing new substituents into the structure of magnesium aspartate (MARCOIN et al. 2002).

Amino acids, the basic components of proteins, are the proper compounds to affect some change in the therapeutic activity and thus have long been applied in therapeutics. The development of bioinorganic chemistry draws the attention of research workers to complexes of amino acid chelates with metallic ions. Introducing amino acid ligands of different structure into magnesium aspartate causes various electronic, lipo- and hydrophilic effects. Its also results in physico-

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chemical changes which are significant factors for pharmaceutical availability (OLEDZKA 1999).

Crystallization water present in a drug influences its dissolution, which in turn influences its availability and therapeutic effect (MEREDITH 1996).

Some more information on the basis of ^1H NMR studies on magnesium coordination with aspartic acid were presented by CIUNIK (1987). The following structure of magnesium-L-aspartate hydrochloride trihydrate has been proven by SCHMIDBAUR et al. (1986). The thermal decomposition of magnesium salts with glycine and methionine was studied by NEAMTU et al. (1986).

The review of the available literature indicates that there have been no studies on mixed ligand complexes of amino acid with magnesium. Consequently, a synthesis of new compounds: magnesium aspartate glycinate and magnesium aspartate arginate, was carried out.

The examination of the structure of these compounds presented hereby was conducted by density functional theory (DFT) at B3 PW11 level. Spectral characteristics of ^1H and ^{13}C NMR and IR obtained experimentally were compared with the data resulting from the calculations and described in other publications (MARCOIN et al. 2004, 2005).

The investigations on the thermal properties of magnesium aspartate and mixed ligand salts provide information on the phase transitions in these salts. This paper presents mainly the measurements of the dehydration process of magnesium complexes using the thermal analysis.

MATERIALS AND METHODS

The preparation of magnesium aspartate has been described previously (MARCOIN et al. 1991). All the reagents used, purchased from Merck and Sigma Company, were chemically pure.

The identification of the synthesized Mg salts was done by the elemental analysis method (C, H, N). The content of magnesium was measured by atomic absorption spectrophotometry (Carl Zeiss Jena model AAF 3) at the wavelength of 285.2 nm.

magnesium aspartate tetrahydrate: $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$

Anal. For $\text{C}_8\text{H}_{14}\text{O}_8\text{N}_2\text{Mg}$: Calcd.(%) C, 26.66; H, 5.55; N, 7.77; Mg, 6.74. Found (%) C 26.08; H, 5.12; N, 7.35; Mg, 6.31 – mol.wt.-360.39, $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$.

Preparation of the magnesium aspartate glycinate pentahydrate and magnesium aspartate arginate heptahydrate (in this work: $\text{Mg}[\text{Asp-Gly}]5\text{H}_2\text{O}$ and $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$).

The complexes of $\text{Mg}[\text{Asp-Gly}]5\text{H}_2\text{O}$ and $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$ were obtained from a reaction of magnesium aspartate and an appropriate amino acid (glycine or arginine) in an aqueous solution at the molar ratio of 1:1. The synthesis was carried out by vigorous stirring for 3 hours at 353 K. The products were isolated from the solution by vacuum evaporation, and then crystallized from methanol and dried at room temperature.

Anal. For $\text{C}_6\text{H}_{20}\text{O}_{10}\text{N}_2\text{Mg}$: Calcd.(%) C, 23.67 ; H, 6.57; N, 9.20; Mg, 7.98. Found.(%) C, 23.44; H, 6.40; N, 8.90; Mg, 7.81. – mol.wt.304.37 – $\text{Mg}[\text{Asp-Gly}] \cdot 5\text{H}_2\text{O}$

Anal. For $\text{C}_{10}\text{H}_{33}\text{O}_{12}\text{N}_5\text{Mg}$: Calcd.(%) C, 27.33; H, 7.51; N, 15.93; Mg, 5.53. Found.(%) C, 28.25%; H, 7.10; N, 7.15; Mg, 5.22. – mol wt. 439.41– $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$

THERMAL ANALYSIS

Thermogravimetry was carried out in air using a Paulik-Paulik-Erdey (MOM, Budapest) Derivatograph. The weight of powder samples was between 20–25 mg. Decomposition was carried out in platinum crucibles at a rate of 2.5 deg/min in a static air atmosphere up to 500 K, using $\alpha - \text{Al}_2\text{O}_3$ as standard material.

Differential scanning calorimetry (DSC) analysis was done. The measurements were performed using a Perkin Elmer DSC-7. The sample weight was 0.50–10 mg and all the sample were heated at a rate of 20 deg /min in a dynamic nitrogen atmosphere, according to the Perkin Elmer program. The decomposition was carried out at the maximum temperature of 500 K.

RESULTS AND DISCUSSION

The magnesium salts analysed were identified by the elemental analysis, IR and ^1H and ^{13}C NMR (MARCOIN et al. 2004, 2005). The elementary and spectral analysis confirmed the course of synthesis. Thus, the compounds were obtained in the form of white powder soluble in water.

The results of thermal analysis of the magnesium salts are summarized in Figures 1 and 2 and in Table 1. The DTA and TG curves were mainly taken into consideration in the evaluation of thermal resistance in the range of 300–500 K. Introducing glycinate or arginate ligands into the structure of the salts caused some change in their thermal properties. The visual results of such changes are shown in the DTA and TG curves in Figs. 1–2. The plateau was observed up to 412 K temperature indicating that no changes occurred in the DTA profile of $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$ (Fig. 1). Comparing the profiles of magnesium aspartate glycinate pentahydrate and magnesium aspartate arginate heptahydrate (Fig. 1) with

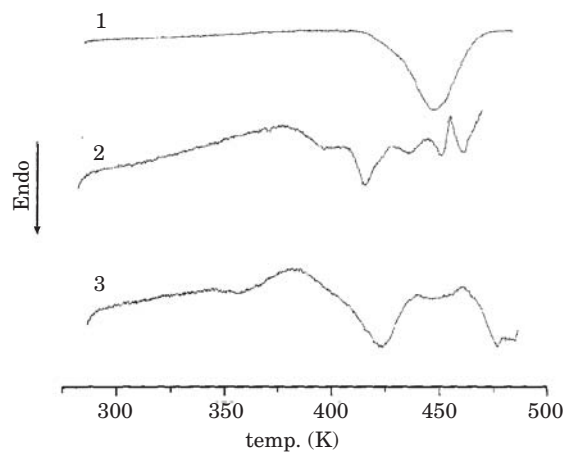


Fig. 1. DTA profiles for : 1- $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$, 2- $\text{Mg}[\text{Asp-Gly}] \cdot 5\text{H}_2\text{O}$,
3- $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$

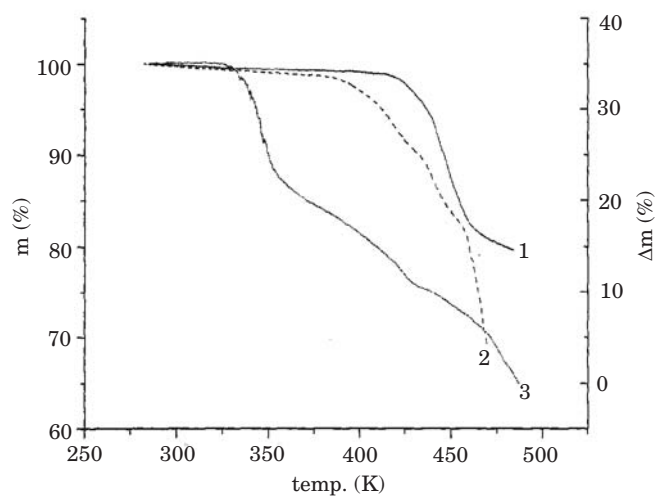


Fig. 2. TG profiles for: 1- $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$, 2- $\text{Mg}[\text{Asp-Gly}] \cdot 5\text{H}_2\text{O}$,
3- $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$

Table 1

DSC for salts: $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$

Compounds	DSC peak T (K)	DH (kJ/mol)
$\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$	448	155.82
	495	49.32
$\text{Mg}[\text{Asp-Gly}] \cdot 5\text{H}_2\text{O}$	406	7.13
	435	8.32
	470	16.84
$\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$	426	44.82
	473	7.12
	498	15.56

the DTA profile of magnesium aspartate tetrahydrate some influence of the additional ligands can be observed. The characteristic peaks are moved towards lower temperatures: for $\text{Mg}[\text{Asp-Gly}] \cdot 5\text{H}_2\text{O}$ to the temperature level of 375 K, and for $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$ to the temperature of 342 K. Comparing the DTA curves for $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$, $\text{Mg}[\text{Asp-Gly}] \cdot 5\text{H}_2\text{O}$ and $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$ one can see some differences. The influence of the ligands (glycinate, arginate) on the thermal properties of the magnesium salts: $\text{Mg}[\text{Asp-Gly}] \cdot 5\text{H}_2\text{O}$ and $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$, can be observed, leading to their decomposition in lower temperature. Above the temperature of 450 K additional endothermic peaks appear in the DTA profile of $\text{Mg}[\text{Asp-Gly}]$ and $\text{Mg}[\text{Asp-Arg}]$.

The TG curves in Fig. 2. illustrate the main thermal process: dehydration of the magnesium salts. The TG curve in Fig. 2 shows a gradual weight loss up to 500 K. The dehydration processes can be represented as shown in Table 1. In the case of magnesium aspartate tetrahydrate the plateau was observed at temperature 412 K. In Fig. 2 four water molecules are liberated from of $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$ in a one step process which began at ca 412 K and finished at 482 K. The weight loss was 20% (4 water molecules). Magnesium aspartate glycinate pentahydrate is stable up to 380 K. In this case two steps of a dehydration process were observed. In the first step, below 285 K, 1.56% of the weight was lost. Then, within the range of 380 K and 468 K the weight loss was of 28.1%. The total weight loss was of 29.6% (5 water molecules). In the case of $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$ the plateau is visible up to 325 K and two dehydration steps are observed: in the first step, within the range of 325 K and 355 K, the weight loss equals 12.5%, and in the second step, at 355 K to 468 K, the weight loss is of 17.1%. The total weight loss was 29.6% (7 water molecules). From the comparative analysis of the TG curves it is possible to draw the following conclusion: the number of molecules of crystallization water previously calculated by elemental analysis was confirmed.

Introduction of an amino acid anion into the original compound molecule influences the changes of its physicochemical properties. The study carried out with the DSC technique was aimed at measuring the enthalpy value in a dehydration process of the salts. The results of the DSC thermal analysis are shown in Table 1. The DSC analysis for $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$ showed the endothermic peak at 448 K, which was connected with the dehydration process, while the heat value of such transition equalled $\Delta H = 155.82 \text{ kJ/mol}$, and at 495 K the value of ΔH was 49.32 kJ/mol. In the case of $\text{Mg}[\text{Asp-Gly}] \cdot 5\text{H}_2\text{O}$ the first endothermic peak was connected with the dehydration observed at 406 K ($\Delta H = 7.13 \text{ kJ/mol}$), the second endothermic peak appeared at the temperature of 435 K ($\Delta H = 8.32 \text{ kJ/mol}$), and the third one – at 470 K ($\Delta H = 16.84 \text{ kJ/mol}$). For $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$ the first endothermic peak was observed at 426 K ($\Delta H = 44.82 \text{ kJ/mol}$). The second endothermic peak indicated the dehydration process at 473 K (value $\Delta H = 7.12 \text{ kJ/mol}$). At the temperature 498 K another endothermic peak is connected with the dehydration process enthalpy value of $\Delta H = 15.56 \text{ kJ/mol}$. The comparison of the results obtained by these two methods, DTA and DSC, has shown some transition of the endothermic peak towards higher values, which was caused by the difference in the heating speed. The curve for $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O}$ shows that dehydration was a one step process, while the curves for $\text{Mg}[\text{Asp-Gly}] \cdot 5\text{H}_2\text{O}$ and for $\text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$ in Fig. 2 imply that in these two cases dehydration is not a one stage process. Based on these experimental results (Fig. 2), with regard to the weight loss caused by the heating of the samples, some conclusions were drawn, which indicated the influence of the chemical structure of a substance on its thermal properties. The main processes of decomposition showed that the stability of these complexes decreased in the following order: $\text{Mg}[\text{Asp}_2] \cdot 4\text{H}_2\text{O} > \text{Mg}[\text{Asp-Gly}] \cdot 5\text{H}_2\text{O} > \text{Mg}[\text{Asp-Arg}] \cdot 7\text{H}_2\text{O}$.

CONCLUSIONS

The results show that thermal decomposition of the hydrated magnesium salts begins with a release of crystallization water. Comparing the thermal stability of the hydrate magnesium complexes with the stability of the basic compound of magnesium aspartate, the influence of additional ligands on the physicochemical properties of the salts is readily observed. In conclusions, we can say that the thermal stabilities of the complexes analysed in the present experiments depend on the nature of the ligands.

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**INFLUENCE OF GLYCINE AND ARGININE LIGANDS ON SOME
PHYSICO-CHEMICAL PROPERTIES OF MAGNESIUM ASPARTATE**

Key words: magnesium aspartate, glycinate and arginate ligands, thermal analysis, dehydration.

Abstract

Hydrate complexes of magnesium aspartate, magnesium aspartate glycinate, magnesium aspartate arginate have been synthesized and characterized by the elemental and spectral analysis.

The formulae of the magnesium complexes were $\text{Mg}(\text{C}_4\text{H}_6\text{O}_4\text{N})_2 \cdot 4\text{H}_2\text{O}$, $\text{Mg}(\text{C}_6\text{H}_{10}\text{O}_5\text{N}_2) \cdot 5\text{H}_2\text{O}$, and $\text{Mg}(\text{C}_{10}\text{H}_{19}\text{O}_5\text{N}_5) \cdot 7\text{H}_2\text{O}$.

The main thermal process: dehydration of the complexes, was studied using the thermoanalytical methods: differential thermal analysis (DTA), thermogravimetric analysis (TG), and differential scanning calorimetry (DSC) measurements. The influence of additional ligands (glycinate or arginate) introduced to the structure of magnesium aspartate on the physicochemical properties of the newly synthesized compounds was analysed.

WPLYW LIGANDÓW GLICYNY I ARGININY NA NIEKTÓRE WŁAŚCIWOŚCI FIZYKOCHEMICZNE ASPARAGINIANU MAGNEZOWEGO

Słowa kluczowe: asparaginian magnezowy, ligandy: glicynianowy i arginianowy, analiza termiczna, dehydratacja.

Abstrakt

Metodą analizy elementarnej i spektralnej scharakteryzowano syntezowane hydraty kompleksów asparaginianu magnezowego, glicynianoasparaginianu magnezowego, arginiano-asparaginianu magnezowego, Kompleksy magnezowe o wzorach : $\text{Mg}(\text{C}_4\text{H}_6\text{O}_4\text{N})_2 \cdot 4\text{H}_2\text{O}$, $\text{Mg}(\text{C}_6\text{H}_{10}\text{O}_5\text{N}_2) \cdot 5\text{H}_2\text{O}$, $\text{Mg}(\text{C}_{10}\text{H}_{19}\text{O}_5\text{N}_5) \cdot 7\text{H}_2\text{O}$.

Zastosowano metody termooanalityczne: różnicową termiczną analizę (DTA), termogravimetryczną analizę (TG), skaningową kalorymetrię różnicową (DSC) do badania głównego procesu termicznego: dehydratacji badanych kompleksów. Potwierdzono wpływ wprowadzonych do struktury asparaginianu magnezowego dodatkowych ligandów glicyny lub argininy na fizykochemiczne właściwości nowo syntezowanych związków.