

# Molybdenum Complexes with Amino Acids as Antihyperglycemic Agent : Preparation and Spectroscopic Studies

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## Abstract

Three novel molybdenum complexes with amino acids were synthesized by the reaction of MoCl<sub>5</sub> and L-Glutamic Acid, Glycine and L- Cysteine, respectively. The orange-brown precipitate indicate the formation of Mo(V) complexes. The complexes were characterized by FTIR spectroscopy and their spectra were then compared to those of the ligands and the Mo(OH)<sub>5</sub>. Two new bands at 968-972 cm<sup>-1</sup> and 732-740 cm<sup>-1</sup> proved new bonds of complexes. Several absorption bands of the free amino acid were disappeared after its complexation to Mo(V). The UV-Vis spectra showed the maximum absorbtion at 345-350 nm.

Keywords: Molybdenum, amino acids, antihyperglycemic, spectroscopic studies

## Introduction

Molybdenum is an essential trace element in living organisms, existing in active sites of molybdoenzymes, proteins which act on redox reactions. The study of the actual state (coordination geometry, oxidation state, etc.) of molybdenum in enzymes, as well as the mechanism followed by the reactions where these enzymes act, has attracted the attention of many researchers, mainly with a view to understanding the role played by molybdenum in these processes. [Macias, 1993 ]

Levina (2007)] and Maurya (2008) reported the research in Mo(VI)-based anti-diabetic complexes. The synthesis of Mo(VI) amino acid complexes were dependent to the ionic strength (Gharib, 2000). However, the predominant metal-based anti-diabetic drugs has been largely focused on Mo (V) and Cr(III) complexes.

The importance of investigating molybdenum complexes with amino acids as possible molybdoenzyme model compounds was recognized as long as 40 years ago. Two molybdenum(V) complexes, [Mo<sub>2</sub>O<sub>4</sub>(acac)<sub>2</sub>(gly)](EtOH)(H<sub>2</sub>O), **1**, and [Mo<sub>2</sub>O<sub>4</sub>(acac)<sub>2</sub>(D,L-val)], **2**, (acac =acetylacetonato, EtOH = ethanol), were synthesized by the reaction of [Mo<sub>2</sub>O<sub>3</sub>(acac)<sub>4</sub>] and amino acids glycine and D,L valine, respectively. The complexes were characterized by elemental and IR spectral analysis. Their structures were determined by the single crystal X-ray diffraction method [Tasner, 2008]. A great deal of effort has been directed towards the synthesis of model compounds of molybdenum(V).

Molybdenum complexes were applied in a research as possible adjuncts in the treatment of diabetes mellitus compared with Vanadium, zinc, chromium, and cobalt. Vanadium is arguably the most thoroughly studied and efficacious insulin-enhancing transition metal; a wide variety of vanadium containing complexes have been tested as candidate anti-diabetic treatments [Thompson, 2004]. Mc Donald (2008) reported the preparation of Mo-ascorbic acid complexes and it's application on treatment of induced diabetic rats. The research of possible role of transition metal complexes as nutraceutical of diabetes also conducted by Flores (2011)

In the present work a series of complexes was synthesized and characterized, using three  $\alpha$ -amino acids ; L glutamic acid, Glycine and L-Cysteine as ligands.

## Experimental Section

### Materials

#### A. Materials

Molybdenum (V) chloride, MoCl<sub>5</sub> salt, was from Sigma Aldrich, All starting amino acids were in the L form (except glycine) from E-Merck; were of Laboratory grade (by E-Merck) and used as such without purification. Sodium hydroxide (E-Merck) was used to adjust the pH.

#### B. Preparation of the Complexes

The Mo(V) complexes of L-Glutamic Acid ligand were prepared in 1:3 [metal:ligand] ratio. To a 25ml water solution of Mo(V)chloride (0.2722 g, 1mmol), NaOH 0.1M was added to adjust the pH. The ligand solution of Glutamic acid then was added (3mmol). The resulting mixture was stirred under reflux for 1h and 80°C. The precipitate product was collected by Buchner filtration, washed with water, and dried in air. The yielding solid was weighing until constant weight. Preparation on the Glycine and Cysteine complexes were quite difficult. The glycinato and cysteinato complexes of Mo (V) also prepared by refluxing the aqueous solution of MoCl<sub>5</sub>, amino acid and NaOH in the molar ratio 1:3:3 for 3 hours. Some trials of these complexes did not yield the precipitation.

### C. Characterization and Measurement

The resulting complexes in this work were characterized by physical properties by observation of the solid performance and the color of the precipitation. The yield was determined by weighing the product and compared with the starting materials. Infra red spectra were recorded on Shimadzu FT-IR 8300 spectrophotometer in the range 4000-400cm<sup>-1</sup> using KBr pellet technique. The UV-Vis spectra were studied in HNO<sub>3</sub> solvent with concentration about 1% b/v by UV Vis spectrometer (Thermo Spectronic), with 1cm<sup>2</sup> quartz cell within the range of 360-650nm. Elemental Analysis was carried out at Faculty of Food Science and Technology, University Kebangsaan Malaysia.

### Result and discussion.

Formation of the Mo(V) complexes was achieved by reaction of the ligand with Mo(V) salts by reflux method. Color changes indicate the occurrence of reaction. The complex formation observed in various pH according to the concentration of Mo(V) ion in water solution which influenced by pH. Products yield and physical data are presented in Table 1.

TABLE 1  
PRODUCT YIELD OF THE COMPLEXES

Complex	M:L ratio	Product and physical data	
		color	Yield (%)
Mo (V) – glutamic acid	1:3	Orange-brown	62.83
Mo (V) – glycine	1:3	Reddish brown	48.50
Mo (V) – cysteine	1:3	Brownies green	17.13

The elemental analysis data are given in Table 2.

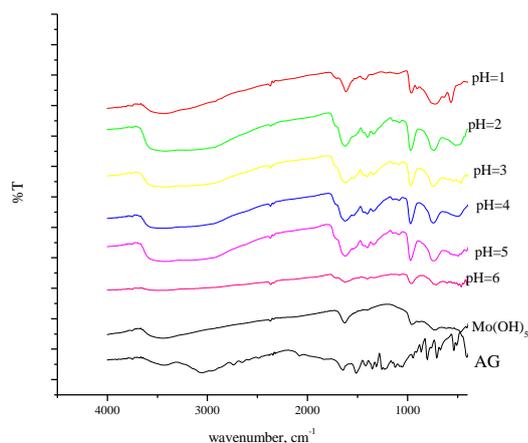
TABLE 2  
RESULT OF ELEMENTAL ANALYSIS OF THE COMPLEXES

Complexes	%C	%H	%N
Mo- Glutamic acid	8.645	3.967	3.987
Mo-glycine	2.821	2.213	4.792
Mo- cysteine	7.544	3.145	5.374

Figs. 1, 2, and 3, showed the FTIR spectra of these products. The characteristic bands also listed in table 3. The Infrared spectra in 4000-400cm<sup>-1</sup> region showed the evidence of complex formation. They were analyzed by comparison with data of the free ligands. Generally, free amino acid have original peaks of stretching vibration of ammonium and carboxylate groups in the broad region of 2600 and 1600cm<sup>-1</sup>, respectively [Barth, 2000]. These spectra showed a clear pattern which shows the difference between the produced complex with their corresponding amino acids. Most of the bands occurring in the spectra of free amino acids are slightly shifted and decreased in intensity in the spectra of the complexes. These changes reflect a changed environment for the coordinated zwitterion in the molybdenum complex. In the region of 400-200 cm<sup>-1</sup> some weak additional bands appear in the spectra of all of the complexes, the vibrational modes associated with Mo-O stretchings (Djordjevic, 1997).

The Infrared spectra of Mo with glutamic acid was shown at Fig. 1. Comparison of the infrared spectral data of complexes and the ligand confirmed that complex formation has occurred as significant shifts in the bands of the

OH groups were observed in the region  $3000\text{-}3500\text{cm}^{-1}$ . The IR spectra of Mo(V) complexes showed the expected characteristic  $\nu_{\text{as}} \text{COO}^-$  band in the region of  $1512.19\text{cm}^{-1}$  is shifted to  $1543.05$  due to metal coordination.

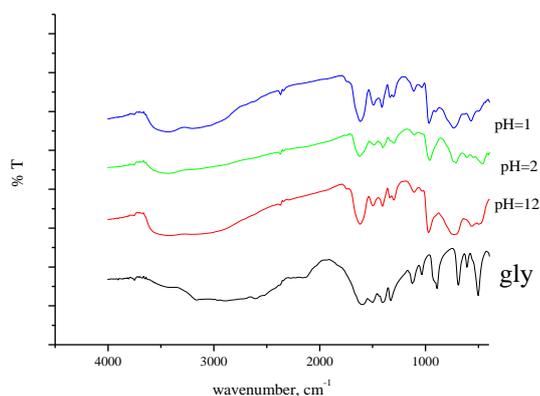


**Fig 1. Infrared spectra of Mo-Glutamic acid complexes**

A sharp band at  $1643.35\text{cm}^{-1}$  in the ligand due to C=O vibration was also shifted to lower frequency ( $1620.21\text{-}1604.77$ ) in the complexes. Moreover, the appearance of additional weak bands in the region  $462\text{-}493$  and  $732.95\text{-}740.67 \text{cm}^{-1}$  which were attributed to  $\nu_{(\text{M-O})}$  and  $\nu_{(\text{M-N})}$ , respectively, confirmed the complexation.

Infrared spectrum confirmed the formation of the complex by m-C-O ( $1543.05\text{cm}^{-1}$ ) and m-N-H ( $3535\text{cm}^{-1}$ ) and the band shifting by about  $40$  and  $30\text{cm}^{-1}$  respectively. The moderately sharp absorption band in the free ligand ( $3000\text{-}3500\text{cm}^{-1}$ ) was shifted to about  $600\text{cm}^{-1}$  may be related to the reorganization in intramolecular hydrogen bonding after the formation of chelating complex. New absorption bands in the far IR region around  $462\text{-}493\text{cm}^{-1}$ , and  $964.41\text{-}972.12 \text{cm}^{-1}$  can be assigned to the Cr-O and Cr-N bonds. Coordination bond in Mo-glu complex was predicted occurred through the COOH group. It was indicated from the disappearance of  $1660\text{cm}^{-1}$  band from glutamic acid [Barth, 2004]. The higher the pH, the more similar to the pattern of  $\text{Mo}(\text{OH})_5$ .

The spectra of Mo-glycine complexes was showed in fig 2.

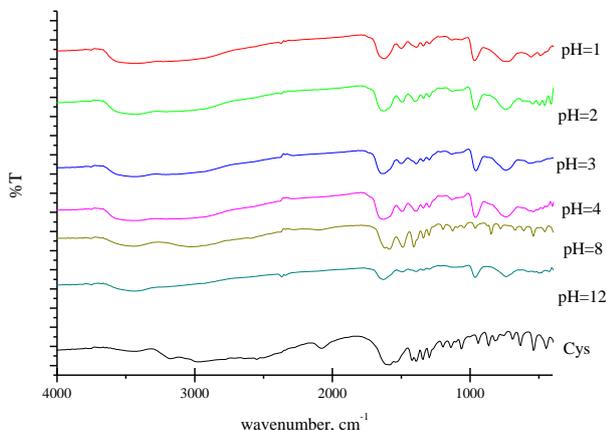


**Fig.2. Infrared spectra of Mo-Gly complexes**

There are some significant differences of FTIR pattern of Mo-Glycine complex with the free ligand. The shift to lower wave number from  $1404.18\text{cm}^{-1}$  (Gly) to  $1381.03\text{cm}^{-1}$  (Mo-Gly complex) correspond to the symmetric vibration of  $\text{COO}^-$ . A study of  $\text{Mo}(\text{Gly})_3$  complex formation reported this shift by  $1400\text{-}1370\text{cm}^{-1}$  [Han, 2010]. A recent publication explained that the N-H stretching vibration at  $3109\text{cm}^{-1}$  in glycine was shifted to higher frequencies ( $3333\text{-}3428\text{cm}^{-1}$ ) in the complex, suggesting that the coordination of the metal ion (in this case, Cu, Cd, Ni, Co, Mn) with the ligand was via the nitrogen atom. Shifting of C-N stretching  $1127$  to ( $1210\text{-}1236\text{cm}^{-1}$ ) also

support this idea [Aileyabola, 2012]. In this work, the N-H stretching vibration was shifted from  $3109.25\text{cm}^{-1}$  to  $3209\text{ cm}^{-1}$  and the C-N stretching vibration shifted from  $1126.43\text{cm}^{-1}$  to  $1111.00\text{ cm}^{-1}$ . Vibration of C=O was shifted from  $1604.77$  (Gly) to  $1620.21$  (Mo-Gly).

The infrared spectra of Mo-Cys Complexes were shown at fig.3



**Fig 3. Infrared spectra of Mo-Cys complexes**

The Infrared spectra of cysteine complex display several significant bands. The asymmetric stretching band of  $\text{COO}^-$  shifted to lower wave number from  $1543.05$  to  $1496.76\text{cm}^{-1}$ , indicating that the carboxylate group was involved in the coordination. Vibration of C=O was shifted from  $1589, 34\text{ cm}^{-1}$  (Cys) to  $1627, 92$  (Mo-Cys). Stretching vibration of  $\text{NH}_2$  were shifted to lower wavenumber, from  $3170.91$  to  $2938.52\text{ cm}^{-1}$  after formation of coordination bond with Mo. According to El-Shahawi [1996], it confirming the participation of the nitrogen atom of the amino group of cysteine in the coordination with metal, with the shifting from  $1195\text{cm}^{-1}$  to  $1126\text{cm}^{-1}$ .

The characteristic absorption in the IR spectra of complexes is listed in Table 3.

**Table 3. Characteristic bands of Mo-AA complexes**

Vibration	Mo-Glu	Glu	Mo-Gly	Gly	Mo-Cys	Cys	Ref
$\nu$ C=O	1620.21	1643.35	1620.21	1604.77	1627.92	1589.34	<b>9,10,11,12, 13</b>
$\nu_{as}$ $\text{COO}^-$	1543.05	1512.19	1496.76	1504.48	1496.76	1543.05	
$\nu_s$ $\text{COO}^-$	1404.18	1419,61	1404.18	1404.18	1388,75	1388.75	
$\delta$ COH	1342	1257,59			1296.16	1296.16	
$\nu$ C-O	1141.86	1126.73;1257.59 [1150]	1111.00	1126.43	1126.46	1141.86 1195.87	
$\delta$ $\text{CH}_2$	1404.18	1419,61 [1440]	1404.18	[1441- 1446]	1388.75	[1424- 1432]	
$\delta$ C-H	1342.66	1311.59 1125	1296	[1333- 1337]	1342.46	[1341]	
$\nu$ N-C		1257.59			1126.43	1195.87	
$\gamma_t$ $\text{CH}_2$ , $\delta$ CH		1226.73	1296	[1310- 1315]		[1303, 1297]	
$\nu$ C-C	1080.14	1075 1056.99	972.12	1033.85	964.41	1064.71	
$\nu$ N-H	3248.13	3062.96	3209	3109.25 [3119]	2993.52	3170.91	
$\nu$ S-H	-	-		-	2337.72	[2551]	
Mo-O	316.33		324.04		339.47		<b>400-200</b>
$\nu$ O-O	<b>872.12</b>			-		-	<b>870</b>

$\nu$ Mo=O	972.12	-	956.59	-	964.41	-	<b>960-978</b>
Mo-N	<b>740.67</b>	-	<b>732.95</b>	-	<b>740.67</b>		

Uv Vis spectrometric studies also conducted to these samples. The coordination of metal to ligands caused a certain change in electronic configuration of the d-orbitals. Complexes of transition metal with electronic absorption at the visible light, the coordination formation is related to the color change, due the change of electronic configuration. In the case of Mo(V), all samples showed color changes from the solution of metal ion (green) and the ligand (white) to a new color of complex. Uv-Vis spectrometer studies give a maximum absorption in the range of 345-350 nm of all Mo complexes in this work. The previous work reported the UV-vis absorption were in range of 320-370 nm (Djorjevic et al. 1997).

The comprehensive analysis is needed to find a definite structure of these complexes. The most popular method is single crystal X-ray diffraction. This method proved the suggested structure by several parameters: the bond length, the angle, and the crystal structure. The final molecular formula and structure can be illustrated by molecular modelling (Djorjevic et al. 1997, Vujevic, 2003).

#### References.

- [1.] Macias, B., Criado, J., And Villa, M., Rodriguez, L., Csatislo, M., Complexes Of Molybdenum(V) And Molybdenum(IV) With Dithiocarbamates Derived From  $\alpha$ -Amino Acids. Reaction Kinetics In Organic Solvents, *Polyhedron*, Vol. 12, No. 23, Pp. 2791-2799, 1993
- [2.] Levina, A., McLeod, A., Seuring, J., and Lay, P. A., 2007, Reactivity of potential Antidiabetic Molybdenum(VI) Complexes In Biological Media: A XANES Spectroscopic Study, *Journal of Inorganic Biochemistry*, , 101, 1586-1593.
- [3.] Maurya, RC., Sahu S., Bohre P., 2008, Synthesis, characterization, antibacterial activity and 3D modelling of some oxoproxomolybdenum (VI) chelates in mixed (O,O) coordination environment involving 2-hydroxy 1 naphthaldehyde and B diketone
- [4.] Gharib, F., Zare, K., Majlesi, K., 2000, Ionic Strength Dependence of Formation Constants, Complexation of Molybdenum(VI) with Glutamic Acid, *J. Chem. Eng. Data*, 45 (5), pp 833–836
- [5.] Tasner, M., Prugovecki, B., Mrvos, B., Branka S., Colig, K., Giester G., and Matkovic, D., Calogovic Synthesis and Crystal Structures of Two Novel Molybdenum (V) Complexes with Glycine and D,L-Valine., *Acta Chim. Slov.* 2008, 55, 928–934
- [6.] Thompson KH., Chiles, J., Yuen VG., Tse, J., McNeill, J.H., Orvig, C., 2004, Comparison of anti-hyperglycemic effect among vanadium, molybdenum and other metal maltol complexes, *J. Inorg. Biochem* 98: 683–690.
- [7.] MacDonald, K., Bailey J, MacRory C, Friis C, Vogels CM, Broderick T, Westcott SA., 2008, A Newly Synthesised Molybdenum/Ascorbic Acid Complex Alleviates Some Effects Of Cardiomyopathy In Streptozocin-Induced Diabetic Rats, *Iran Biomed J.* Jul;12(3):143-52.
- [8.] Flores, C.R; Puga, M.P.; Wrobel, K.; Garay Sevilla, M.E.; Wrobel, K. 2011, Trace Elements Status In Diabetes Mellitus Type 2: Possible Role Of The Interaction Between Molybdenum And Copper In The Progress Of Typical Complications, *Diabetes Res Clin Pract.* Mar;91(3):333-41.
- [9.] Barth, A., 2000: The Infrared Absorption of Amino Acid Side Chains, Progress in Biophysics and Molecular Biology), a review, *Progress in Biophysics & Molecular Biology*, 74 ,141–173.
- [10.] Djordjevic, C., Vuletic, N., Jacobs, B.A., Lee M., and Sinn Ekk., 1997, Molybdenum(VI) Peroxo  $\alpha$ -Amino Acid Complexes: Synthesis, Spectra, and Properties of  $\text{MoO}(\text{O}_2)_2(\alpha\text{-aa})(\text{H}_2\text{O})$  for  $\alpha\text{-aa}$  ) Glycine, Alanine, Proline, Valine, Leucine, Serine, Asparagine, Glutamine, and Glutamic Acid. X-ray Crystal Structures of the Glycine, Alanine, and Proline Compounds, *Inorg. Chem.* 1997, 36, 1798-1805
- [11.] Han, J.H., Chi, Y.S., 2010, Vibrational and Electronic Spectroscopic Characterizations of Amino Acid-Metal Complexes. *J. Korean Soc. Appl. Biol. Chem.* 53(6), 821-825.
- [12.] Aileyabola .T.O, Ojo. IA., Adebajo, A.C., Ogunlusi G.O., Oyetunji, O., Akinkumi E., O., Adeoye, A.O., 2012, Synthesis, Characterization and Antimicrobial Activities of Some metal (II) amino acids' complexes, *Advances in Biological Chemistry*, 2: 268-273.
- [13.] El Shahawi, 1996, Spectroscopic and Electrochemical Studies of Chromium Complexes with Some Naturally Occurring Ligands Containing Sulphur, *Spectrochimica Acta*, 59: 139-148.
- [14.] Vujevic G., Janiak, C., 2003, Structural studies of Bis (cyclopentadienyl)molybdenum-amino acid complexes, *Z. Anorg. Allg. Chem.* 629, 2585-2590.