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Research Article

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Study for effect of pH on l-arginine and hydroxyurea interactions with transitional metal ions

Harshada Gurav,Sangeeta Parab*, A.V.Chitre,

Chemistry Department, Jai Hind College, Churchgate, Mumbai- 400020.

Email : sangeetaparab2003@yahoo.com,sangeetaparab2012@gmail.com

Abstract

No* is a free radical with one free electron and as such it is very highly reactive and particularly it interacts with transitional metals. Nitric oxide, gas is an important signaling molecule in the body of mammals, including humans and is an extremely important intermediate in chemical industry in biological systems there are many enzymes, which contain transitional elements like iron, copper and manganese, which are the most probable sites for nitric oxide to react. Such type of interactions results in considerable modification of the enzyme functions resulting pathological and even genetic disorders. This needs a critical amount of nitric oxide in the system for proper functioning.

To observe the effects of NO*, various NO* donor compounds are used. Hydroxyurea (HU) is shown to increase the levels of NO*.L-Arginine is one of the non- essential amino acids. In the body L-Arginine is used to make nitric oxide, which reduces blood vessel stiffness, increases blood flow and improves blood vessel function.

The effect on maximum wavelength of some transitional metals Cu, Fe (II), Fe(III), Mn, Cr and Ni with change in pH have been studied individually in presence of Hydroxyurea (HU) with varying amounts .This study also done for the effect of varying amounts of L-Arginine on Metal ion solutions. To observe how arginine itself acts on transitional metal ions with change pH. The evaluation of these spectra is carried out for its binding parameters with the help of Scatchard plots[18-20]. The work has revealed certain very significant and interesting data which can have a lot of bearing on many chemical, biological and environmental aspects.

Keywords: Scatchard, hydroxyurea, transitional, binding.

Introduction

Nitric oxide – small inorganic molecule which was probably best known to general public as pollutant in car exhaust, became biological molecule of 1990's. Its importance was recognized by the award of a Nobel prize to Furchgott, Ignarro and Murad in 1998'for their discoveries concerning nitric oxide as a signaling molecule in the cardiovascular system'

Nitric oxide plays major role in human physiology. NO functions as a neurotransmitter, a macrophage derived defense agent against foreign organism and regulate blood flow as vasodilator [1-6] Nitric oxide forms complexes with all transitional metals to give complexes called metal nitrosyla. NO can serve as a one electron pseudo halide. Nitric oxide group can also bridge between metal centers through N-atom in variety of geometries[7].

Nitric oxide is produced in the body by enzyme called nitric oxide synthase, which converts the amino acid L-arginine to nitric oxide and L-citrulline. There are three types of nitric oxide synthase: brain, endothelial and inducible. NO plays several major roles in human physiology. Nitric oxide functions as a neurotransmitter, a macrophage-derived defense agent against foreign organisms and regulates blood flow as vasodilator. Nitric oxide has great physiological importance and forms the basis of several current or considered therapeutic methodologies. Nitric oxide has good site and a bad side, while excess Nitric oxide in septicaemia,

inflammation and stroke causes severe damage, while localized production of small quantities of nitric oxide is essential for normal body function.

Hydroxyurea represents an approved treatment for sickle cell anemia and acts as nitric oxide donor under oxidative conditions in vitro. Treatment of hydroxyurea with hydrogen peroxide and copper (II) sulphate produces 'NO-LIKE' species capable of nitro sating morphine that eventually decomposes to nitrite (NO^{-2}) and nitrate (NO^{3-}), the stable oxidative decomposition products of nitric oxide.

Hydroxyurea reduces the incidence of painful crises in patients with sickle cell disease and has recently been approved for the treatment of this condition. A number of in vitro studies show that the oxidation of hydroxyurea results in the formation of nitric oxide, which also has drawn considerable interest as a sickle cell disease therapy. While patients on hydroxyurea demonstrate elevated levels of nitric oxide-derived metabolites, little information regarding the site or mechanism of the in vivo conversion of hydroxyurea to nitric oxide exists

In the body L-arginine is used to make nitric oxide, which reduces blood vessel stiffness, increases blood flow, and improves blood vessel functions. L-arginine is an amino acid that has numerous functions in the body. It helps the body get rid of ammonia (a waste product), is used to make compounds in the body such as creatin, L-glutamate and L-Proline and can be converted to glucose and glycogen if needed. L-arginine is used to make the nitric oxide a compound in the body that relaxes blood vessels.

Hence we feel that it will be interesting to see how arginine itself acts on these transitional metals. So we propose to study metal- arginine interactions and the effects of these interactions on these entities itself.

The free radical nitric oxide has direct influence on the spectral properties of transitional metals and particularly it has binding interactions with some of them are observed. Since arginine is precursor of nitric oxide synthesis in human body its interaction with transitional elements becomes important [7-9]. Since many transitional elements like Cu, Zn, Mg and Mn are required for many biological processes like enzyme activity. Nitric oxide preferentially binds to iron (Fe) atom of heam group in proteins; it can also interact with other metal sites in proteins. NO functions as a neurotransmitter, a macrophage derived defense agent against foreign organism and regulate blood flow as vasodilator. Nitric oxide forms complexes with all transitional metals to give complexes called metal nitrosyla. NO can serve as a one electron pseudo halide. Nitric oxide group can also bridge between metal centers through N-atom in variety of geometries.

Experimental Work

All the chemicals used for the work are of A.R. grade of S. D.Fine or Merck. Spectral analysis carried out with Shimadzu model 2450 U.V.-Visible spectrophotometer.

Transitional metal ions selected for the work are Cu, Mn, Ni, Fe (II), and Fe (III), in the form of $CuSO_4$, $KMnO_4$, $NiSO_4$, $K_2Cr_2O_7$These metal ion solutions are studied for its λ_{max}values[13].

The pH of metal ion solution is determined first and the pH of solution is first increased by about 0.5 and to this solution varying amounts of L-Arginine is added then next again after determining the pH of metal ion solution the pH of solution is decreased by about 0.5 and to this solution varying amounts of L-Arginine is added. The same study is carried out in presence of other binding substance i.e. Hydroxyurea. And effect on spectra is studied with Scatchard plot[18].

Metal ions	Original pH	Increasing pH by 0.5	Decreasing pH by 0.5
$CuSO_4$	6.243	6.743	5.745
$KMnO_4$	6.441	6.941	5.941
$NiSO_4$	6.955	7.495	6.495
$K_2Cr_2O_7$	6.310	6.810	5.81

Results and Discussion

a) Metal ion solutions of Cu, Mn, Ni, and Cr were used to find their respective λmax.

Metal ion solution	λ_{max}.
$CuSO_4$	805 nm
$KMnO_4$	395nm
$NiSO_4$	389 nm
$K_2Cr_2O_7$	354nm

b) Metal ion solution with increasing pH and varying amount of L-Arginine and HU added for binding interactions by spectral study and Scatchard plots to calculate binding parameters.

c) Metal ion solution with decreasing pH and varying amount of L-Arginine And HU added for binding interactions by spectral study and Scatchard plots to calculate binding parameters.

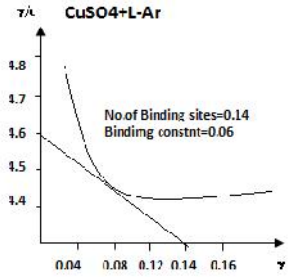

Fig.1

Incresing pH Study of L-Ar and HU

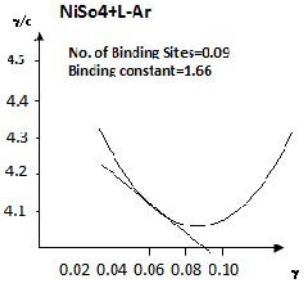

Fig.2

$KMnO_4$ has no +ve Value

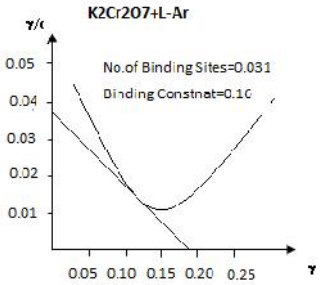

Fig.3

Fig.1,2 and 3 gives Scatchard plotes for $CuSO_4$+L-Ar,$NiSO_4$+L-Ar and $K_2Cr_2O_7$+L-Ar with incresing pH respectively

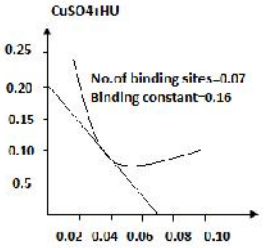

Fig.4

$KMnO_4$ has not getting +ve value

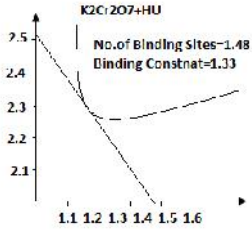

Fig.5

$NiSO_4$+HU has no proper nature is obtained

Fig.6

Fig 4 gives Scatchard plot for $CuSO_4$, Fig 5 for $K_2Cr_2O_7$, and Fig 6 for $NiSO_4$

Now similar study is carried out with decreasing pH.

$CuSO_4$ has no proper nature

Fig. 7

$KMnO_4$ has not getting +ve value

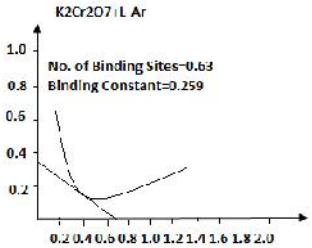

Fig 8

Fig.9

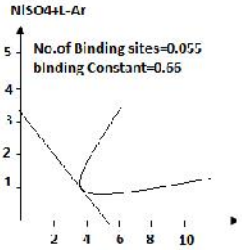

Fig.10

Fig. 7 and Fig 8 gives Scatchard plot for $CuSO_4$and $K_2Cr_2O_7$ respectively with varying amount of HU and Fig 9, 10 gives and Scatchard plot for. $K_2Cr_2O_7$and $CuSO_4$ respectively with varying amount of L-Arginine.

I) Table 1 gives binding parameters between for 3 cm^3 metal ion solution with increasing pH and with varying amount of L-Arginine and HU is Added.

Table 1

Solutions		**0-0.5cm^3L-Arginine with increasing pH**		**0-0.5cm^3 HU with increasing pH**	
3.0cm^3 of	λmax (nm)	No. of binding sites = n'	Binding constant = K'	No. of binding sites = n'	Binding constant = K'
$CuSO_4$	805	0.4	0.06	0.035	0.022
$KMnO_4$	525	0.8	0.10	0.062	0.055
$NiSO_4$	389	0.09	1.66	0.4	0.76
$K_2Cr_2O_7$	354	0.1	0.05	0.031	0.16

II) Table 2 gives binding parameters between for 3 cm^3 metal ion solution with decreasing pH and with varying amount of L-Arginine and HU is added.

Table 2

Solutions		**0-0.5cm^3L-Arginine with decreasing pH**		**0-0.5cm^3 HU with decreasing pH**	
3.0cm^3 of	λmax (nm)	No. of binding sites = n'	Binding constant = K'	No. of binding sites = n'	Binding constant = K'
$CuSO_4$	805	0.07	0.16	No. proper nature to graph	
$KMnO_4$	525	0.77	0.28	0.02	0.065
NiSO4	389	0.055	0.66	No. proper nature to graph	
$K_2Cr_2O_7$	354	0.1	0.05	0.031	0.16

Conclusion

From the graph it is observed that the binding interactions are different for different transitional metal ions for decreasing pH as follows:-

Increase of Cu, Mn and Cr there is decrease in the binding sites between the interactions of L-Arginine and HU there decrease in the association cost of Cu, Mn, and Ni and slight increase in case of Cr with increase of pH While at lower pH there is decrease in the binding sites in Mg and Cr, while in case of Ni, and Cu binding sites Of Arginine are very small and with HU no proper binding are observed. As far as association cost is consider there is reduction in the binding strength of binding for Mn with HU and increase in the binding strength with HU as compared to Arginine

From these observations it can be suggested that the binding of Arginine as well as HU is very much influence by pH of the medium. Particularly with increasing pH the effect appears to be much stronger. Also it can be seen that the binding with the metal to Arginine and HU is considerably pH dependent

References

1) Snyder S. Science, 54, 171-78(1992).
2) R. F., Vanhoutte P. M. FASEB J, 3, 2007-18 (1989);
3) Moncada S. and Higgs A, New Engl. J. Med, 329, 2002-12 (1993);
4) Lowenstien C.J.,Dienernam J. L.,Snydern S. H.,ANN. Intern Med. 120,227-37 (1994);
5) Ignarro L. J. FASEB J, 3, 31-36 (1989);
6) Anggard E. The Lancet, 343, 1199-1211 (1994);
7) Chakraborty K, Resonanc, 8 (4), 57-61 (2003);
8) Harald H. H., W. Schmidt and Uttrich W, Cell 78, 919-26 (1994).
9) A.K. Szardenings, M.F. Gordeev, and D.V. Patel, *Tetrahedron Lett.,* 1996,37,3635
10) Henry Y.,Lepoivre M., Drapier J.C.,Ducrocq C.,Boucher J. L., Guissani A., FASEB J,1,1124-34 (1993).
11) Holme D.J. and Peck, H.Anal. Biochem. P.395, Longman, London 1983.
12) Instrumental methods of analysis; Willard Merrit, Dean, Settle.(Seventh edition), CBS publishers & distributers, (1986), (pg. 159-166)
13) Spectroscopy, Clusters and molecular beam; N. P.Singh, Sublime publications (1999), (Pg.9-21)

18) G. Scatchard, A.N.Y.ASc. 51, 660, 1949
19) J.L.Irvin & E.M.Irvin, J.Prio.chem. 206, 39, (1954)
20) Peacock A.R. & Skerette N.M. Trans, Fareday Soc. 52, 261, 1956.
21) Harshada Gurav, Sangeeta Parab, A.V.Chitre, International Journal of Pharmaceuticals and drug Analysis.2016; 58 – 63
22) Sangeeta Parab, A.V. Chitre, society of free radical research- India BulletinVol.6, 2007, pg.7-9

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