INTERNATIONAL JOURNAL OF PHARMACEUTICS & DRUG ANALYSIS
VOL. 3 ISSUE 9, 2015; 322 – 325 ; http://ijpda.com; ISSN: 2348-8948

REVIEW ARTICLE

STUDY OF BINDING PARAMETERS FOR INTERACTION BETWEEN NITROGLYCERINE AND SOME PROTEINS AND AMINO ACIDS.

Poonam Shinde, *Sangeeta Parab, A.V.Chitre

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

Ex- Head Chemistry Department ,Sophia college, Mumbai-400026

Date Received: 26th September 2015; Date Accepted: 15th October 2015 Date published: 31th October 2015

Email: vprabhu74@yahoo.com

Abstract: Nitroglycerin belongs to a class of drugs called nitrates. Nitroglycerin has been used to treat angina pectoris and heart failure for over 130 years. Nitroglycerin (NG), also known as nitroglycerine, trinitroglycerin, trinitroglycerine, or nitro, is more correctly known as glyceryltrinitrate or more formally: 1, 2, 3-trinitroxypropane. It is a heavy, colorless, oily, explosive liquid most commonly produced by treating glycerol with white fuming nitric acid under conditions appropriate to the formation of the nitric acid ester. Nitroglycerine metabolises to Nitric oxide in vascular smooth muscle cells. Nitroglycerine is used to make nitric oxide a compound in the body that relaxes blood vessels. In the present study we proposed to observe the effect of this nitroglycerine with some amino acids, proteins and carbohydrates in both Ultraviolet and visible region (with addition of colour developing reagents). Effect on spectra is studied in terms of binding interaction like the binding sites and binding association constants. This Study is found to provide interesting and significant data, which possibly may have correlation with biological effects by NO* on these amino acids and proteins.

Key words: Nitroglycerine, Amino acids, Proteins binding

INTRODUCTION:

Nitroglycerin (NG) or Glycerol trinitrate (GTN) is an aliphatic nitrate ester containing compound that is important for manufacturing of explosives and rocket propellants and as a pharmaceutical vasodilator. It is commonly found in the waste streams and soils of munitions and fire cracker manufacturing facilities and pharmaceutical plants [1]. Concerns about toxicity and explosion hazards have led to increased efforts to develop safe and cost effective methods for treating GTN laden waste streams. A number of early studies on environmental fate of NG revealed toxicity to algae, invertebrates and vertebrates and further suggested that NG was recalcitrant to degradation [2]. NG affects the cardiovascular system, blood and nervous system of experimental animals and suffered by hypotension, tremors, ataxia, lethargy etc. Acute exposure to NG can cause headache, nausea, vomiting, occasionally diarrhoea, sweating and light headedness[3]. High exposure can cause abdominal cramps, vomiting, depression or mania, mental confusion, convulsions, paresthesia or paralysis, apasia, impaired vision, breathing difficulties, methaemoglobinemia and blue skin (Cyanosis), bradycardia, circulatory collapse or death[4] .

NG is a potent vasodilator of veins, arterial conductance vessels, and collaterals that has minimal effects on arteriolar tone. At the cellular level, NG is biotransformed by a still unknown enzymatic process in endothelial cells, smooth muscle, and to some extent platelets, causing it to release the vasodilator and anti-aggregatory principle nitric oxide. The two major drawbacks of nitrate therapy that have been shown to be important are the rapid development of nitrate tolerance and endothelial dysfunction within several days of prolonged NTG treatment[5].

The free radical nitric oxide has direct influence on the spectral properties of amino acid, protein and particularly it has binding interactions with some of them are observed. Since nitroglycerine is precursor of nitric oxide synthesis in human body its interaction with amino acids and proteins becomes important. Since many Amino acids like Glutamic acid, l-arginine and proteins like Amylase, bovine serum albumin, Papain, Egg Albumin are required for many biological processes like enzyme activity. NO functions as a neurotransmitter, a macrophage derived defence agent against foreign organism and regulate blood flow as vasodilator. NO can serve as a one electron pseudo halide. Nitric oxide group can also bridge between metal centres through N-atom in variety of geometries. UV Spectroscopy method is one of the instrumental

analytical methods that are widely used in pharmaceutical industries for the assay of pharmaceutical products, because it is simple, easy, less time consuming and an economical method[5]. The main objective of this study is to determine Binding parameters for Interaction between NG and Proteins, Amino Acids etc.

MATERIALS & METHODS

Chemical and Reagents : - All the chemicals used for the work are of A.R. grade of S.D.Fine Chem. or Merk.

Instruments :- UV-Visible spectrophotometer (Shimadzu modelUV-2450) and Electrical balance (Type Citizen CY 204).

Experimental:-

Amino acids - Glutamic acid, L-arginine, Proteins , Amylase, Egg Albumine, Papain , Bovine serum albumin and Starch and Fructose were selected as representative compounds of each class. These Biological solutions are studied at its λ_{max}.0.01M aqueous solution of these were used for spectroscopic study. To 3.0 ml of these biological solutions (Amylase, BSA, Egg Albumin Glutamic Acids , L-Arginine) and visible solutions (Amylase, BSA, Egg Albumin Glutamic Acid L-Arginine) varying amount of (0.005-0.1 ml) Nitroglycerine is added and effect on spectra is studied with the help of scatchard plot [7-9].The study is carried out also in presence of other binding substance .

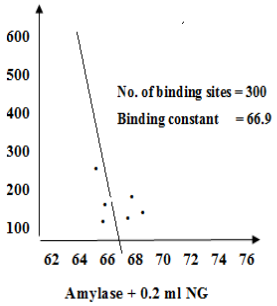
RESULTS AND DISCUSSIONS

a) Biological solution-nitroglycerine binding interactions by scatchard plots to calculate binding parameters. Table 1 gives comparison of binding parameters of Nitroglycerine between UV and Visible region , when variable amount of Nitroglycerine is added to 3.0 ml of biological solution.

TABLE 1: Comparison of Binding Parameters of Biological solutions

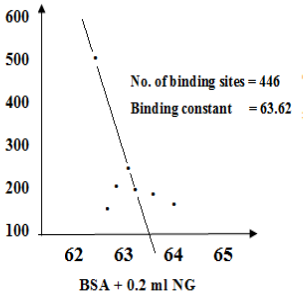
Biological solutions		0.01 - 0.2 Cm^3 NG (UV Region)		0.005 - 0.1 Cm^3 NG (Visible Region)		
3ml of	λ_{max} nm	No. of binding Sites = n′ = n′	Binding constant = K′	λ_{max} nm	No. of binding Sites = n′	Binding constant = K′
Amylase	276	300	66.9	575	16.25	170
Bovine serum Albumin	276	446	63.62	602	2.5	42.5
Egg Albumin	276	1000	71.6	591	10.27	30.88
Glutamic Acid	202	222.22	70.2	436	9.25	166
Papain	268	125	67.3	590	8.42	162
L-Arginine	202	23.3	66	590	9.11	56.9
Fructose	251	9.79	14.45	---	------	--------
Starch	---	--------	---------	592	7.14	12.8

UV Region Scatchard plots :-



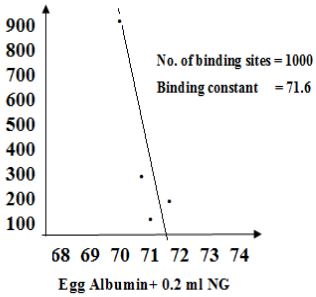
Amylase + 0.2 ml NG

Fig 1



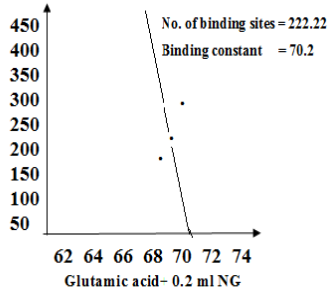
BSA + 0.2 ml NG

Fig 2



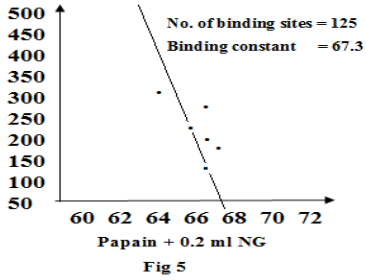
Egg Albumin+ 0.2 ml NG

Fig 3



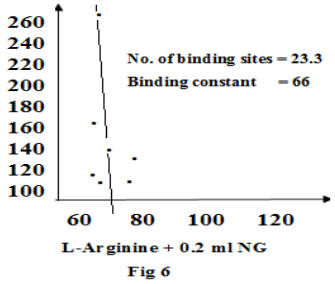
Glutamic acid– 0.2 ml NG

Fig 4



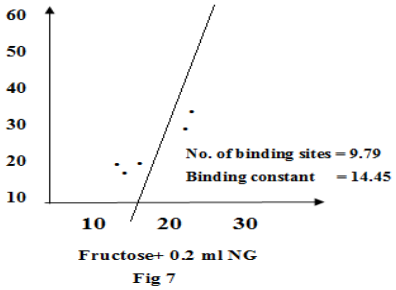
Papain + 0.2 ml NG

Fig 5



L-Arginine + 0.2 ml NG

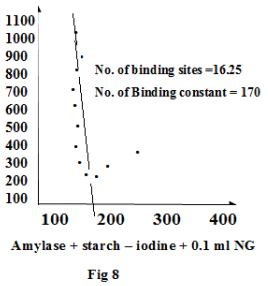
Fig 6



Fructose+ 0.2 ml NG

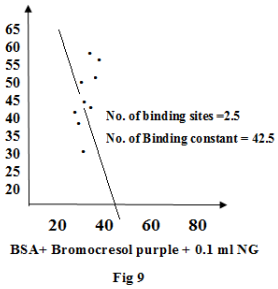
Fig 7

Visible Region Scatchard plots :-



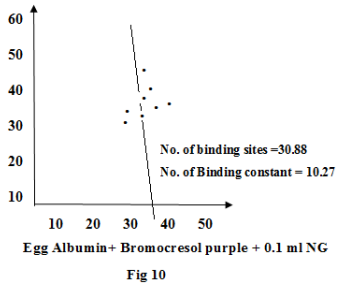
Amylase + starch – iodine + 0.1 ml NG

Fig 8



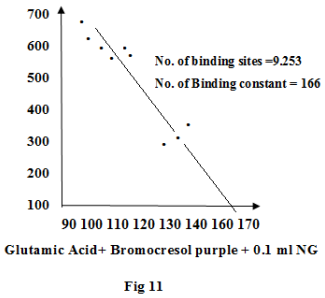
BSA+ Bromocresol purple + 0.1 ml NG

Fig 9



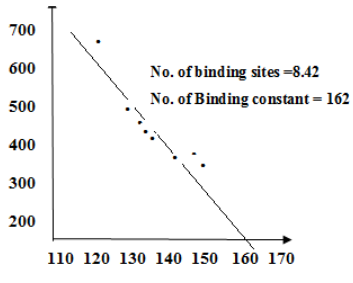
Egg Albumin+ Bromocresol purple + 0.1 ml NG

Fig 10



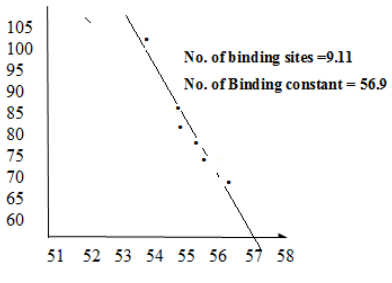
Glutamic Acid+ Bromocresol purple + 0.1 ml NG

Fig 11



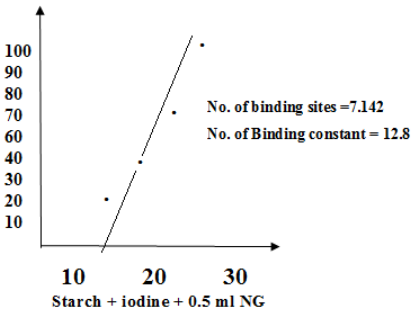
Papain+ Bromocresol purple + 0.1 ml NG

Fig 12



L- aginine + Bromocresol purple + 0.1 ml NG

Fig 13



Starch + iodine + 0.5 ml NG

Fig 14

Fig 8 Amylase + Starch – iodine + 0.1 ml NG, Fig 9 BSA + bromocresol purple + 0.1 ml NG, Fig 10 Egg Albumin + bromocresol purple + 0.1 ml NG , Fig 11 Glutamic acid ++ bromocresol purple + 0.1 ml NG , Fig 12 Papain + bromocresol purple + 0.1 ml NG, Fig 13 L-Arginine ++ bromocresol purple + 0.1 ml NG, Fig 14 Starch + iodine + 0.5 ml NG

CONCLUSIONS

From the above data it was observed that the NG reacts differently with individual Amino Acids and Proteins but with over all good binding.The observation in UV region show better interaction as compare to the values in visible region suggesting the interference due to bromocresol purple. Bromocresol purple might be interfering probe.

As regards Carbohydrate the data is insufficient at this time and will have to be studied more but there is certainly interaction between Starch and NG. Thus NG has side effect in terms of interactions with Proteins and Carbohydrates.

REFERENCES

1) Chen et al.; Foster MW ; Zang , J ; Mao, L ; Rockman , HA ; Kawamoto,T;Kitgawa, K; Nakayama ; KI et al. (2005) . "An essential role for mitochondrial aldehyde dehydrogenous in Nitroglycerine bioactivation " ProcNatl.Acad.sci.USA 102 (34) : 12159-12164
2) Ignore LJ, Lippton H, Edwards JC, Baricos WH, Hymen AL, Kadowitz PJ, Gruetter CA.Mechanism of vascular smooth muscle relaxation by Organic nitrates , nitrites , nitroprusside and nitric oxide. Evidence for the involvement of S- nitrosothiols are active are active intermediates J.Pharmacol Exp Ther; 218 : 739-749.
3) Bosegard s, Alldeerhive J, Poulsen HE Preventive administration of intravenous N-acetylcysteine and development of tolerance to isosorbide dinitrate in patient with angina pectoris.Circulation 1992;85 : 143 - 149
4) The Scitech journal ISSN 2347 - 7318
5) International Current Pharmaceutical Journal 2011, 1(1):1-5
6) Snyder S. H., Science, 54, 171-78(1992).
7) George Scatchard , Ann. NY Acad sci. 51,660, 1949
8) J. L. Irvin & E. M. Irvin, J. Prio. chem. 206, 39, (1954)
9) Peacock A.R. & Skerette N.M. Trans, Fareday Soc. 52, 261, 1956.