

Azo Complexes: Role in Cancerous Diseases

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ABSTRACT

Carcinogenesis is caused by mutation and epimutation of the genetic material of normal cells, which upsets the normal balance between proliferation and cell death. This results in uncontrolled cell division and the evolution of those cells by natural selection in the body. In fact, there is a higher percentage of cancer among chemists than in the general population. More and more compounds are being identified as having carcinogenic activity in animals and are therefore suspect in humans. The object of this work is to compare the ligand *o*-hydroxy benzene-azo-2 naphthol with those of benzene azo-2 naphthol in forming alkali-metal complexes and to study the role of former complexes in cancerous diseases. *o*-*o*'-dihydroxy azo compounds form coordination complexes more readily than *o*-hydroxy azo-compounds, and in the former case the metal chelates are also markedly stable. For the metal complexes of *o*-*o*'-dihydroxy azo dyes, that structure is to be favoured in which the metal is held between the azo groups and both the hydroxyl groups. The work on azo-complexes was extended in which a series of mixed ligand complexes of alkali-metal salts of different organic acids with this ligand were synthesized having general formula MLOH-BAN.

Keywords: Azo complexes, Carcinogenesis, Cancer, *o*-hydroxy benzene-azo-2 naphthol, azo-2 naphthol.

INTRODUCTION

Cancer is a formidable disease that is killing increasing number of people every year in virtually all the countries of the world. Surgery and radiation therapy have a great curative potential for localized tumors. Unfortunately, by the time such tumors are detected they have usually spread to other organs and the only treatment for disseminated cancer is chemotherapy although immunotherapy holds encouraging promise for the future. The circumstances will be improved as we recognize and eliminate many of the environmental carcinogens. Some epidemiologists estimate that up to 90 percent of all cancers are produced by environmental factors.

Cancer certainly, is a social evil since it places second in claiming deaths but it has proved to be very hard to establish the direct dependence of its origin upon the living conditions of the populations.

It has been established that a wide variety of chemicals can induce cancer. For the present discussion chemical carcinogens can be divided into certain groups in which azo-compounds play a vital role.

MATERIAL AND METHODS

In this research work, I have tried to analyze regulatory documents, detail review of related literature and research papers etc.

RESULTS AND DISCUSSION

According to Bernarol Peyrithe "Cancer is a disease which is just as difficult to define as it is to cure". Cancers are generally differentiated by two characteristics, their origin (tissue), and the way they develop and grow. The successive steps by which a normal cell becomes malignant have not been delineated. Nevertheless, it is well known that a wide variety of chemicals can induce cancer. For the present discussions, chemical carcinogens can be divided into five groups: polycyclic aromatics, biological alkylating agents, aromatic amines and azo-compounds, N-nitroso-amines and amides, and metallic substances.

Actually a number of differences have been observed between cancer and normal cells. Compared with normal cells cancer cells have:

- (i) Lower pH
- (ii) Lower calcium ion and higher potassium ion concentration.

We have characterized the azo-complexes formed by the interaction of benzene azo-2 naphthamine with sodium and potassium salts of various organic acids like IN2N (1-nitroso 2-naphthol), 8HQ (8-hydroxy quinoline), ONP (ortho-nitrophenol) and 2H3NA (2-hydroxy 3-naphtholic acid) in ethanolic medium and studies their role in cancerous disease by measuring their pH values. This work is highly interesting as the complexes contain azo group and NH₂ group. Both have cancer

producing tendency. Therefore, this work throws some more intense light on the chemical aspects of some of the developments in cancer chemotherapy with the hope that it will attract the additional chemists into the war on cancer.

We have observed that the pH of ligand ortho hydroxyl azo-2 naphthylamine in absolute ethanol at room temperature is at pH 11.1. As we go on adding various salts e.g. M1N2N, MONP and M2H3NA having amounts 500 mg, 1gm, 1.5gms, 2 gms and 2.5 gms for every mentioned salts separately, we have seen that the pH decreases.

The pH measurement was taken at atmospheric pressure and at 22-25°C. The pH values are listed in the following table.

Table 1

Ligand	Salt added in milligrams	pH
OH-BAN=L2 in 95% ethanol	-	9.5
	500	9.3
	1000	9.0
	1500	8.8
	2000	8.5
	2500	8.2
	Salt M8HQ added in milligrams	pH
	500	8.1
	1000	8.8
	1500	8.4
	2000	8.0
	2500	7.7
	Salt MONP added in milligrams	pH
	500	8.9
	1000	8.4
	1500	7.9
	2000	7.4
	2500	6.9
	Salt M2H3NA added in milligrams	pH
	500	8.8
	1000	8.2
	1500	7.6
	2000	7.0
	2500	6.4

Apart from β -naphthylamine we have azo group having 0-0' substituents as OH and NH₂ which have electron releasing nature. Therefore, electron density on azo group is maximum in this case and thus it has the maximum carcinogenic tendency.

By exogenic synthesis in human system some unsaturated groups and binding sites having high electron density are formed, then they may produce cancer. For example some forms of cancer is linked with the saline composition of the water that one regularly drinks. There is an ethnic group members which invariably drink water which contains a low concentration of magnesium salts, the incidence of

carcinoma of the stomach in this group is statistically higher than in others.

To see the role of azo-complexes in cancerous disease we took azo-complexes formed by the interaction of azo-ligands like benzene azo-2-naphthol, ortho-hydroxy benzene azo-2-naphthol, ortho-carboxyl benzene azo-2-naphthol, ortho-hydroxy benzene azo-2-naphthylamine and sodium and potassium salts of 1-nitroso 2-naphthol, 8-hydroxy-quinoline, ortho-nitrophenol and 2-hydroxy 3-naphthoic acid in ethanol.

The complexes have been synthesized and characterized by elemental analysis, decomposition temperature and infra red spectra. Since cancer cells have lower calcium ion and higher potassium ion concentration. Therefore, azo-complexes with these calcium and potassium salts may throw some light on to lower the concentration of potassium by attracting it towards -N=N-group of the ligands taken. In this manner cancerous activity may be lowered.

Due to exogenic synthesis inside our system, it may be that (-N=N-) group is temporarily formed. Since due to higher electron density on nitrogen, it comes under the category of carcinogen, hence we thought that if it forms complexes by the salts which are taken orally, then the electron density of nitrogen of -N=N-group may be certainly lowered and thus carcinogenic activity may be reduced.

If concentrations of potassium inside the biological system is increased then the cell may be cancerous. In this case also, the (-N = N-) group is useful to lower the concentration of potassium and thus the cancerous activity of cells may be reduced. In either cases the study is important and useful.

A series of mixed ligand complexes of alkali metal salts were synthesized having general formula MLOH-BAN. Where M = Li, Na and K, L= deprotonated organic acids; 1-nitroso 2-naphthol(1N2N), 8-hydroxy quinoline(8-HQ), ortho-nitrophenol(ONP), 2-hydroxy 3-naphthoic acid(2H3NA), salicylic acid, salicylaldehyde, and OH-BAN (ortho- hydroxy-benzene -azo-2-naphthol). The complexes were stable when stored under dry condition e.g. in a desiccator. All the complexes of ligand are colored either green, dark violet or brown. When heated, they underwent decomposition at a temperature higher than the melting point of ligand, OH-BAN. The complexes broke on heating to form the simple salts and ligand; and as such threw light on the fact that the bonding in these complexes was not strong. On the basis of analytical result and infra-red studies, these complexes were characterized.

O-hydroxy-benzene azo-2-naphthol formed coordination complexes more readily than benzene azo-2-naphthol and were comparatively much more stable. The higher decomposition temperatures of the complexes than the azo-ligand suggested that the compounds were genuine and not a stoichiometric mixture of the two ingredients. The ligand OH-BAN was multidentate and, therefore, formed cyclic metal complexes. The presence of two-OH groups in the o-o' positions to the azo group suggested possibility of intra-molecular hydrogen bonding stronger than the o-monohydroxy-azo ligand. Thus the ligand OH-BAN formed the stable complexes as the metal was complexed in macrocyclic form.

CONCLUSION

A number of differences have been observed between cancer and normal cells. e.g. compared with normal cells, cancer cells have lower pH and different potassium isotope ratio. On this basis we determined the pH of ligand OH-BAN in ethanol medium and also various pH values obtained when we add alkali metal

salts of different organic acids taken in alcoholic solution of the ligand. After each addition the mixture as a whole was refluxed over a hot plate using magnetic stirrer and then cooled.

On the basis of observation in Table 1 we may argue that OH-BAN has more carcinogenic effect compared to BAN. Thus this type of organic compounds may be used in synthesizing chemotherapeutic drugs for cancerous diseases.

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