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## Conductometric Studies on the Charge Transfer Interaction of Some Genetic Bases with 4-Nitroquinoline-1-Oxide

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**ABSTRACT:** 4- Nitroquinoline-1-oxide (4-NQO) is a carcinogenic compound. In this paper the charge transfer interaction between acceptor 4-NQO and Genetic Bases like Adenine, cytosine, Uracil has been studied with the help of Conductometric Studies.

**KEYWORDS:** 4-NQO, Adenine, cytosine, Uracil, Conductometric studies, Cancer, Charge Transfer Interaction.

### I. INTRODUCTION

Cancer has been defined as an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissue and persists in the same excessive manner after the cessation of the stimuli which evoked the change. This change may occur due to physical or chemical interaction of a carcinogenic compound with four major classes of organic compounds available in living cells. These compounds are protein, carbohydrates, lipids and nucleic acids. The mutagenic<sup>1,2,3,4,5</sup> and carcinogenic<sup>6</sup> activities of 4-NQO have already been reviewed. Its interaction with nucleic acids has been studied *in vivo*<sup>7,8,9,10,11</sup> and *in vitro*<sup>12,13,14</sup>. However, the nature of its binding to DNA and hence the carcinogenic mechanism of 4-NQO has yet been fully explored. Since 4-NQO is a potent carcinogen<sup>15</sup> and acts as a good electron acceptor. The charge transfer interaction of this carcinogen<sup>16</sup> with some of the DNA<sup>17</sup> moieties (genetic bases), such as, adenine, cytosine and uracil has been studied using electrical conductance measurement in order to provide additional evidence on its charge-transfer actions as an acceptor<sup>18</sup> and hence on the mechanism of its carcinogenesis.<sup>19,20</sup>

### II. EXPERIMENTAL

The donors (adenine, cytosine, uracil) were obtained from Fluke and have been used as such. The acceptor, 4-nitroquinoline-1-oxide (4-NQO), was procured from Sigma. Solvent dimethyl sulfoxide was AR grade (B.D.H.) Stock solutions of donor and acceptor of appropriate concentration were prepared by w/v in the above solvent. Electrical conductance were measured by Phillips PR-9500 conductivity bridge and conductivity cell (immersion of dip type) having cell constant 0.8178.

All the measurements were made at 50 Hz. Conductivity cell was standardized each day with N/50 KCl solution using Lind, Zwolenik and Fuoss<sup>21</sup> constants. The conductivity experiments have been performed as follows:

- By using Gutmann's<sup>21-24</sup> technique to study the charge transfer complexation process, the equimolar stock solutions of donors and acceptor were prepared and varying the volumes of donor and acceptor.

### III. RESULTS AND DISCUSSION

On mixing a solution of genetic base (adenine, cytosine or uracil) with a solution of 4-NQO<sup>25</sup> in the DMSO solvent, an appreciable increase in conductance was noticed with the increase in donor concentration and keeping the acceptor concentration constant. At this stage, there may be doubt that the relative increase in

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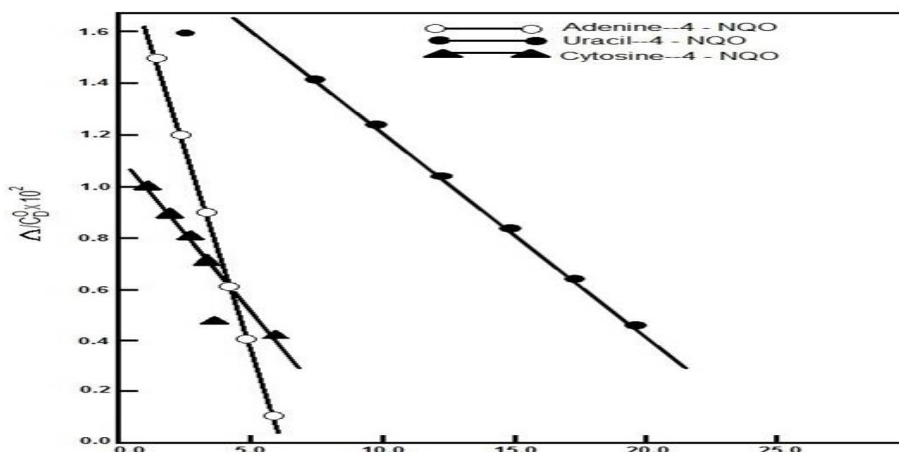


FIG. 1.1 Plots of  $\Delta$  versus  $\Delta/C_D^0$  for Adenine, Uracil, Cytosine and 4-NQO complexes in Dimethyl Sulphoxide.

conductance may be due to the increase in donor concentration and not due to charge transfer interaction. This problem has been solved by taking the conductance of donor and acceptor solution separately. Now on mixing the equal amount of donor and acceptor solution, the conductance increases appreciably more than that of separate component. This appreciable increase in conductance is due to charge transfer interaction and not due to the donor concentration. Thus, this relative increase in conductance of solution may be interpreted due to the charge transfer from donor to acceptor.

Charge transfer interaction between genetic bases and 4-NQO was studied in dimethylsulfoxide solvent. The titration technique has indicated that DNA bases (adenine, cytosine & uracil) FIG. 1.1, form 1:1 complexes with 4-nitroquinoline-1-oxide.

The solvent dimethylsulfoxide used in this study is non-conducting. The genetic bases show little conductance. A representative molar ratio plot for uracil: 4-NQO complex is shown in FIG. 1.2. On mixing 1ml of donor and 1ml of acceptor solution, an appreciable increase in conductance was noticed. Similarly, an increase in refractive index may be interpreted due to the transfer of charge from donor to acceptor. The equilibrium constant data (Table 1.1) indicate the following complexing strength of donors: adenine>cytosine>uracil.

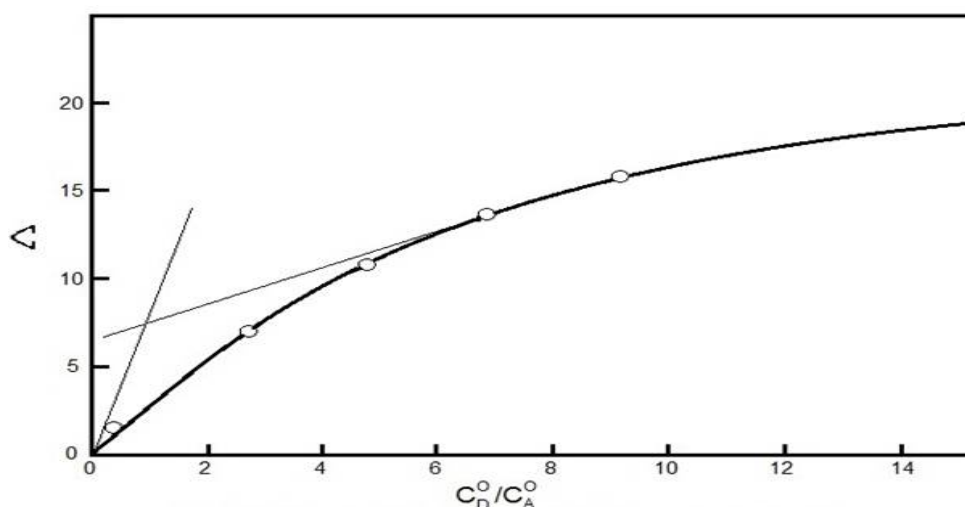


FIG. 1.2 Molar ratio plot for the Uracil-4 - NQO complexes in Dimethyl Sulphoxide determined by electrical conductance method.

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Table 1.1 Equilibrium Constant ( $K_1$ ) and Extent of Polarization ( $\rho$ ) Data for 1:1 Molecular Complexes of 4-NQO with some genetic bases in DMSO at 32 °C

| Genetic Bases | Concentration Range of donor* | $K_1$ (dm <sup>3</sup> mol <sup>-1</sup> ) | Extent of polarization $\rho \times 10^3$ |
|---------------|-------------------------------|--|---|
| Adenine       | 0.008-0.625M                  | 28.0±4.00                                  | 303.00                                    |
| Cytosine      | 0.013-0.156M                  | 12.5±2.00                                  | 217.00                                    |
| Uracil        | 0.054-0.500M                  | 7.9±0.25                                   | 80.00                                     |

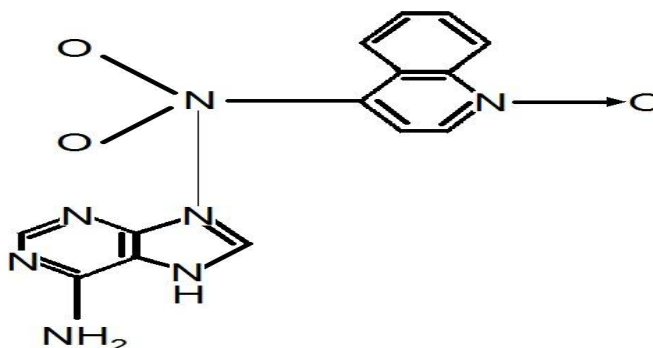
\*The concentration of the acceptor (4-NQO) was kept constant at ca.  $2 \times 10^{-4}$  M in each case.

The equilibrium constant of guanine : 4-NQO complex could not be determined due to the less solubility of guanine. However, it is clear from the equilibrium constant data that purine base (adenine) forms stronger complex than the pyrimidine bases (thymine, cytosine & uracil). The site of interaction of the DNA bases cannot be located by the electrical conductance technique.

However, from the equilibrium constant data it may be proposed that n- $\pi^*$  charge-transfer plays an important role in the interaction of DNA bases<sup>26,27</sup> with 4-NQO.

Based upon the above experimental results, a model for the carcinogenesis<sup>28,29,30,31</sup> of 4-NQO may be proposed, DNA and RNA are basic units of nucleic acid. Adenine, cytosine and uracil are constituent units of DNA and RNA in a human-being who takes betel quid<sup>32</sup>, 4-NQO enters his body where it may interact with adenine, cytosine or uracil under favorable conditions forming charge transfer complexes.

In such charge transfer complexes, there is distinct possibility of n- $\pi^*$  interaction as shown below:



Present model requires further work *in vivo* to propose a definite mechanism for the carcinogenesis of 4-NQO. This model finds support from the work of Tsibris,<sup>33</sup> *et al.* on the interaction of adenine with flavin, where the interaction takes place from N<sub>9</sub> position of adenine because it is highest occupied molecular orbital (HOMO).

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## IV. CONCLUSION

Cancer has been defined as an abnormal mass of tissue the growth of which exceeds and is uncoordinated with that of normal tissue and persists in the same excessive manner after the cessations of the stimuli which evoked the changes. 4-NQO is present in betel quid, in human beings who takes betel quid 4-NQO (acceptor) enters his body where it may interact with genetic bases (adenine, cytosine or uracil) under favorable conditions forming charge transfer complexes. In this paper these charge transfer complexes studied by conductometric studies, by this interaction the normal functions of the cell become disturbed leading towards the abnormality in the function of the cell. This abnormality may later on appears in the form of mutagenesis which transforms into carcinogenesis.

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