OPTICAL STUDIES OF PENICILLIN GROUP IN RELATION TO THEIR MEDICAL ACTIVITY

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ABSTRACT

The study of Medical activity of antibiotics is gaining momentum now a days owing to the importance of their curative values. The Medical Activity correlated to molecular interactions, can be studied by various physical techniques, at present optical methods like Refractometry and Polarization are used to study the activity of a few antibiotics like Penicillin. The Refractive Indices Mean Molecular Polarizability Diamagnetic Susceptibilities and Electron Ionisation Cross Section are interpreted in terms of dosages and the toxic effects if any due to over dosages are discussed critically.

Keywords: Refractometry, Medical Activity, Antibiotics, Diamagnetic susceptibilities, and Electron Ionisation Cross Section.

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1. INTRODUCTION

Antibiotics are chemical substances excreted by some microorganisms, which inhibit the growth and development of other microbes. The study of the physical and optical properties of antibiotics plays a vital role in drug designing and understanding their pharmacological activities. Molecular biology & Biomolecular engineering are the two fields of research of much important in this direction. Though many physical techniques like UV, Visible, IR, NMR, Raman and Laser have been used to study the pharmacological activities in terms of chemical activities, but not much work has been done in utilizing optical Polarizabilities and related properties like Diamagnetic Susceptibilities, molecular ionisation cross-section as tools in this field. Rao et al [1] and Murthy et al [2, 3] and Murthy and Jeevan Kumar [4] have been successfully used the techniques of the Polarizabilities in the confirmations of Biopolymers, synthetic polymers and Liquid crystals. This paper reports the study of Molecular Polarizabilities of few antibiotics (Penicillin Group), structures of these antibiotics are shown in the Fig. 1, by using Lippincot δ -function potential model, Molecular vibration method and through Bond Refractions and using the same to determine diamagnetic susceptibilities, electron ionisation cross-section and to correlate Q values with the degree of covalency on one hand and with the effective number of electrons on the other hand. And the results are discussed critically.

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2. THE METHOD

2.1 Mean molecular polarizabilities

Methods used to determine Mean Molecular Polarizabilities are

1. The method based on Lippincot – δ -function Potential Model [5].
2. Molecular Vibration method [6].
3. Mean Molecular Polarizabilities through bond refractions [7].

The first two methods are based on Quantum Mechanical approach and Vibrational spectroscopic parameters respectively.

The last method is an empirical relation developed by Murthy et-al and it is based on the bond refractions.

Final expressions governing the above methods are given below.

2.2 Lippincot – δ -function potential method

$$\alpha_M = 1/3(\Sigma\alpha_{||p} + \Sigma\alpha_{||n} + \Sigma 2\alpha_{\perp}) \quad (1)$$

Where $\alpha_{||}$ - parallel bond components from the δ -function model.

$\alpha_{||n}$ - parallel components from the non bonded region electrons.

$\alpha_{\perp}$ - perpendicular bond components from atomic δ -function model.

2.3 Molecular vibration method

$$\alpha_M = \Sigma n_i/3 (b_L + 2b_T)_i \quad (2)$$

Where b_L and b_T are the longitudinal and transverse Polarizabilities of i^{th} and n_i is the number of bonds of i^{th} kind in molecule.

2.4 Method based on bond refractions

$$\alpha_M = 3/4\pi N \Sigma(R_{\infty})_I \quad (3)$$

Where N is Avogadro's number ΣR_{∞} is the summations of the bond refractions of various bonds present in the molecule.

2.5 Diamagnetic susceptibilities χ_M [8].

Diamagnetic susceptibilities and Mean molecular Polarizabilities depend upon the effective number of free electrons which will be free to take part in magnetic and optical interactions. In view of these considerations a semi empirical relation was proposed by Rao et-al [4], which is given as

$$\chi_M = (\gamma_m \sigma^1) \alpha_M \quad (4)$$

$\gamma = (0.9)^n$ represents saturation state of the molecule with n denoting the number of unsaturation rings and bonds present in the molecule.

σ^1 is the degree of the covalency of the characteristic group. And $m = 0.72 \times 10^{19}$ is characteristic constant. The diamagnetic susceptibility values of Penicillin group compounds are

determined here by substituting α_M values calculated by various methods in the above expression.

2.6 Molecular electron ionization cross-section [9]

The molecular electron ionization (Q) of the various antibiotics is calculated utilizing diamagnetic susceptibilities using Rao and Murthy's relation.

$$Q = 0.278 \gamma \chi_M \quad (5)$$

The mean molecular polarizabilities, diamagnetic susceptibilities and molecular electron ionization cross sections of various antibiotics such as few compounds of penicillin group are determined by the above methods and are listed in the tables 1, 2, 3 & 4, respectively.

3. RESULTS AND DISCUSSIONS

From table 1 it is seen that the agreement among mean molecular polarizability values obtained by Lippincot – δ -function method, Molecular Vibration method, Bond refractions and Addition bond Polarizabilities are very good. Since the experimental values of α_M for these compounds are not available, it is not possible at present to compare these values with the experimental values. Since bond Polarizabilities are accepted as one of the standard method to evaluate α_M by Le Fevre [10], the values obtained by this method may be taken as reference datum for comparison. However, the good agreement among the results reveals, beyond doubt, their reliability as well as the applicability of these theoretical methods for the evaluation of mean molecular Polarizabilities of antibiotics.

A glance at the tables 2 & 3 reveals the good agreement among the values of χ_M and Q values obtained by using α_M (from Lippincot – δ -function method, Molecular vibration method and Additions bond Polarizabilities), values. However the comparison of χ_M and Q is also not possible as they are not reported so far. But Subbaiah [9] applies these methods for many systems and theoretically computed values were reported to have good agreement with the experimental values. Hence χ_M and Q values calculated for these antibiotics are taken to be fairly reliable.

In the case of molecular ionization cross-section, the concept of $Q_{\text{effective}}$ is used. The substances which are added to the main group are treated as separate group, then the activity of the entire antibiotics can be explained in terms of the activity of the main group + that of the substituents. For example in cyclic compounds, the effective Q can be fit with the calculated Q by the following relationship.

$$Q_{\text{eff}} = Q_{\text{main group}} + \alpha \log \pi (\Delta p_i) \quad (6)$$

Where p_i refers to the effective number of electrons of substituent group i and α is constant and is equal to 1×10^{-16} the $Q_{\text{effective}}$ values of these antibiotics are listed in table 4 and they are also in good agreement with the computed Q values.

A graph is drawn between $Q^{1/2}$ and $\sigma^{1/2}$ [Fig. 2]. This shows a regular variation there by showing that the ionization activity and degree of covalency are well related through the number of free electrons (available for reaction) present in the antibiotics [11]. Thus the electron ionization cross section could be correlated to the degree of covalency on one hand and with the effective number of electrons on the other hand. The larger the values of Q, the higher the efficiency of the molecule to partake in the reaction. This is also reflected in increase in value of σ , the degree of covalency. We could thus see that $\sigma^{1/2}$ is proportional to $Q^{1/2}$, with a maximum deviation being about 8%. Efforts to quantify the relation between Q and the reactivity of the antibiotics are in progress.

Fig. 1: Some Natural and semi synthetic penicillins showing the basic core of 6-aminopenicillanic acid with side chains which differ, thereby conferring special properties.

Fig. 2: Relation of Q with σ .

Table 1: Mean molecular polarizabilities ($\alpha_M \times 10^{23}$ c.c.) obtained by different methods.

Compound	Lippincot δ function method	Molecular vibration method	From bond refractions	From addition of bond polarizabilities
Penicillin – G	3.614	3.779	3.386	3.649
Penicillin – V	3.691	4.004	3.504	3.769
Penicillin – F	3.331	3.712	3.051	3.490
Phenethicillin	3.894	4.231	3.684	3.988
Methicillin	3.945	4.362	3.753	4.018
Ampicillin	3.866	4.061	3.569	3.884

Table 2: Diamagnetic susceptibilities ($\chi_M \times 10^6$ C.G.S. units).

Compound	Lippincot δ function method	Molecular vibration method	From addition of bond polarizabilities
Penicillin – G	60.967	63.753	61.558
Penicillin – V	48.502	52.609	49.525
Penicillin – F	54.005	60.172	56.575
Phenethicillin	49.165	53.419	50.347
Methicillin	38.792	42.884	39.505
Ampicillin	64.480	67.752	64.800

Table 3: Molecular electron ionization cross sections ($Q \times 10^{16}$ cm²).

Compound	Lippincot δ function method	Molecular vibration method
Penicillin – G	12.356	12.920
Penicillin – V	9.830	10.662
Penicillin – F	11.041	12.195
Phenethicillin	9.964	10.826
Methicillin	7.862	8.691
Ampicillin	13.068	13.731

Table 4: The relation of Q with σ .

Compound	Q	σ	Q_{eff}
Penicillin – G	12.356	0.321	12.176
Penicillin – V	9.829	0.250	10.023
Penicillin – F	11.047	0.309	11.000
Phenethicillin	9.964	0.241	9.178
Methicillin	7.862	0.187	10.059
Ampicillin	13.068	0.318	12.954

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