CHAPTER V

CENTRALLY ACTING MUSCLE RELAXANTS

Abstract

In the world of pharmacology, the prescription of a medicine and its dosage play important role. Different physico-chemical methods are in vogue in describing the interactions of the drug molecule with host target among them, the chief being spectroscopic, chromatographic and quantum mechanical techniques. Very recently the projection of molecular electron ionization cross section in relation to medicinal parameters, protein binding, bioavailability, log P and half life period has been used as a method of evaluating the dosage of medicinal compound.

The molecular electron ionization cross section ‘Q’ is evaluated from the molecular polarizability and diamagnetic susceptibility. The application of electron ionization cross section ‘Q’, in calculating the dosage of medicinal compounds is presented in this chapter on centrally acting muscle relaxants. These include Methocarbamol, Meprobamate, Metaxalone, Carisoprodol, Dantrium and Baclofen. This method compared favourably with the reported methods. For example the evaluated dosage of Meprobamate is 1.660 grams per day agree with the supported dosage value 1.60 grams per day. Similarly Metaxalone has the calculated dosage value 3.069 grams per day compared to the reported dosage value 3.200 grams per day. Thus the present method enables a new approach in finding out the dosage and drug activity which involves less cumbersome theoretical and computational difficulties.
5.1 INTRODUCTION:

Strains, sprains and other muscle injuries can result in pain, stiffness and muscle spasms. Muscle relaxants do relax muscles ease discomfort and stop muscle spasms. Muscle pain is the characteristic feature of several conditions. For example, in certain viral fevers such as Chicken gunya, the patient experience severe muscle pains. Similarly in case of Arthritis, the patient will be thrown into discomfort initially and may become disable in severe condition. People belonging to risky jobs in various fields such as workers in mine, software engineers suffer from joint pains and severe chronic back pain. During injuries in particular athletes during sports, post operative conditions, as side effects of several antimicrobial drugs induction, during accidents, also at the time of various infections, during over exercise, centrally acting muscle relaxants play an important role in releasing the pain. In view of the increasing importance to these conditions, muscle relaxant drugs have been selected and studied. The discovery of central acting muscle relaxants dates back to 1910. Berger and Bradely in 1946, observed the muscle relaxant activity present in large number of glycerol mono ether and analogues.

Skeletal muscle relaxants (See and Ginzburg, 2008a) consist of both anti spasticity and spasmodic agents. Approximately 2 million people per year report using a skeletal muscle relaxant, primarily for back pain, with an estimated 3,00,000 of the patient being elderly. Sparmolytic agents generally work by either enhancing the level of inhibition, or reducing the level of excitation. The benzodiazepines, such as diazepam, interact with the GABA receptor in the central nervous system (Miller, 1998) and Baclofen is considered to be an effective as diazepam in reducing spasticity (Cazalets et al., 1998) and cause much less sedation. Dantrolene is a spasmolytic agent with a unique mechanism of action out side the CNS.

Other common spasmolytic agents include Methocarbomol, Carisoprodol, Chlorzoxazone, Metaxalone and Orphenadrine. Meprobamate, a potent adenosine reuptake inhibitor and related drugs include Carisoprodol and Tybamate.

5.2.1 MEPROBAMATE:

Introduction: Meprobamate was first synthesized by Bernard John Ludwig and Frank Milan Berger at caster products in 1950.
It became the first blockbuster psychotropic drug in American history (Andrea, 2009). It is classified under substituted alkanediols and analogues.

**Chemistry:** A good member of 1,3–alkanediols and their structural analogues have been reported to be potent muscle relaxant drugs.

**Structure:** Molecular structure of Meprobamate is given in Fig: (5.1)

**Mechanism of Action:** Meprabomate binds to GABA receptors (Rho et al., 1997) which interrupt neuronal communication in the reticular formation and spinal cord, causing sedation and altered perception of pain. It has the ability to activate currents even in the absence of GABA also and a potent adenosine reuptake inhibitor (ADORI) (Phillis and Delong, 1984), (De Long et al., 1985). Related drugs include Carisoprodol and Tybamate.

**Indications:** Meprobamate gives short term relief of anxiety, and tension. It has anticonvulsant and muscle relaxant properties.

**Toxicity:** Drowsiness, sluggishness, unresponsiveness, or coma, loss of muscle control, severe impairment or cessation of breathing, or shock.

### 5.2.2 METHOCARBAMOL:

**Introduction:** Methocarbamol is a central muscle relaxant used to treat skeletal muscle spasms. Methocarbamol is a white powder, sparingly soluble in water and chloroform and soluble in alcohol.

**Chemistry:** It is the carbamate of guaifenesin (Bruce et al., 1971) and has the empirical formula C_{11}H_{15}NO_{5}.

**Structure:** The molecular structure of Methocarbamol is given in Fig: (5.2)

**Indications:** It is employed in the treatment of muscle spasm caused by musculoskeletal disorders, tetanus and injury. Methocarbamol is also used in the treatment of Parkinsonism, cerebrovascular mishaps and cerebral palsy.

**Toxicity:** Potential side effects include drowsiness, dizziness, upset stomach, blurred vision and fever.
Serious side effects include the development of a severe skin rash or itching, slow heart rate, jaundice, persistent nausea, vomiting.

5.2.3 CARISOPRODOL: (Toth and Urts, 2004), (Chon et al., 2004), (Litterell et al., 1993)

Introduction: A centrally acting skeletal muscle relaxant whose mechanism of action is not completely understood but may be related to its relative actions. It is used as an adjunct in the symptomatic treatment of musculoskeletal conditions associated with painful muscle spasms.

Structure: Molecular structure of Carisoprodol is presented in Fig: (5.3).

Mechanism of Action: Carisoprodol is a central nervous system depressant that act as a relative and skeletal muscle relaxant. Carisoprodol interrupts neuronal communication within the reticular formation and spinal cord, resulting in radiation and alteration in pain perception. Its exact mechanism of action is not yet known.

Indications: For the relief of discomfort associated with acute, painful, musculo skeletal conditions.

Toxicity: Symptoms of over dose include drowsiness, giddiness, nausea, indigestion, or rash. Other adverse effects attributed to therapeutic use of Carisoprodol include dizziness, irritability, insomnia, diplopia, temporary loss of vision, ataxia, weakness, headache and dysarthria.

5.2.4 DANTROLENE: Chemically, Dantrolene is a hydantoin derivative, but does not exhibit antiepileptic activity like ether hydantoin derivative such as Phenytoin.

Mechanism of Action: Dantrium has been shown to produce relaxation by affecting the contractive response of the muscle at a site beyond the myoneural junction. In skeletal muscle, Dantrium dissociates excitation – contraction coupling (Krause et al., 2004), probably by interfering with the release of Ca$^{2+}$ from the sarcoplasmic reticulum by binding to the ryanodine receptor1. Ryanodine receptor mediates the release of calcium from the sarcoplasmic reticulum, an essential step in muscle contraction.

Structure: Molecular structure of Dantrolene is specified in Fig: (5.4)
**Indications:** It is currently used for the management of the fulminant hyper metabolism of skeletal muscle, characteristic of malignant hyperthermia crises in patient of all ages.

**Toxicity:** Symptoms of overdose include muscular weakness and alternations in the state of consciousness (eg, lethargy, coma), vomiting diarrhea.

**5.4.5 BACLOFEN:** *(Dzitoyeva et al., 2003), (Mezler et al., 2001), (See and Ginzburg, 2008a).*

**Chemistry:** Baclofen is a gamma- amino – butyric acid (GABA) derivative used as a skeletal muscle relaxant. It is especially useful in treating muscle spasticity associated with spinal cord injury.

**Structure:** The molecular structure of Baclofen is given in Fig (5.5)

**Mechanism of Action:** It is a capable of inhibiting both monosynaptic and polysynaptic reflexes at the spinal level, possibly by hyper polarization of afferent terminals, although action at supra spinal site may also occur and contribute to its clinical effect.

**Indications:** For the elevation of signs and symptoms of spasticity resulting from multiple sclerosis, particularly for the relief of flex or spasms and concomitant pain, claws and muscular rigidity.

**5.2.6 METAXALONE:** Metaxalone is a muscle relaxant used to relax muscle and relieve pain caused by strains, spains and other musculoskeletal conditions. *(See and Ginzburg, 2008b), (Elenbaas, 1980).* It is considered to be moderately strong muscle relaxant, with relatively low incidence of side effects.

**Structure:** Molecular structure of Metaxalone is given in Fig: (5.6)

**Mechanism of Action:** The mode of action of this drug has not been clearly identified, but may be related to sedative properties. Metaxalone does not directly relax tense skeletal muscles in man. The mechanism of action in humans may be due to general central nervous system depression.

**Indications:** For the treatment of painful peripheral musculoskeletal conditions and spasticity from upper motor neuron syndromes.
Figure: (5.1) Molecular structure of Meprobamate

Figure: (5.2) Molecular structure of Methocarbomol
Figure: (5.3) Molecular structure of Carisoprodol

Figure: (5.4) Molecular structure of Dantrolene
Figure: (5.5) Molecular Structure of Baclofen

Figure: (5.6) Molecular structure of Metaxalone
5.3 METHODS OF INVESTIGATION: (Murthy and Raghuram, 2007) (Murthy et al., 2007). (Murthy et al., 2008)

5.3.1 THEORETICAL METHODS:

The mean molecular polarizability of these drugs has been derived by theoretical approaches of Lippincott and Stutmann, additivity of bond refractions and additivity of bond polarizability. The details of these approaches are given in earlier papers of Murthy (Rao et al., 1976), (Murthy et al., 1979), (Rao and Murthy, 1979) (Rao et al., 1979), (Murthy et al., 1980), (Subbaiah et al., 1983), (Murthy et al., 1991), (Subbaiah et al., 1994), (Murthy et al., 1996), (Murthy and Sreenivasulu, 1997) and (Murthy et al., 2003) and explained in Chapter II.

5.3.1.1 Lippincott –δ-Function Model: (Lippincott and Stutmann, 1964), (Lippincott et al., 1966)

The evaluation of molecular polarizability by Lippincott method is a four step process.

1) The parallel component of polarizability of each bond.
2) The contribution of the non bonded region of electrons to parallel component polarizability.
3) The estimation of perpendicular component of polarizability from atomic polarizability knowing the number of degree of freedom.
4) Determination of mean molecular polarizability from the above components.

The methods of evaluation of the above components of polarizability are given Chapter II.

Using bond lengths of the bonds, the parallel components of polarizability of bond region and non bonded region of electrons are calculated. The perpendicular component of polarizability is evaluated from the atomic polarizability by appropriate equation given in Chapter II.

From these values molecular polarizability is calculated using the expression.

\[ \alpha_M = \frac{1}{3} \left[ \sum \alpha_{\|} + \sum \alpha_{\perp} + \sum 2 \alpha_{\perp} \right] \]

-----------------------(5.1)

The details of the above equations and various terms are given in Chapter II.
The bond length of all bonds and other relevant information on parameters like H, C are taken from the latest edition of CRC Hand Book, 85th edition (David R. Lide, 2004). The δ –function strengths and reduced electronegativities are taken from the work of Lippincott and Stutmann (Lippincott and Stutmann, 1964) (Lippincott et al., 1966). The values of $\sum \alpha_{\parallel P}$, $\sum \alpha_{\parallel n}$ and $\sum 2 \alpha_{\perp}$ for the centrally acting muscle relaxant drugs are calculated by Lippincott δ function method, are reported in Table (5.1).

5.3.1.2 BOND POLARIZABILITY: The data on bond polarizability required to calculate mean molecular polarizability is taken from the values reported by Le F’evre (Le F’evre, 1965).

The formula for calculating $\alpha_M$ is given by

$$\alpha_M = n_1 \alpha_{(c=c)} + n_2 \alpha_{(c\rightarrow c)} + \cdots = \sum_n n_j a_j$$  \hspace{1cm} (5.2)

Where $\alpha_{(c=c)}$, $\alpha_{(c\rightarrow c)}$ etc. are the mean bond polarizabilities of respective bonds and $n_1, n_2$ etc. are the number of bonds of $1^{st}, 2^{nd}$ etc. A detailed discussion is given in Chapter II.

5.3.1.3 BOND REFRACTIVITY: The information regarding bond refractivities of various bonds present in these systems are taken from Le Fevre (Le F’evre, 1965)

$$\alpha_M = \left[ \frac{3}{4\pi N} \right] \gamma (R_{\infty})_1$$ \hspace{1cm} (5.3)

$$\alpha_M = (0.0396 \gamma R_{\infty})_i$$ \hspace{1cm} (5.4)

Where, N is Avogadro number, $\gamma = M/\rho$ is the density or Molar density, $R_{\infty}$ is the Molar refraction of at infinitive wave length is given by

$$R_{\infty} = [R_{\infty}]n_1 + [R_{\infty}] n_2 + [R_{\infty}] n_3 + \cdots = \sum_i n_i (R_{\infty})_i$$ \hspace{1cm} (5.5)

Where $n_1, n_2$ --- are the number of bonds of a particular kind with bond refractivity, $(R_{\infty})_i$.

The molecular polarizabilities of these antiepileptic drugs calculated by the above methods are reported in Table (5.2).

5.3.1.4 DIAMAGNETIC SUSCEPTIBILITY ($\chi_M$): The diamagnetic susceptibility calculated by method of Murthy et al. Murthy et al (Rao et al., 1979),( Murthy et al., 1996) from $\alpha_M$
obtained by different methods through equation (5.6) along with the experimental values through VSM are reported in the Table(5.3).

The necessary equation for evaluating the diamagnetic susceptibility \( \chi_M \) is given by equation (5.6). The terms are explained in Chapter II.

\[
\chi_M = \gamma m \sigma \alpha_M
\]

\---------------------

\[(5.6)\]

5.3.1.5 MOLECULAR ELECTRON IONIZATION CROSS SECTION (Q):

An introductory note on molecular electron ionization cross section (Q) and its relation to molecular polarizability and diamagnetic susceptibility have already been given in chapter II. Beran and Kevan (Beran and Kevan, 1969a),(Beran and Kevan, 1969b) observed proportionality between molecular polarizability and susceptibility on one hand, susceptibility and electron ionization cross section on the other hand. The dependence of Q on \( \alpha_M \) and \( \chi_M \) became expressive in the form of mathematical relation. The unsaturated bonds also affect the values. So, Rao et al., (Rao et al., 1979) modified the equation of Beran and Kevan to equation (5.7).

\[
Q \text{ (in } 10^{-16} \text{cm}^2) = 0.278 \gamma \chi_M
\]

\---------------------

\[(5.7)\]

The Q values for the present system are reported in Table (5.4). Before making an analytical discussion of the results on molecular electron ionization cross section Q, it is felt necessary to have a comparative study of Q with protein binding (PB), Bioavailability (BA), Log P and Half life period (HL). The detailed discussion about these medicinal parameters was given in Chapter I. The Q value of these medicinal systems along with PB, BA, Log P and HL are reported in Table (5.5). The required data of these medicinal compounds is taken from drug bank wikipedia.

5.3.2 EXPERIMENTAL METHOD: The diamagnetic susceptibility can be experimentally determined by using Vibrating Sample Magnetometer.

**Vibrating Sample Magnetometer (VSM):** VSM measures the moment of the sample caused due to the influence of external magnetic field. The sample may be a diamagnetic, paramagnetic, ferromagnetic and antiferromagnetic substance. The present experimental results are obtained using VSM from IIT, Madras, Chennai. India. The detailed information regarding VSM is given in Chapter II.
Two drugs belonging to centrally acting muscle relaxants namely Carisoprodol and Baclofen responded to experimental determination of diamagnetic susceptibility by vibrating Sample Magnetometer method. The magnetic moment at various fields (G) are reported in Table (5.3.1) and (5.3.2). The comparative theoretical and experimental $\chi_M$ values are reported in Table (5.3).

5.4 THE PRESENT STUDY:

The analytical applicability of $Q$ on the parameters PB, BA, Log P and HL is studied more comprehensively and their interdependence along dosage and is discussed through the analytical formula which reads as (Murthy et al., 2010a), (Murthy et al., 2010b), (Murthy et al., 2011).

$$\beta=[(Q/D)^{2/3}L \text{ (LogP)}]^{\alpha/5}$$

So from the above mathematical equation, dosage of a drug can be estimated with the known medicinal parameters and $Q$ and thus calculated dosages are compared with the experimental dosage values. In Table (5.6) the evaluated dosage values and suggested dosages are presented.

5.5 RESULTS AND DISCUSSION:

The mean molecular polarizability obtained by different methods such as Lippincott method, bond refraction and bond polarization method show similarity in their values to each other which give strong support to the theoretical basis. For example, the molecular polarizability obtained by Lippincott method in case of Meprobamate is 217.923 in $10^{-25}$ cm$^3$ and that of bond refraction is 209.161 in $10^{-25}$ cm$^3$ is near to the $\alpha_M$ values obtained from bond polarizability 204.674 in $10^{-25}$ cm$^3$. Same in the case with other medicinal compounds related to centrally acting muscle relaxants.

The electron ionization cross section, ‘$Q$’ values obtained from diamagnetic susceptibilities also agree well with each other. The ‘$Q$’ value of Methocarbomol drawn by Lippincott method is 4.150 in $10^{-16}$ cm$^2$ agree well ‘$Q$’ value obtained from bond polarizability method 4.549 in $10^{-16}$ cm$^2$ and bond refraction method 4.992 in$10^{-16}$ cm$^2$. Similarly Baclofen exhibit identical Q values derived from three methods. i.e through Lippincott method, the value is 9.855 in $10^{-16}$ cm$^2$, by bond refraction method 9.855 in $10^{-16}$ cm$^2$,and by bond polarizability method It is 9.577 in $10^{-16}$ cm$^2$. 
The experimental diamagnetic susceptibility value of Baclofen (50.0 in $10^{-6}$ C.G.S Units) is near the value obtained from Bond refraction 49.237 in $10^{-6}$ C.G.S Units. Similarly the experimental value of Carisoprodol is 142.5 in $10^{-6}$C.G.S. Units against the theoretical value 144.447 in $10^{-6}$C.G.S Units. The experimental value of $\chi_M$ for Carisoprodol is less compared to the theoretical value of diamagnetic susceptibility is due to the presence of other constituent medicinal compound (eg: Paracetmol) which may decrease the value. The data obtained from VSM is given in Table (5.3.1) and (53.2) and comparative theoretical and supportive practical data is reported in Table (5.3).

The comparative theoretical and supportive experimental values of ‘Q’ drawn from VSM are given in Table (5.4). It is observed that the reported value of ‘Q’ obtained from $\chi_M$ of VSM exhibit proximate values against the theoretical values. For example, Baclofen has the ‘Q’ value 10.13 in $10^{-16}$ cm$^2$ as supportive value and 9.855 in $10^{-16}$ cm$^2$ as theoretical value.

A close look at the dosage of the medicines calculated and reported show the following features. The calculated dosage of Baclofen is 0.035 grams per day agree with the reported dosage value i.e., 0.040 grams per day. Similarly Metaxalone has the calculated value 3.069 grams per day against the reported value, 3.2 grams per day. The evaluated and supported dosage values were reported in Table (5.6)

An analytical approach on Q and medicinal parameters reveal some observations. Generally the medicinal compounds, having similarity in their structure, are analyzed. In case of certain centrally acting muscle relaxant such as Meprobamate, Methocarbamol, Carisoprodol, Dantrium etc, an increase in ‘Q’ shows observable decrease in half life period. For example the ‘Q’ value of Methocarbamol is 4.99 in $10^{-16}$ Cm$^2$, which is lower than Baclofen (‘Q’ value 9.85 in$10^{-16}$ cm$^2$) and has increased dosage value i.e .5.79 grams per day than the dosage value of Baclofen i.e. 0.04 grams per day. Other drugs such as Metaxalone and Dantrium reveal the same analysis. The dosage value of Metaxalone is 3.2 grams per day against the ‘Q’ value 9.60 in $10^{-16}$ cm$^2$.Similar analysis was done in other two more drugs, Meprobamate and Carisoprodol. The half life period is less i.e. 8 hrs with increased Q value 32.52 in $10^{-16}$ cm$^2$ and decreased dosage i.e. 1.4 grams per day in case of Carisoprodal when compared to Meprobamate Q value 5.51 in $10^{-16}$ cm$^2$, dosage value 1.6 grams per day and half life 10 hrs. From the above discussion
it can be understood that the drugs with high ‘Q’ value are to be preferred, so that a decrease in dosage and number of side effects can be experienced.

The relation between the ‘Q’ value, and other medicinal parameters compared to dosage value is under study. The data regarding ‘Q’ and other medicinal parameters is given in Table (5.5)

A possible explanation for this behavior may be given as follows. An increase in electron transportation activity reported by higher electron ionization cross section will tender the chemical reaction to be faster. Hence an incidence of electron from the place of malignity will make the process of curing faster. Thus very little dosage of the medicine will be sufficient. A long continued impingent of the electrons on the malignant cells might develop saturation effects. Hence the life time of the drug for limited time is suggested. Thus an increase in ‘Q’ explains lower half life and lower dosage. A continued dosage of such medicine might result in undesirable toxic effects.
Table 5.1 Molecular Polarizability by Lippincott method (in $10^{-25}$ cm$^3$)

<table>
<thead>
<tr>
<th>S. No</th>
<th>Name of the drug</th>
<th>$\sum \alpha \parallel p$</th>
<th>$\sum \alpha \parallel n$</th>
<th>$\sum 2\alpha \perp$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Methocarbamol</td>
<td>430.328</td>
<td>5.339</td>
<td>177.978</td>
</tr>
<tr>
<td>2</td>
<td>Meprobamate</td>
<td>382.642</td>
<td>21.731</td>
<td>217.923</td>
</tr>
<tr>
<td>3</td>
<td>Carisoprodol</td>
<td>492.219</td>
<td>21.731</td>
<td>316.701</td>
</tr>
<tr>
<td>4</td>
<td>Metaxalone</td>
<td>458.610</td>
<td>6.919</td>
<td>218.710</td>
</tr>
<tr>
<td>5</td>
<td>Dantrium</td>
<td>647.136</td>
<td>31.621</td>
<td>206.102</td>
</tr>
<tr>
<td>6</td>
<td>Baclofen</td>
<td>376.060</td>
<td>22.762</td>
<td>225.595</td>
</tr>
</tbody>
</table>

Table 5.2 Molecular Polarizabilities ($\alpha_M$) in $10^{-25}$ cm$^3$

<table>
<thead>
<tr>
<th>S. No</th>
<th>Name of the drug</th>
<th>From $\alpha_M$ by Lippincott method</th>
<th>From $\alpha_M$ by Bond Polarizability</th>
<th>From $\alpha_M$ by Bond Refraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Methocarbamol</td>
<td>204.549</td>
<td>224.189</td>
<td>246.026</td>
</tr>
<tr>
<td>2</td>
<td>Meprobamate</td>
<td>217.923</td>
<td>204.674</td>
<td>209.161</td>
</tr>
<tr>
<td>3</td>
<td>Carisoprodol</td>
<td>276.884</td>
<td>254.379</td>
<td>263.640</td>
</tr>
<tr>
<td>4</td>
<td>Metaxalone</td>
<td>228.708</td>
<td>234.075</td>
<td>247.086</td>
</tr>
<tr>
<td>5</td>
<td>Dantrium</td>
<td>294.953</td>
<td>280.999</td>
<td>285.091</td>
</tr>
<tr>
<td>6</td>
<td>Baclofen</td>
<td>208.139</td>
<td>219.322</td>
<td>225.693</td>
</tr>
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</table>
Table 5.3 The diamagnetic susceptibility values in $10^{-6}$ C.G.S. Units

<table>
<thead>
<tr>
<th>S.No</th>
<th>Name of the drug</th>
<th>Theoretical Values</th>
<th>Experimental values of $\chi_M$ by V.S.M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>From $\alpha_M$ by Lippincott method</td>
<td>From $\alpha_M$ by Bond Refraction</td>
</tr>
<tr>
<td>1</td>
<td>Methocarbamol</td>
<td>20.479</td>
<td>24.631</td>
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<td>2</td>
<td>Meprobamate</td>
<td>28.974</td>
<td>27.808</td>
</tr>
<tr>
<td>3</td>
<td>Carisoprodol</td>
<td>151.702</td>
<td>144.447</td>
</tr>
<tr>
<td>4</td>
<td>Metaxalone</td>
<td>43.737</td>
<td>47.382</td>
</tr>
<tr>
<td>5</td>
<td>Dantrium</td>
<td>57.292</td>
<td>55.376</td>
</tr>
<tr>
<td>6</td>
<td>Baclofen</td>
<td>45.407</td>
<td>49.237</td>
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</tbody>
</table>

Table 5.3.1 The diamagnetic susceptibility values of Carisoprodol obtained from VSM

<table>
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<th>Field(G)</th>
<th>Moment(emu)$\times10^4$</th>
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<td>2000.0</td>
<td>1.3</td>
</tr>
<tr>
<td>3500.0</td>
<td>1.9</td>
</tr>
<tr>
<td>4500.0</td>
<td>2.3</td>
</tr>
<tr>
<td>6000.1</td>
<td>2.4</td>
</tr>
<tr>
<td>7000.1</td>
<td>4.0</td>
</tr>
<tr>
<td>8000.1</td>
<td>4.2</td>
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<tr>
<td>9000.1</td>
<td>5.4</td>
</tr>
<tr>
<td>10000.2</td>
<td>5.6</td>
</tr>
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</table>
Table 5.3.2 The diamagnetic susceptibility values of Baclofen obtained from VSM

<table>
<thead>
<tr>
<th>Field(G)</th>
<th>Moment(emu) x10^4</th>
</tr>
</thead>
<tbody>
<tr>
<td>12500.2</td>
<td>3.3</td>
</tr>
<tr>
<td>14000.3</td>
<td>4.0</td>
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<td>5.2</td>
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<tr>
<td>18000.3</td>
<td>6.3</td>
</tr>
<tr>
<td>19000.3</td>
<td>7.8</td>
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</table>

Table 5.4 Electron ionization cross section values in 10^{-16} cm²

<table>
<thead>
<tr>
<th>S.No</th>
<th>Name of the drug</th>
<th>From α_M by Lippincott method</th>
<th>From α_M by Bond Refraction</th>
<th>From α_M by Bond Polarizability</th>
<th>From experimental values of ‘χ_M’ by V.S.M</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Methocarbamol</td>
<td>4.150</td>
<td>4.992</td>
<td>4.549</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>Meprobamate</td>
<td>5.872</td>
<td>5.515</td>
<td>5.447</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>Carisoprodol</td>
<td>34.040</td>
<td>32.525</td>
<td>31.382</td>
<td>32.088</td>
</tr>
<tr>
<td>4</td>
<td>Metaxalone</td>
<td>8.864</td>
<td>9.602</td>
<td>9.097</td>
<td>--</td>
</tr>
<tr>
<td>5</td>
<td>Dantrium</td>
<td>11.467</td>
<td>11.084</td>
<td>10.925</td>
<td>--</td>
</tr>
<tr>
<td>S. No</td>
<td>Name of the drug</td>
<td>Q in ($10^{-16}$ cm$^2$)</td>
<td>Protein Binding (%)</td>
<td>Bioavailability (%)</td>
<td>Log P</td>
</tr>
<tr>
<td>------</td>
<td>------------------</td>
<td>--------------------------</td>
<td>---------------------</td>
<td>---------------------</td>
<td>-------</td>
</tr>
<tr>
<td>1</td>
<td>Methocarbamol</td>
<td>4.992</td>
<td>50</td>
<td>50</td>
<td>0.1</td>
</tr>
<tr>
<td>2</td>
<td>Meprobamate</td>
<td>5.515</td>
<td>50</td>
<td>50</td>
<td>0.7</td>
</tr>
<tr>
<td>3</td>
<td>Carisoprodol</td>
<td>32.525</td>
<td>60</td>
<td>50</td>
<td>2.1</td>
</tr>
<tr>
<td>4</td>
<td>Metaxalone</td>
<td>9.603</td>
<td>50</td>
<td>50</td>
<td>2.3</td>
</tr>
<tr>
<td>5</td>
<td>Dantrium</td>
<td>10.925</td>
<td>50</td>
<td>70</td>
<td>1.7</td>
</tr>
<tr>
<td>6</td>
<td>Baclofen</td>
<td>9.855</td>
<td>30</td>
<td>50</td>
<td>1.3</td>
</tr>
</tbody>
</table>

**Table 5.6 Dosage values in grams per day**

<table>
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<tr>
<th>S. No</th>
<th>Name of the drug</th>
<th>α</th>
<th>β'</th>
<th>Calculated dosages</th>
<th>Reported dosages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Methocarbamol</td>
<td>0.048</td>
<td>1.089</td>
<td>4.893</td>
<td>5.79</td>
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<tr>
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<td>Meprobamate</td>
<td>0.117</td>
<td>1.428</td>
<td>1.660</td>
<td>1.60</td>
</tr>
<tr>
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<td>Carisoprodol</td>
<td>0.148</td>
<td>1.773</td>
<td>1.534</td>
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<tr>
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<td>Metaxalone</td>
<td>0.029</td>
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<td>1.098</td>
<td>2.066</td>
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<tr>
<td>6</td>
<td>Baclofen</td>
<td>0.016</td>
<td>1.229</td>
<td>0.035</td>
<td>0.040</td>
</tr>
</tbody>
</table>
REFERENCES


