DETERMINATION OF MOLECULAR DESCRIPTORS FOR ILLEGAL DRUGS BY GC-FID USING ABRAHAM SOLVATION MODEL

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The Abraham solvation parameter model is a good approach for analyzing and predicting biological activities and partitioning coefficients. The general solvation equation has been used to predict the solute property (SP) behavior of drug compounds between biological barriers. Gas chromatography (GC) retention time can be used to predict molecular descriptors, such as E, S, A, B & L for existing and newly developed drug compounds. In this research, six columns of different stationary phases were used to predict the Abraham molecular descriptors more accurately. The six stationary phases used were 5% phenylmethyl polysiloxane, 6% cyanopropylphenyl 94% dimethylpolysiloxane, 5% diphenyl 95% dimethylpolysiloxane, 100% dimethylpolysiloxane, polyethylene glycol and 35% diphenyl 65% dimethylpolysiloxane. Retention times (RT) of 75 compounds have been measured and logarithm of experimental average retention time $Ln(RT_{exp})$ are calculated. The Abraham solvation model is then applied to predict the process coefficients of these compounds using the literature values of the molecular descriptors (Acree Compilation descriptors). Six correlation equations are built up as a training set for each of the six columns. The six equations are then used to predict the molecular descriptors of the illegal drugs as a test set. This work shows the ability to extract molecular information from a new compound by utilizing commonly used GC columns available with the desired stationary phases. One can simply run the new compound in GC using these columns to get the retention time. Plugging in the retention time into the developed equations for each of the column will predict the molecular descriptors for the test compound and will give some information about the properties of the compound.

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TABLE OF CONTENTS

Page

LIST OF TABLES

Page

LIST OF FIGURES

Page

CHAPTER 1

INTRODUCTION

For better drug development, drug candidate's ADMET (adsorption, distribution, metabolism, elimination and toxicity) properties need to be predicted in the early stages of drug discovery. The prediction can be done experimentally (*in vitro* and *in vivo*) or computationally. But the experimental work includes animal studies which can be difficult, expensive and have a high chance of failure. Also, there can be failures due to unsatisfactory effectiveness, poor solubility, low bioavailability, unfavorable pharmacokinetic properties, toxicity concerns, drug-drug interactions and drug degradation. A computational approach may be a good consideration to sort out the properties of the drug candidates in the very early development stage. It is less time consuming and minimizes waste of valuable resources [1-3].

Computational techniques are useful tool to predict the appropriate chemical features of a drug molecule while passing through the biological membranes. Activity and distribution of a drug depend on the interaction with the biological membranes. Partition coefficients between an aqueous or a gas phase and lipid phase predict drug permeability across these membranes [19]. Usually a series of structurally similar drugs like molecules are studied to predict the effect of various functional groups on the partitioning [69, 70]. In this approach these drugs like molecules are first studied experimentally. Second, the experimental data are used to set up a computational model to explain the effect of various functional groups on the absorption and/or permeability of the parent compounds. Then the computational model serves to predict the chemical features of the parent compound. Experimental data obtained with a chromatographic method and the theoretical data from quantum mechanical method (CODESSA-PRO, ISIDA etc.) are used to develop a computational model [71]. However, a better approach to study biological processes is

to model experiments that can be studied rather easily. Chromatographic processes are suitable for studying a large number of compounds. So the idea of developing a direct connection between chromatographic processes and biological processes by combining chromatographic data with computational data would be a fruitful approach.

Gas chromatography is a modern separation technique in which the separation of compounds is based upon the partition, or distribution, of the analytes between two phases in a dynamic system. The two phases consist of a gaseous mobile phase and a liquid or solid stationary phase [4]. The distribution constant is determined by the column temperature and the extent of intermolecular interactions between the solute and stationary phase. The mobile phase transports the analyte through the column but does not participate in the retention mechanism. The conditions generally used in analytical GC are small sample size, low column pressures, and low-molecular mass gases as the mobile phase [5-7]. Therefore, it is the solute-stationary phase interaction that is responsible for the selectivity differences for various stationary phases [8]. For effective selectivity optimization, a wide range of stationary phases are required, which are distinguished by their capacity for varied intermolecular interactions [9]. Polarity and the selectivity of the stationary phase need to be considered before approaching the characterization of the stationary phase in GC. In general, polarity is the capacity of a stationary phase for all intermolecular interactions consisting of dispersion, dipole-type and hydrogen bonding [10-12]. The selectivity is the relative capacity of the stationary phase to enter into inter-molecular interactions [13].

Gas chromatography is a good technique to study the distribution of drug compounds between different organic phases. The retention time obtained on a given stationary phase can be used to model biological activities that involve the transfer of drug molecules from the gas phase to the biological phase, like in the case of an air pollutant traversing the nasal cavity (Figure 1.1).

In the present study we try to establish a correlation between the partitioning behavior of the drug compounds and several biological phases.

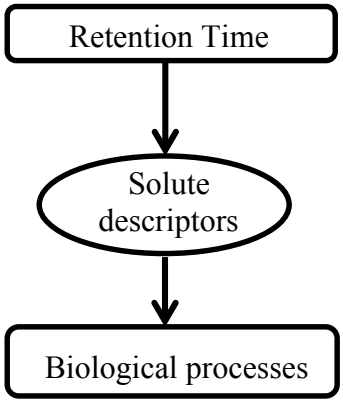


Figure 1.1: Connection between retention time and biological process [68]

Drugs need to cross the blood brain barrier (BBB) to enter into the central nervous system (CNS). The process of drugs penetrating through the BBB is rate-limiting [14]. This process depends on the permeability of the BBB to a drug and the steady-state distribution of the drug between brain and blood [15]. The Abraham solvation model is a good way to predict the ADMET property of the drug molecules. It is two linear free energy relationships [16-18], one of which describes transfer process of the drug between two condensed phases

$$SP = c + e \cdot \mathbf{E} + s \cdot \mathbf{S} + a \cdot \mathbf{A} + b \cdot \mathbf{B} + v \cdot \mathbf{V} \quad (1)$$

and the other one involves gas-to-condensed phase transfer

$$SP = c + e \cdot \mathbf{E} + s \cdot \mathbf{S} + a \cdot \mathbf{A} + b \cdot \mathbf{B} + l \cdot \mathbf{L} \quad (2)$$

SP is the dependent variable. It is the property of a series of solutes in a fixed phase. The independent variables, known as descriptors (E, S, A, B, L, V) are also solute properties. They describe the ability of the solute to participate in the solute-solvent interaction. The c, e, s, a, b, v, l are called the process coefficients which describe the solvent interaction with the solute. Of the five descriptors in equation (1) and (2), the E and L or V can be found in the literature [1,13, 20-

22]. E can be obtained from the refractive index, V can be calculated from the bond and atom contribution, and L is related to the solute size and solute-solvent dispersion interaction. So these descriptors can be simply calculated from the structure of the solute [67]. The other three descriptors S, A and B need to be determined experimentally. For a given solute the retention time is obtained experimentally and then the natural log of the retention time (lnRT) is assigned to equation (1) or (2). The S, A and B descriptors can be calculated from the best fit observed and calculated lnRT values. The process coefficients in Equations (1) and (2) are obtained by multiple linear regression analysis of experimental logarithm of retention times for a particular column.

Molecular descriptors used in Abraham's Solubility model are helpful for understanding what barriers a drug compound will traverse as well as giving an indication towards the drug molecule acidity, basicity and polarizability. This particular model can be applicable to both chemical processes (*e.g.*, solubility [23-30] and partition/extraction) [31-38] and biological interest (*e.g.*, skin permeation [39], nasal pungency [40] eye irritation [41], brain-blood partition [42] and permeation [43], human and rat [44] intestinal absorption, tissue-blood partition [46], aquatic toxicity) [47-52]. The mathematical form of linear free energy relationships (LFER) is easy to make partitioning measurements for all of the processes. The measured data then can be used to predict partitioning behavior of solutes for difficult environments, like cocaine crossing the blood brain barrier. A drug molecule passes through numerous biological and chemical barriers to reach its final destination in the brain to bind to a specific receptor and to exert its activity as a stimulant. This involves a series of complicated events. The current experimental techniques, such as single photon computed tomography (SPECT), magnetic resonance imaging (MRI), and positron emission tomography (PET), to measure BBB partitioning are not considered the high throughput screening (HTS) methods which has become a demand in preclinical drug discovery. [54].

The Abraham general solvation model is an example of a predictive method. It describes the measured solute properties in terms of molecular solute descriptors. The same solute descriptors can be used for every process, such as, blood-to-tissue partitioning, Draize eye scores, aquatic toxicities, air-to-blood partitioning and do not need to calculate a different set of descriptors for these each time. The advantage of the Abraham model can be seen in the following illustration:

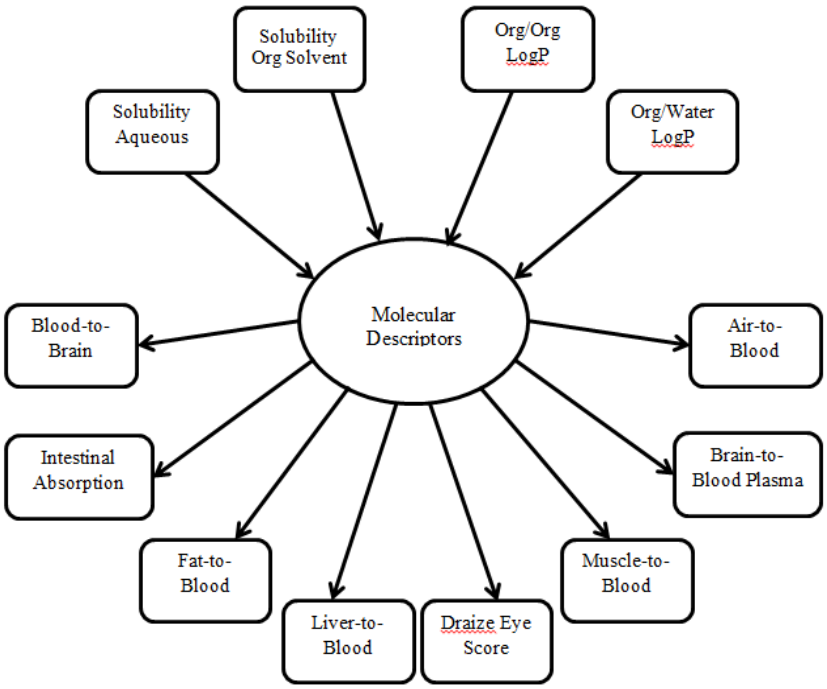


Figure 1.2: Molecular descriptors are interchangeably used in all Abraham models [1].

Inwards arrows represent calculation of the molecular descriptors from experimental measurements like solubilities, partitioning behavior like air-to-blood, blood-to-brain, intestinal absorption and once the descriptors are known, they can be used to estimate biological properties represented by the outwards arrows for which a process equation is available. As will be discussed

later, the solute descriptors have physical significance, and their numerical values contain encoded information pertaining to the different types of molecular solute-solubilizing media interactions.

Models like the Abraham model can predict and describe complicated biological and chemical interactions. This model has advantages over the oldest model, octanol/water system. The Abraham solvation model not only describes physical interactions but more importantly biological interfaces. “The octanol-to-water partition coefficient of a molecule is easy to obtain and provides a rough estimate of its hydrophilic/lipophilic properties. The octanol–water phase boundary, however, only represents a physical, not a biological interface” [53].

In the present study, we are in the process of developing an Abraham model correlation equation for illegal drugs and predicting the molecular descriptors for these. The known molecular descriptors for about 75 compounds have been collected from the published literatures [1, 13, 20-22]. The process coefficients in Equations (1) and (2) are obtained by multiple linear regression analysis of experimental logarithm of retention time for a particular column as those give the best fit observed and calculated ln(RT) values. Of the five descriptors in equation (1) and (2), the E and L can be found in the literature for the target drug compound [1, 13, 20-22]. To obtain the other three descriptors for a drug, the known ln(RT) can be assigned in equation (1) and (2) with the calculated process coefficients and the unknown descriptors can be predicted. To obtain these values gas chromatography experiments are needed to establish retention times for a large database of compounds and then predict values for the target drug compounds.

1.1 Review of Abraham Solvation Parameter Model

Since chemical reactions occur in solution, the solute/solvent interactions have major importance in chemistry and biochemistry. These interactions can be studied through empirical equations that can be related to selected properties with parameters of solutes and/or solvents. In a solution, solutes and solvents can undergo various types of interactions including dispersion forces, dipole-dipole polar interaction, hydrogen bonding, London forces and so on [59]. Abraham and his co-workers proposed a linear free-energy relationship model that describes these solute-solvent interactions. It can correlate solute properties (SP), such as partitioning [33,63], chromatographic properties [64], blood-brain distribution [41], human intestinal absorption [65], with a standard set of parameters of solutes and/or solvents. These parameters represent the solute influence on solute-solvent interactions. The numerical values of these parameters are used to describe different characteristics of a structure to provide information about the property being studied. The equation co-efficient or process co-efficient corresponds to the chemical information of the phases on these interactions.

The Abraham model relies on two linear free energy relationships LFER that describes transport-related properties of solutes as equilibrium transfer between two phases. The basic Abraham model describes the partitioning of a solute from a gas phase to a condensed phase, and the partitioning between two condensed phases.

$$SP = c + e\mathbf{E} + s\mathbf{S} + a\mathbf{A} + b\mathbf{B} + l\mathbf{L} \text{ (gas-condensed phase)} \quad (1)$$

$$SP = c + e\mathbf{E} + s\mathbf{S} + a\mathbf{A} + b\mathbf{B} + v\mathbf{V} \text{ (condensed-condensed phase)} \quad (2)$$

SP is the dependent variable. It is the property of a series of solutes in a fixed phase. In our study we may consider it as the logarithm of the drug's retention time, that is the distribution of drug molecules between the stationary phase and mobile phase in gas chromatography. The independent

variables, known as descriptors, are also solute properties. **E** is the excess molar refraction descriptor, **S** is dipolarity/polarizability descriptor of the solute, **A** is measurement of the solute hydrogen-bond acidity, **B** is the solute hydrogen-bond basicity, **V** is the McGowan volume of the solute and **L** is the logarithm of the solute gas phase dimensionless Ostwald partition coefficient into hexadecane at 298 K. **E, S, A** and **B** provide the tendency of the given solute to undergo various solute-solvent interactions. **V** and **L** represent the solvent cavity term that will accommodate the dissolved solute. These two descriptors, **V** and **L ,** will also describe the general solute-solvent interactions. There are more than 4,000 solutes available with known solute descriptors. The advantage of these descriptors is they can be easily experimentally determined by gas-liquid chromatography [13]. The E and V or L can be calculated from the structure of a compound. S, A and B need to be determined by direct experimental measurements or via back-calculation from the partition measurements [66].

1.1.1 E: Excess Molar Refraction

The excess molar refraction, E, is the refractive index function that gives an indication of the polarizable electrons for a molecule. It is a measure of the ability of the polarizable electrons in the molecule to be involved in the solute-solvent dispersive interactions. E is calculated as the difference between the molar refraction of the molecule and the molar refraction of the alkane with the same McGowan volume V.

$$E = MR\ (observed) - MR\ (for\ alkane\ of\ the\ same\ V) \quad (3)$$

where the units of E are $cm^3mol^{-1}10^{-1}$. **E** can be determined from the molecular fragment or substructure values for a given compound.

The McGowan's volume in molar refraction, MRx, can be calculated as [15].

$$MRx = V*[(\eta^2-1)/ (\eta^2+2)] \quad (4)$$

V is the McGowan's volume (units is $(cm^3/mol)/10$), and η is the pure liquid solute refractive index at 25℃.

1.1.2 S: Dipolarity/Polarizability

S is termed as the solute's dipolarity or polarizability. It measures the tendency of a solute to engage in dipole-dipole and induced dipole-dipole interactions. It can be determined experimentally which reflects the interactions involving both induced and stable polarity on the solute. Gas liquid chromatographic (GLC) data can be used to measure the polarity of the solute using polar stationary phase. It is difficult to separate the contributions of dipole-dipole interactions from those of induced dipole-dipole interactions [60]. So a combined polarizability/dipolarity descriptors was introduced instead of only considering dipole moment [61].

1.1.3 A: Hydrogen Bond Acidity and B: Hydrogen Bond Basicity

A and B are the hydrogen bond acidity and basicity descriptors that describe the hydrogen donor and acceptor capacity of the solute. It was developed successfully by Abraham using the equilibrium constant for the 1:1 reaction in tetrachloromethane at 298 K.

$$A\text{-}H + B \leftrightarrow A\text{-}H\text{---}B$$

by the hydrogen bond (HB) acidity 'A' factor of the AH molecule and by the hydrogen bond basicity 'B' factor of the B molecule, through the relation (11).

$$\text{Log } K_{AB} = -1.094 + 7.354\ A.B \quad (5)$$

A is the solute descriptor for hydrogen bond solute acidity, **B** is the solute descriptor for the hydrogen bond solute basicity, $\log K_{AB}$ is the average hydrogen bond acidity and basicity for solutes in carbon tetrachloride.

When a molecule is surrounded by a large excess of solvent molecules, it is capable of forming hydrogen bonds. So there is a difference in hydrogen bond characteristics of a molecule in solvent than that of a solute in a single hydrogen bond acid or base. There are significant differences in hydrogen bond basicity between the bulk solvent and monomeric solute depending on their association with each other. Abraham A and B descriptors are effective for not only the associated compounds such as alcohols, but also for the non-associated compounds.

1.1.4 L: Ostwald Solubility

The L is the logarithm of the solute's Ostwald solubility coefficient, and is defined as gas-to- hexadecane partition coefficient at 25°C. It includes both the cavity effect and general London dispersion effect of the process. This process can be shown as:

$$\text{Solute (gas phase)} \rightleftharpoons \text{Solute (hexadecane)} \quad (6)$$

$$L = [\text{solute}]_{\text{hexadecane}} / [\text{solute}]_{\text{gas phase}} \quad (7)$$

The L can be measured experimentally from solute's retention volume by gas-liquid chromatography. For this, a hexadecane stationary phase is used at 25^0C. It is not applicable for large, nonvolatile solute molecules as they do not readily elute from the Hexadecane liquid stationary phase. For large, nonvolatile compounds Apolane-87 is used as a suitable replacement stationary phase solvent [62].

1.1.5 V: McGowan Volume

The McGowan volume, **V** is used in two condensed phase partition systems. It is calculated from the bonds and atoms found in the solute molecule. Within a solute, all the bonds are treated equal, i.e., a single bond, double bond, and triple bond are treated equally regardless of their hybridization. The number of bonds in a molecule can be obtained as follows:

$$B = N-1+R \tag{8}$$

where B is the number of bonds, N is the total number of atoms, and R is the total number of ring structures.

V is related to the size of the molecule as well as to the size of the solvent cavity. The V descriptor is calculated by counting the total number of bonds (Bn) between bonding atoms and by the addition of atomic volume fragments (10). Here the total number of bonding atom is equal to 1.

$$V = \Sigma\, n_{\text{atom of type}} / V_{\text{atom of type i}} - 6.58\ B \tag{9}$$

Here $V_{\text{atom of type I}}$ is the atomic volume fragments.

1.1.6 Process Co-Efficients

Eqs (1) and (2) provide valuable information through the co-efficients reflecting solute-solvent interactions that corresponds to the solvent phase. These co-efficients are e,s,a,b,v,l also known as the process coefficients. The **e**-coefficient provides the measure of the solvent dispersion interactions. It shows how the phase or the solvent interact with the solute through π and n-electron pairs. Normally the e is positive, but the presence of an electronegative atom in the phase may make it negative. The **s**-coefficient reflects the ability of the solvent phase to undergo dipole-dipole induced interaction with a solute. The **v** and **l**- coefficients include both the endoergic and exoergic

solute-solvent effects that arise through solute polarizability. The **a** and **b**-coefficients reflect the complementary hydrogen bond basicity and acidity respectively [13]. The **c**-coefficient is an independent term generated by the multi linear regression analysis (MLRA) analysis. The value of **c** contributes to the cavity formation and related to the non-polar interaction to the retention [73]. These are for gas-to-condensed phase partitions because in gas phase there are no interactions. For partitions between two condensed phases, the coefficients in eq.(1) refer to differences between the properties of the two phases. The positive value indicates that the solute will favor the condensed phase. The negative value indicates it will favor the gas phase.

Thus Abraham model can be used to predict and characterize interactions within in a system. If the predictive method for system has already been created it is easy to understand how a specific gas phase solute would interact with solvent. All one would have to do is to insert the solute descriptor values for that certain gas phase into the system.

1.2 Gas Chromatography

1.2.1 Origin of GC

Modern gas chromatography was first described by Martin and James in their publication in Bichem. J. 50, 679 (1952). James and Martin separated volatile fatty acids. They used nitrogen gas as the mobile phase and silicone oil and stearic acid, which came from diatomaceous earth, as the stationary phase [55]. Griffin and George manufactured the first commercial GC system in 1954.

Then in early 1960s a packed column technique was developed, and capillary column development was in progress at the same time. In 1980s chemically bonded fused silica capillary

columns were first introduced. Since then till now GC is still evolving and developing new technologies.

1.2.2 Gas Chromatography Instrumentation

Gas chromatography (GC) is a well-established analytical technique used in industrial and academic laboratories because of its high sensitivity, accuracy and precision. It is a separation technique in which the separation of compounds is based upon partition, or distribution, of the analytes between two phases in a dynamic system. GC involves partitioning of analytes between a solid stationary phase or liquid stationary phase retained on a solid sorbent or a column wall and a gaseous mobile phase. In order to transport the analytes through the column, the analytes must be sufficiently volatile for them to be present in the gas phase in the experimental condition. The association between the vaporized solute and the carrier gas which simplifies the chromatographic process is very little. One of the major limiting factors for the application of this technique is the analyte volatility. The greater the affinity of the compound for the stationary phase, the more the compound will be retained by the column. Also it will take longer time to be eluted and detected. All solute molecules spend the same amount of time in the gas phase.

The main component of the gas chromatography is the column in which the separation takes place. For better separations there are some factors that need to be considered such as the source and control of carrier gas through the column, sample introduction and detection of the components as they elute from the end of the column. The column is placed in a thermostatically controlled oven. Also there are three controlled heated zones, for the inlet, column and detector. The basic gas chromatograph is represented in Figure 1.3.

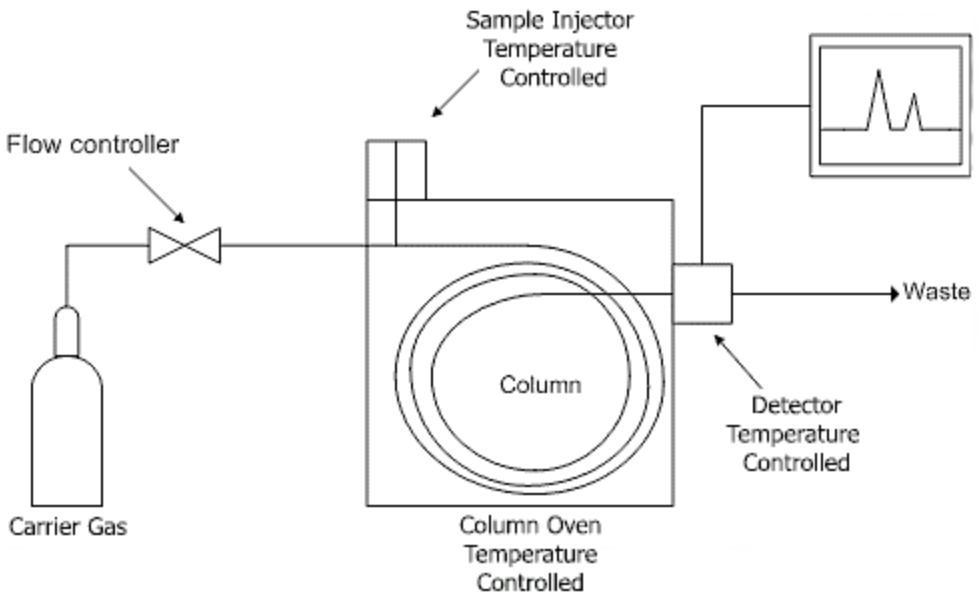


Figure 1.3: Schematic diagram for GC instrumentation

The sample is first introduced into the instrument via an inlet with a continuous flow of the carrier gas. Inside the chromatograph the sample is vaporized in the inlet and the carrier gas sweeps the sample through the thermostated column. The individual components emerge from the column and give rise to an electrical signal in the detector. The gas flow through the column and the detector needs to be optimized separately. Then the detector signal is conducted to a recording device. The concentration profiles of the components are called the peak and they can be identified from their characteristic retention time.

The separation in GC involves adsorption and partition/bonded phase mechanisms for which the following factors must be considered:

- Sample type
- The carrier gas or mobile phase

- Column oven
- Sample injection system
- The type of column
- The detector

1.2.2.1 Sample Type

The sample must be thermally stable and have an appreciable vapor pressure at the column temperature to move with the gaseous mobile phase. So GC can be applied to permanent gases, non-ionized organic molecules and many organometallic compounds. Also the non-volatile compounds can be converted to more volatile by derivatization and stable derivatives before the separation. Care must be taken while running a mixture of volatile and non-volatile components, as the non-volatile solutes can be deposited in the system which may interfere with the subsequent analyses.

1.2.2.2 Carrier Gas or Mobile Phase

The function of the carrier gas is to transport the sample through the column. The carrier gas for GC should be inert toward the analyte, dry and free of oxygen to prevent the degradation of the column. Impure gases produce noisy baselines that reduce sensitivities, precision and quantitative analysis. The carrier gas can influence resolution through its effect on column efficiency as solute diffusion rates in various gases are different. The most popular carrier gases in GC are hydrogen, nitrogen and helium. A constant gas flow is maintained so the retention times will not vary.

1.2.2.3 Column Oven

Column oven is temperature controlled and houses the column. The oven temperature is programmed at a variety of rates with isothermal periods set as desired. It responds rapidly and accurately to the temperature program profile. The low thermal mass cools down fast at the end of the analysis.

The temperature of the oven has an effect on the time a sample is going to be retained by the column. At higher temperatures, the sample tends to elute faster. But it leads to less interaction between the sample and stationary phase, causing poor separation. The optimum temperature is when a balance is maintained between the oven run time and separation.

The temperature can be isothermally controlled or programmed. In an isothermal method, a constant column temperature is maintained during the analysis process. The advantage of isothermal separation is it gives optimal resolution. But this method is limited to samples having narrow boiling point range. A sample having components with boiling points more than 100°C apart cannot be separated with a single isothermal run. In a programmed temperature method, separation involves increasing column temperature during the run. It allows separation of broad boiling range samples in a single run. The run begins at low temperature to resolve the low retention components. As the run progresses, the temperature is increased incrementally to reduce the retention time of the high retention compounds. Highly resolved separation occurs if the temperature is ramped at a slow rate. For reproducible retention times, the oven temperature must be held to ±0.1°C or better.

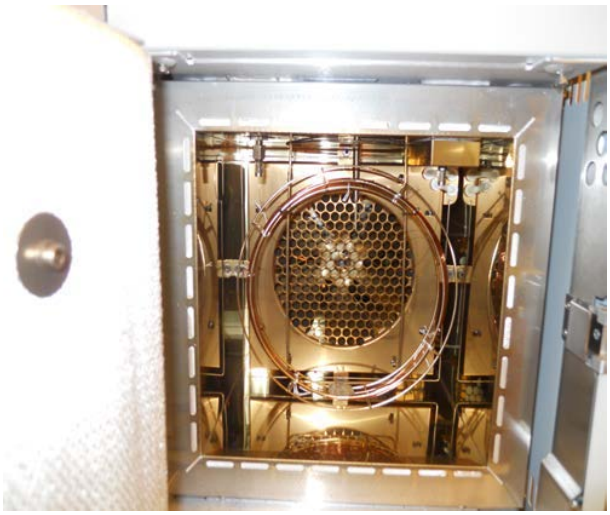


Figure 1.4: Column oven

1.2.2.4 Sample Injection System

The inlet system or injection port must deliver the correct amount of sample to the column so the column is not overloaded or the linear range of the detector is not exceeded. Also the sample needs to be vaporized readily and delivered to the column as a sharp band. But caution must be applied that the injector is not hot enough to decompose the sample. Temperature is set 50°C above the boiling point of the highest boiling sample. If the temperature is too low, the shape of the peak will be poor. Sample is introduced by means of a microsyringe through a septum made of elastomer or rubber which seals the inlet system as the syringe needle is withdrawn. But there can be difficulties during the injection process. Selective vaporization may occur from the syringe needle [56] during needle insertion into the hot vaporization chamber and from the residue remaining in the needle after the bulk of the sample is injected. Most needles are made of stainless steel. The syringe should be gas-tight at the column back pressure to prevent the loss of sample.

To avoid the peak broadening during the separation process a small volume of sample needs to be introduced into the column. To prevent unwanted cooling during fusion and vaporization of solid or liquid samples a well maintained heat capacity system is also needed. Also it should be taken into account that the solvent peak is not co-eluting with the solute peak. So to meet these requirements a good inlet system is needed. So inlet liners are introduced to the system to provide proper mixing of sample vapor with carrier gas, efficient transfer of heat to the sample and to prevent non-volatile materials interfering the column. In capillary chromatography there are several types of injection system. Two popular types are:

A. Split/splitless
B. On-column

1.2.2.4.1 Split Injection

In split injection the sample is injected after evaporation and homogenous mixing with the carrier gas. Then it is split into two unequal portions. The smaller portion passes through the column and the rest is vented to waste. The amount of sample entering the column is related to the split ratio times the amount of sample injected. The split ratio is determined by the relative magnitude of the two flow-rates. The disadvantage of this mode is that most of the sample is wasted.

1.2.2.4.2 Splitless Injection

In splitless injection a relatively large volume of dilute sample is introduced to the column. The carrier gas velocity is much lower. Therefore the sample stays in the injection port much longer and the temperature of the injection port is low enough for effective sample vaporization.

This system is usually applied for trace analysis. But it doesn't work well for samples containing high molecular mass, low volatility or low thermal stability. Also it places high solvent load on the column.

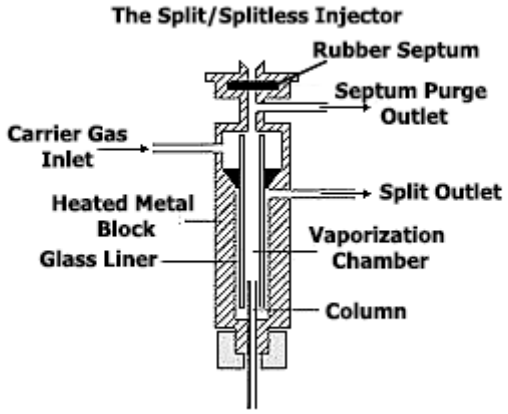


Figure 1.5: Split/splitless injector

1.2.2.4.3 On-Column Injection

To minimize the discrimination effect or catalytic decomposition on the metal surface, the sample is directly introduced on the open tubular column. The injector is initially cooled so that the sample will not vaporize. After injection the injector is rapidly heated to begin separation. Equilibrium is established prior to elution. This is used for thermally labile compounds and mixtures having a wide range of boiling points.

1.2.2.5 Column Type

As selectivity and the efficiency of the separation are determined by the column chemistry, it is considered the heart of the separation process in GC. There are two types of columns used in GC- Packed columns and open tubular or capillary columns. Packed columns are ones which are constructed from stainless steel or Pyrex glass packed with a suitable adsorbent. Typically these columns are 0.5-3 m long with a 3mm or 6mm outside diameter and 2-4mm inside diameter. But

open tubular columns are most popular for GC separation. These columns are usually polymer-clad flexible fused silica with bonded and/or cross-linked immobilized stationary phase on the wall of the column. They are 5-50m long, 0.1-1.0mm internal diameter and the stationary film thickness is 0.1-0.5um. Factors that affect the performance of the column are stationary phase chemistry, column diameter, film thickness, and column length [57-58].

Table 1.1: Recommended Stationary Phases according to the Compound's Polarity [57-58]

Polarity of the compound	Types of Compounds	Preferred Stationary Phases Composition
Polar Compounds containing Br, Cl, F, O, N,P,S other than C and H atom	Alcohols, amines, carboxylic acids, diols, ether, ketones, esters, thiols	20% diphenyl/80% dimethyl siloxane; 6% cyanopropylphenyl/94% dimethyl siloxane; 14% cyanopropylphenyl/86% dimethyl siloxane; 35% diphenyl/65% dimethyl siloxane; 50% diphenyl/50% dimethyl siloxane; 50% cyanopropylphenyl/50% dimethyl siloxane; ethylene glycol; alkylene glycol
Polarizable C and H atoms only, C=C or C=C bonds	Alkenes, arenes, alkynes	80% biscyanopropyl/20% cyanopropylphenyl siloxane; 90% biscyanopropyl/10% cyanopropylphenyl siloxane; biscyanopropyl siloxane; 1, 2, 3-tris(2-cyanoethoxy)propane
Non-Polar C and H atoms only, C-C bonds	alkanes	methyl silicone; 50% n-octyl/50% methyl siloxane; dimethylsiloxane; 5% diphenyl/95% dimethylsiloxane; silphenylene polymer

For stationary phase selection the rule is "likes dissolves like". The polarity of the compound should be close enough to that of the stationary phase for a well resolved separation. That is, polar compounds are most likely retained by the polar stationary phase than the non-polar phase.

The column diameter can also affect the efficiency and sample capacity of the column. As the internal diameter increases, the sample capacity increases but the efficiency of the column decreases.

Film thickness is also a determining factor for separation in GC. Thin film coatings decrease the column bleed and increase the resolution, signal-to-noise, and the maximum running temperature. Thin film coatings also decreases the retention time. Thick films have reduced interactions with the column tubing and have greater the sample capacity. However, thicker films, tend to produce peak broadening and poor resolution, as well as increase the retention time.

The last factor is the column length. The general length of the column is 10m to 100m. For screening purposes or simple samples where low resolution is enough, shorter columns are usually used. The long columns are used in case of high resolution, complex or volatile samples. Usually if the column length increases the resolution will also increase. Open tubular columns have high resolution power, greater sensitivity, reduced analysis time and greater chemical inertness.

Figure 1.6: Capillary column

1.2.2.6 Detector

The detector simply detects the presence of compounds in the gas stream as it leaves the column. Detectors can be concentration sensitive and mass sensitive. Concentration sensitive detector depends only on the concentration of the analyte. Mass sensitive detector depends on the mass of the analyte entering the detector per unit time. The column flow rate has an effect on the detector's response. At constant concentration, the response of a mass sensitive detector is

proportional to the flow rate while that of the concentration sensitive detector is constant. Another characteristic of all detectors is their baseline noise level when no peak is present. Excessive detector noise degrades quantitative accuracy and precision. Drifting baseline can also degrade performance. The purpose of the detector is to produce an electrical response proportional to the sample concentration. At high concentration, the response tends to become non-linear. At low concentration, the limit of detection is defined as the concentration that gives a response three times the system noise level.

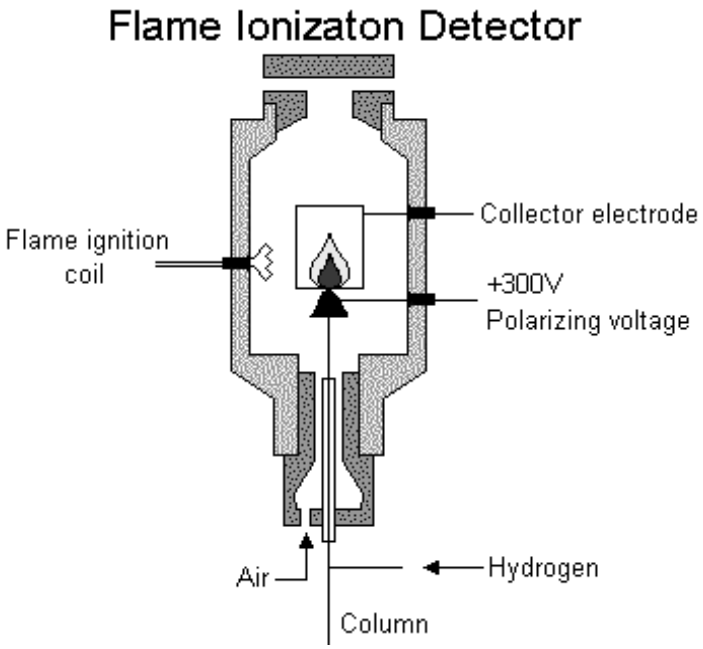


Figure 1.7: Flame ionization detector

There are several types of detectors available. Flame ionization detector (FID) is the universal detector specifically designed for gas chromatography. This detector is robust, sensitive and specific for organic compounds. For this research a FID detector is used, which consists of a base in which the eluent from the column is mixed with the hydrogen gas. There is a polarized jet and a cylindrical electrode that surround the flame. For combustion purpose air is supplied. In a stainless steel or aluminum body a flame ignition coil is placed. Electrical connection to the

collecting electrode and a polarizing voltage to the detector jet are applied. When the eluent burns it generates ions, there is a potential difference between the jet and the collector electrode and ionization current is detected. The current is amplified by the electrometer, producing a response that is proportional to the amount of carbon entering the flame per unit time.

1.3 Conclusion

Abraham solvation parameter model can be combined with GC experiment to establish predictive models for various applications including applications of environmental importance, physicochemical and biological properties of pharmaceutical importance. The information we get from the predicted Abraham molecular descriptors can help chemists, environmental scientists, and others to choose appropriate solvents for a particular solvation system. In present study, we are in the process of developing equations for GC stationary phases and also for predicting solute descriptors for illegal drugs from the gas chromatography retention data and structural information. Once the drug's descriptors are calculated, they can be used to predict the partitioning behavior of the molecule through different biological barriers. This experiment is also feasible since no elaborate experimental condition is needed. The partition coefficients can simply be determined by measuring the retention time and using retention time in appropriate equations. The partition co-efficient gives information whether the chemical will cross the biological membrane or not. It also corresponds to the effect of solvent phase on solute-solvent phase interactions. It reflects the chemical information of the solvent phase and also characterizes it.

CHAPTER 2

EXPERIMENTAL METHODOLOGY

2.1 Research Purpose

The purpose of the research is to experimentally determine molecular descriptors for certain drug compounds and analyze them with the Abraham model. Gas chromatography is used to characterize the drug compounds. Chromatographic data (retention time) can be used to calculate the molecular descriptors and then it can be related with the biological data as discussed in chapter one. GC data on a given stationary phase can be modeled for biological process involving transfer of a solute from the gas phase to a receptor or receptor area [68].

This correlation can predict the partitioning behavior of drug molecules across numerous biological barriers like the blood brain barrier (BBB). Gas Chromatography is a routine technique to analyze illegal drugs. The benefit of the Abraham model lies in the newly developed column equations; one can measure the retention time of a compound or a new drug on one of the six columns (with corresponding equations) and predict partitioning across numerous biological barriers.

2.2 GC Instrumentation

The gas chromatography system used has a Flame Ionization Detector (FID) (Thermo Fisher Scientific, Model GC FOCUS SERIES, Serial No. 10901012) connected to a Dell computer with ChromQuest software to run the analytical instrument. In the experiment, the GC system is used to obtain the retention time of each sample which will be used in the calculation of the solvation parameter model of Abraham.

Six different columns were used in the experiment to develop six Abraham equations based on the five unknowns in Equation 1. Columns TR-5, TR-1MS, TG-1301MS and TG-5MS were purchased from Thermo Scientific, column ZB-WAX and ZB-35 were purchased from Zebron. A summary of the columns stationary phases are shown in Table 2.1

Table 2.1: Summary of the Column Stationary Phase

Column	Stationary Phase	Polarity	Max. Temp.	Recommended
TR-1MS	100% dimethyl polysiloxane	non-polar	380°C	Chlorinated and nitroaromatic compounds
TG-5MS	5% diphenyl 95% dimethyl polysiloxane	low-polarity	350°C	Semivolatiles, Phenols, Amines
TR-5	5% phenyl methyl polysiloxane	Low-Polarity	350°C	Alcohols, free fatty acids, aromatics, flavours and low polarity pesticides
TG-1301MS	6% cyanopropylphenyl 94% dimethyl polysiloxane	Mid-polarity	280°C	Alcohols, Volatile organics, Oxygenates, Residual Solvents
ZB-35	35% phenyl 65% dimethylpolysiloxane	Mid-polarity	360°C	Aroclors, Semi-volatiles Amines, Drugs of Abuse, Pharmaceuticals, Steroids, Pesticides
ZB-Wax Plus	polyethylene glycol	polar	280°C	Esters, Alcohols, Ketones, Glycols, Aromatic Isomers

All compounds, both illegal drugs and chemical compounds were dissolved and diluted in methanol, dichloromethane, dimethylsulfoxide or acetonitrile to obtain the solution for injection. For the solid, the concentration of the compound is 1 mg/ml; for the liquid, the concentration is 1mg /ml. The chemical compounds with low boiling point are diluted in dichloromethane or DMSO, like acetone, ethanol, ethyl acetate, methyl acetate, butanone, and benzene, because the methanol solvent peak co-elutes with the peak of interest. The flow rate of helium carrier gas is 1.5 ml per minute. The initial oven temperature is set at 50°C, with a hold time of 2.00 min. Then the temperature is increased at a rate of 15°C per minute with 5.00 min hold time to the final temperature depending on the maximum temperature of the column. The average maximum oven

temperature is 260-330°C, prep-run timeout is 10.00 min, and equilibration time is 0.50 min. The detector temperature for FID is 200°C. The injection volume of the sample is primarily 1µL. But it was varied to 5 µL depending on the peak area of the sample. Also the split ratio is varied. Methanol was used to wash the needle for pre and post injection of the samples with 3 cycles. In addition, the needle was rinsed with the sample itself 3 times before injection. Each sample was run 3 times to reproduce the data. The columns were conditioned between each sample run for 2 times to make sure no analyte from the previous run was interfering with the retention time of the desired sample. Summary of method development are shown in Table 2.2.

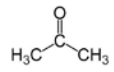
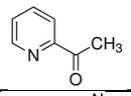
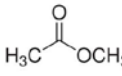
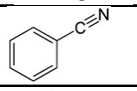
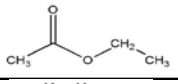
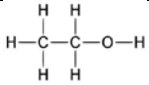
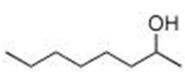
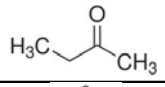
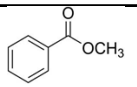
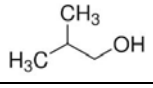
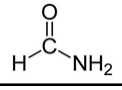
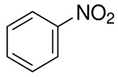
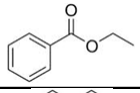
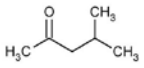
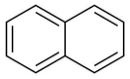
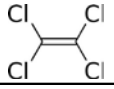
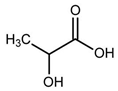
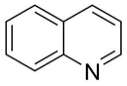
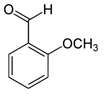
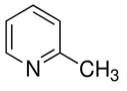
Table 2.2: Method Development

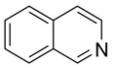
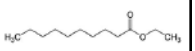
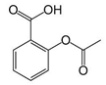
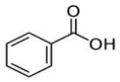
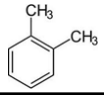
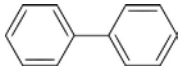
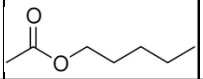
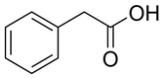
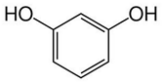
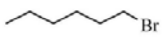
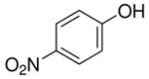
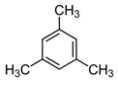
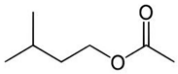
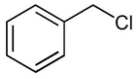
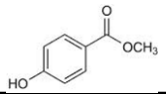
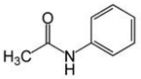
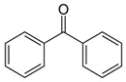
Column Dimensions	30m x 0.32 mm ID x 0.25 µm film thickness
Sample concentration	1mg/mL
Solvents	MeOH, DCM, DMSO
Injection Volume	1.0µL
Split Ratio	50:1
Split Mode	Split
Injection Temperature	240°C
Carrier gas	Helium
Carrier Flow Rate	1.5 mL/min
Initial Oven Temperature	50°C (hold for 2 min)
Final Oven temperature	360°C (depending on column temperature, hold for 5 min)
Ramp	15^{0}C/min
Prep run time	10.00 min
Equilibration time	0.5 min
Detector	FID
Detector temperature	200°C

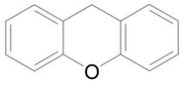
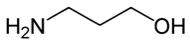
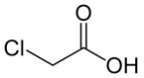
2.3 Chemicals

A diverse set of compounds covering a wide range of boiling points and size were selected. List of the compounds with their structures and boiling points are shown in Table 2.3.

Table 2.3: Physical and Chemical Properties of the Chemical Compounds

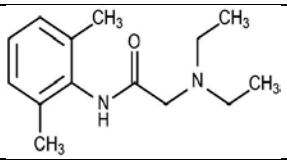
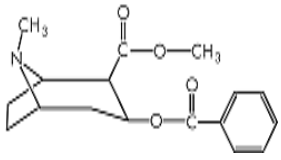
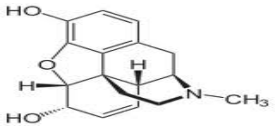
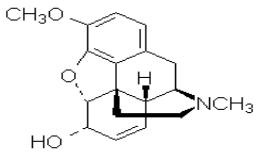
Solute	Structure	Boiling point	Solute (cont'd)	Structure	Boiling point
Acetone		56.5	2-acetylpyridine		189
Methyl Acetate		56.9	Benzonitrile		191
Tetrahydrofuran		66	o-cresol		191
Ethyl Acetate		77	N,N-Dimethylaniline		194
Ethanol		78.5	2-octanol		195
2-butanone		79.6	Methyl Benzoate		199.6
Benzene		80.1	Nonylamine		201
N-propyl alcohol		97.2	Acetophenone		202
2-Methyl-1-propanol		108	formamide		210
Toluene		110.6	nitrobenzene		210.9
Pyridine		115.2	Ethyl benzoate		213
methyl isobutyl ketone		115.9	N,N-Diethylaniline		217
Acetic Acid		118	Naphthalene		218
tetrachloroethylene		121.1	Acetamide		222
lactic acid		122	Quinoline		237
morpholine		129	o-anisaldehyde		238
2-picoline		129	Propylene Carbonate		240

Solute	Structure	Boiling point	Solute (cont'd)	Structure	Boiling point
Chlorobenzene		132	Isoquinoline		242
pentan-1-ol		139	Ethyl decanoate		245
aspirin		140	Benzoic Acid		249
1,2-Dimethylbenzene		144	biphenyl		255
amyl acetate		148	1-chloronaphthalene		263
N,N-Dimethylformamide		153	m-toluic acid		263
alpha pinene		155	Phenylacetic Acid		265.5
Bromobenzene		156	Resorcinol		277
1-bromohexane		158	4-nitrophenol		279
1,3,5-Trimethylbenzene		164.7	acenaphthene		280
2-chlorophenol		175	2-Chlorobenzoic acid		285
Octylamine		176	Vanillin		285
Caffeine		178	iso-pentyl acetate		287.6
Benzyl chloride		179	methyl-4-hydroxybenzoate		298.6
1,2-Dichlorobenzene		180	1-nitronaphthalene		304
diiodomethane		181	Acetanilide		304
phenol		181.7	Benzophenone		305.4

Solute	Structure	Boiling point	Solute (cont'd)	Structure	Boiling point
Aniline		186	xanthene		312
3-Amino-1-propanol		188	Phenanthrene		332
Chloroacetic acid		189	3-nitrobenzoic acid		341

Illegal and prescription drugs of cocaine, codeine, lidocaine and morphine were studied. Information of these drugs is tabulated in Table 2.4.

Table 2.4: Physical and Chemical Properties of Drug Compounds

Compound	Chemical Structure	Molecular Formula	Molecular Weight (g/mol)	Boiling Point ($^{\circ}$C)
Lidocaine		$C_{14}H_{22}N_2O$	234.34	181
Cocaine		$C_{17}H_{21}NO_4$	303.35	187-188
Codeine		$C_{18}H_{21}NO_3$	299.36	250
Morphine		$C_{17}H_{19}NO_3$	285.34	254

Chemical compounds in Table 2.4 are standard organic compounds which have similar functional groups with the drug samples. The solvents used to dissolve the drug samples and the

compounds are HPLC grade methyl alcohol (Spectrum Chemical Mfg. Corp.) and analytical grade dichlormethane (Spectrum Chemical Mfg. Corp.), DMSO, ACN.

After running the GC system, Equation (1) was used to solve Abraham solvation parameter model with retention times of each compound and using the experimental gas-to-liquid partition coefficient data (E, S, A, B and L) from literature [35-38]. The statistical product and service solutions (SPSS) software is used to calculate the process coefficients (c, e, s, a, b, and l) by multiple linear regression analysis from the experimental logRT, where RT is retention time. Then using these co-efficients the calculated logRT is obtained.

2.4 Multiple Linear Regression Analysis

Multiple linear regression analysis (MLRA) is a statistical technique correlating two or more independent variables (*x*) and a dependent variable (*y*) to produce equation coefficients. A two independent variable system can be shown mathematically as follows:

$$y = a + b_1x_1 + b_2x_2 \quad (8)$$

where a is the regression constant, b_1 and b_2 are the equation coefficients for the independent variables x_1 and x_2, respectively. The variable being predicted is the dependent variable, whereas the variables predicting the dependent variable are the independent variables. The latters are also known as the predictor or regressor. Multiple linear regression analysis is commonly used to create specific linear free-energy relationships including the Abraham solvation parameter model. This highly sophisticated method is easy to execute with various software including Microsoft's Excel and SPSS. It is to be noted that several values are needed for each variable used in the multiple linear regression analysis. One needs approximately thirty values in order to make a regression of good quality that includes five variables.

2.5 Standard Deviation

The standard deviation is the average distance, or deviation, from the mean. It is basically the average amount of variability in a set of data. It can be defined mathematically as follows:

$$sd = \sqrt{\frac{\sum(x - \bar{x})^2}{n - p - 1}}$$

where *s* is standard deviation, Σ is (mathematical summation), x is individual data, $\bar{x}$ is the mean of the data set, n is the number in the sample size, and p is the number of independent variables.

A low standard deviation represents there is a low spread of data with a good relationship among the data points. A high standard deviation represents a poor relationship among the data points. For multiple linear regression analysis a low standard deviation is favorable since it represents a regression equation that is a good representation of the qualities of the data set.

2.6 Correlation Coefficient

The correlation coefficient, *r*, reflects the linear relationship between two variables. It is usually ranged between -1 and +1. The sign of the correlation coefficient determines the direction of how the variables are correlated. Positive signs reflect a direct relationship between the two variables; the variables change in the same direction. Negative signs reflect an indirect relationship between the two variables; the variables change in opposing directions. The correlation coefficient squared, r^2 or R^2, is the percentage of variance in one variable that is accounted for by the variance in the other variable. It is also known as co-efficient of determination. The R^2 would be equal to one, if the individual predicted or calculated values based on the equation matched the individual experimental or observed values. In this situation, a plot of experimental values on the x axis and the calculated values on the y-axis, will create a completely straight line.

2.7 Construction of the Spread Sheet

The calculated logRT used in Microsoft excel solver is to minimize the sum of squares on the set of described system equations. System equations consists of the six equations using the known process coeffients (*c,e,s,a,b,v* and *l*) as equation coefficients. These process coefficients for each of the column have been calculated by MLRA by using SPSS software. The E, L and V values are set as constant and the values for these can be found in the literature. The overall sums of squares are set at a minimum to fit the targeted cells S, A and B where A and B are set as constrained variables with a value of (≥ 0) as acidity and basicity can't be negative. S is set as unconstrained variable. The solving method used here is the generalized reduced gradient (GRG) non-linear solving method which is used for problems that are non-linear. It gives at least a local optimal solution and the solution for S, A and B can be obtained by excel solver.

CHAPTER 3

RESULTS AND DISCUSSION

3.1 Result and Data

More than 75 compounds were run on the GC three times each for each of the six columns. This becomes the training set for building up the equations for calculating descriptors. From the average of three runs, the logarithm of retention time is calculated, as well as standard deviation and RSD. These data for the six columns are shown from Tables 3.1 to 3.6.

Table 3.1: Retention Time for Compounds in TR-5 (5% phenyl methyl polysiloxane) Column

Solute	RUN1	RUN2	RUN3	AVG	SD	RSD
1,3,5-Trimethylbenzene	6.492	6.483	6.483	6.486	0.005	0.08
1,2-dichlorobenzene	7.292	7.285	7.300	7.292	0.008	0.103
1,2-dimethyl benzene	5.61	5.612	5.618	5.613	0.004	0.074
1-bromohexane	6.113	6.108	6.107	6.109	0.003	0.053
1-chloronaphthalene	10.778	10.772	10.773	10.774	0.003	0.03
1-nitronaphthalene	12.57	12.57	12.572	12.571	0.001	0.009
2-acetylpyridine	7.258	7.255	7.253	7.255	0.003	0.035
2-butanone	2.675	2.647	2.645	2.656	0.017	0.632
2-chlorobenzoic acid	10.612	10.652	10.6	10.621	0.027	0.256
2-chlorophenol	6.76	6.76	6.767	6.762	0.004	0.06
2-methylcyclohexane	6.272	6.272	6.268	6.271	0.002	0.037
2-picoline	4.602	4.602	4.597	4.6	0.003	0.063
3-amino-1-propanol	4.865	4.857	4.867	4.863	0.005	0.109
3-nitrobenzoic acid	12.262	12.265	12.263	12.263	0.002	0.012
Acenaphthene	11.613	11.612	11.61	11.612	0.002	0.013
Acetamide	4.503	4.422	4.448	4.458	0.041	0.928
Acetanilide	10.608	10.608	10.605	10.607	0.002	0.016
acetic acid	2.873	2.863	2.867	2.868	0.005	0.176
Acetone	2.348	2.343	2.342	2.344	0.003	0.137
Acetophenone	7.657	7.668	7.672	7.666	0.008	0.101
alpha-pinene	6.14	6.132	6.135	6.136	0.004	0.066
amyl acetate	5.808	5.812	5.808	5.809	0.002	0.04
Aniline	6.607	6.6	6.605	6.604	0.004	0.055
benzoic acid	9.1	9.16	9.128	9.129	0.03	0.329
Benzonitrile	6.685	6.69	6.698	6.691	0.007	0.098
Benzophenone	12.705	12.712	12.713	12.71	0.004	0.034
benzyl chloride	7.007	7.003	7.007	7.006	0.002	0.033
biphenyl	10.69	10.688	10.683	10.687	0.004	0.034

bromobenzene	6.115	6.107	6.102	6.108	0.007	0.107
caffeine	15.357	15.417	15.387	15.387	0.03	0.195
chloroacetic acid	4.087	4.068	4.137	4.097	0.036	0.87
chlorobenzene	5.008	5.003	5.008	5.006	0.003	0.058
Cocaine	9.957	9.952	9.965	9.958	0.007	0.066
Codeine	18.302	18.208	18.285	18.265	0.05	0.274
ethanol	2.3	2.27	2.273	2.281	0.017	0.724
ethyl acetate	2.727	2.691	2.718	2.712	0.019	0.691
ethyl benzoate	8.733	8.735	8.73	8.733	0.003	0.029
ethyl decanoate	10.685	10.685	10.687	10.686	0.001	0.011
formamide	4.947	4.95	4.952	4.95	0.003	0.051
iso-pentyl acetate	5.4	5.392	5.39	5.394	0.005	0.098
isoquinoline	9.665	9.665	9.655	9.662	0.006	0.06
lactic acid	5.803	6.092	5.88	5.925	0.15	2.526
Lidocaine	15.832	15.795	15.828	15.818	0.02	0.128
methyl acetate	2.425	2.412	2.417	2.418	0.007	0.271
methyl benzoate	7.96	7.96	7.953	7.958	0.004	0.051
methyl isobutyl ketone	3.748	3.743	3.745	3.745	0.003	0.067
methyl-4-hydroxybenzoate	11.228	11.217	11.22	11.222	0.006	0.051
Morphine	9.962	9.963	9.98	9.968	0.01	0.101
morpholine	4.492	4.492	4.49	4.491	0.001	0.026
N,N-diethylaniline	9.253	9.255	9.255	9.254	0.001	0.012
N,N-dimethylaniline	7.895	7.897	7.895	7.896	0.001	0.015
N,N-dimethylformamide	4.293	4.29	4.292	4.292	0.002	0.036
naphthalene	8.897	8.902	8.893	8.897	0.005	0.051
nitrobenzene	7.937	7.94	7.935	7.937	0.003	0.032
nonylamine	8.418	8.415	8.413	8.415	0.003	0.03
N-propyl alcohol	2.513	2.333	2.337	2.394	0.103	4.293
o-anisaldehyde	9.413	9.415	9.415	9.414	0.001	0.012
octyl amine	7.313	7.297	7.295	7.302	0.01	0.135
pentan-1-ol	4.058	4.058	4.067	4.061	0.005	0.128
phenanthrene	13.943	13.945	13.94	13.943	0.003	0.018
phenol	6.607	6.62	6.617	6.615	0.007	0.103
phenylacetic acid	9.398	9.423	9.393	9.405	0.016	0.171
propylene carbonate	6.792	6.793	6.81	6.798	0.01	0.149
pyridine	3.778	3.797	3.795	3.79	0.01	0.275
quinoline	9.428	9.437	9.437	9.434	0.005	0.055
resorcinol	9.685	9.68	9.687	9.684	0.004	0.037
tetrachloroethylene	4.572	4.572	4.572	4.572	0	0
tetrahydrofuran	2.83	2.805	2.802	2.812	0.015	0.547
toluene	4.015	4.003	3.997	4.005	0.009	0.229
vanillin	10.818	10.817	10.82	10.818	0.002	0.014
xanthene	12.96	12.973	12.975	12.969	0.008	0.063

N/A: 4-nitrophenol, Aspirin, Diiodomethane, m-toluic acid, o-cresol do not elute for this column

Table 3.2: Retention Time for Compounds in TR-1MS (100% dimethyl polysiloxane) Column

SOLUTE	RUN1	RUN2	RUN3	AVG	SD	RSD
1,3,5- Trimethylbenzene	8.620	8.623	8.622	8.622	0.002	0.018
1,2-dichlorobenzene	9.143	9.150	9.150	9.148	0.004	0.044
1-bromohexane	8.038	8.042	8.047	8.042	0.005	0.056
1-chloronaphthalene	12.572	12.558	12.560	12.563	0.008	0.060
1-nitronaphthalene	14.257	14.260	14.258	14.258	0.002	0.011
2-acetyl pyridine	9.003	8.997	8.997	8.999	0.003	0.038
2-butanone	4.475	4.485	4.478	4.479	0.005	0.115
2-chlorophenol	8.678	8.683	8.678	8.680	0.003	0.033
2-methyl cyclohexanone	8.217	8.218	8.223	8.219	0.003	0.039
2-picoline	6.575	6.573	6.572	6.573	0.002	0.023
3-amino-1-propanol	6.457	6.445	6.450	6.451	0.006	0.093
acenaphthene	13.408	13.422	13.417	13.416	0.007	0.053
acetanilide	12.295	12.257	12.250	12.267	0.024	0.197
acetic acid	4.653	4.638	4.658	4.650	0.010	0.224
acetone	4.322	4.225	4.128	4.225	0.097	2.296
acetophenone	9.423	9.450	9.428	9.434	0.014	0.152
alpha-pinene	8.360	8.362	8.353	8.358	0.005	0.057
amyl acetate	7.733	7.742	7.743	7.739	0.006	0.071
aniline	8.395	8.400	8.400	8.398	0.003	0.034
benzene	5.010	5.030	5.033	5.024	0.013	0.249
benzoic acid	10.485	10.495	10.503	10.494	0.009	0.086
benzonitrile	8.415	8.405	8.400	8.407	0.008	0.091
benzophenone	14.418	14.412	14.412	14.414	0.003	0.024
benzyl chloride	8.903	8.887	8.885	8.892	0.010	0.111
biphenyl	12.467	12.465	12.467	12.466	0.001	0.009
bromobenzene	8.152	8.145	8.147	8.148	0.004	0.044
chlorobenzene	7.012	7.007	7.000	7.006	0.006	0.086
diiodomethane	8.880	8.880	8.893	8.884	0.008	0.084
ethyl acetate	4.580	4.572	4.577	4.576	0.004	0.088
ethyl alcohol	3.930	3.935	3.935	3.933	0.003	0.073
ethyl benzoate	10.515	10.502	10.495	10.504	0.010	0.097
ethyl decanoate	12.503	12.500	12.498	12.500	0.003	0.020
formamide	6.697	6.647	6.605	6.650	0.046	0.693
isopentylacetate	7.433	7.418	7.408	7.420	0.013	0.170
isoquinoline	11.408	11.395	11.392	11.398	0.009	0.075
lactic acid	7.547	8.065	7.613	7.742	0.282	3.642
methyl acetate	4.245	4.245	4.247	4.246	0.001	0.027
methyl benzoate	9.733	9.737	9.737	9.736	0.002	0.024
methyl Isobutyl ketone	5.710	5.705	5.703	5.706	0.004	0.063
methyl-4-hydroxybenzoate	12.907	12.895	12.843	12.882	0.034	0.264
morpholine	6.277	6.272	6.273	6.274	0.003	0.042
N,N-diethyl aniline	11.068	11.063	11.067	11.066	0.003	0.024

N,N-dimethyl aniline	9.717	9.717	9.712	9.715	0.003	0.030
N,N-dimethyl formamide	6.087	6.130	6.133	6.117	0.026	0.421
naphthalene	10.793	10.817	10.800	10.803	0.012	0.114
nitrobenzene	9.653	9.633	9.635	9.640	0.011	0.114
nonyl amine	10.333	10.332	10.343	10.336	0.006	0.059
n-propyl alcohol	4.080	4.085	4.080	4.082	0.003	0.071
o-anisaldehyde	11.957	11.955	11.952	11.955	0.003	0.021
octylamine	9.268	9.272	9.278	9.273	0.005	0.054
pentane-1-ol	6.043	6.033	6.033	6.036	0.006	0.096
phenanthrene	15.665	15.665	15.657	15.662	0.005	0.029
phenol	8.468	8.470	8.473	8.470	0.003	0.030
phenylacetic acid	11.187	11.187	11.185	11.186	0.001	0.010
propylene carbonate	8.255	8.255	8.248	8.253	0.004	0.049
pyridine	5.725	5.737	5.723	5.728	0.008	0.132
quinoline	11.177	11.175	11.173	11.175	0.002	0.018
resorcinol	11.353	11.373	11.403	11.376	0.025	0.221
tetrachloroethylene	6.647	6.647	6.645	6.646	0.001	0.017
tetrahydrofuran	5.020	4.942	4.878	4.947	0.071	1.438
toluene	6.103	6.100	6.100	6.101	0.002	0.028
vanillin	12.487	12.487	12.532	12.502	0.026	0.208
xanthene	14.718	14.720	14.725	14.721	0.004	0.024
Lidocaine	16.358	16.377	16.378	16.371	0.011	0.069
Cocaine	11.962	11.963	11.963	11.963	0.001	0.005
Morphine	11.963	11.965	11.967	11.965	0.002	0.017
Codeine	18.27	18.253	18.265	18.263	0.009	0.048

N/A: 1-bromohexane, 2-chlorobenzoic acid, 3-nitrobenzoic acid, 4-nitrophenol, Acetamide, Aspirin, Caffeine, Chloroacetic acid, m-toluic acid, o-cresol do not elute for this column

Table 3.3: Retention Time for Compounds in ZB-WAX Plus (polyethylene glocol) Column

SOLUTE	RUN1	RUN2	RUN3	AVG	SD	RSD
1,3,5-trimethylbenzene	7.082	7.083	7.082	7.082	0.001	0.008
1-bromohexane	6.100	6.113	6.110	6.108	0.007	0.111
1,2-Dichlorobenzene	9.343	9.340	9.340	9.341	0.002	0.019
1,2-Dimethylbenzene	6.492	6.480	6.485	6.486	0.006	0.093
2-acetylpyridine	10.290	10.283	10.285	10.286	0.004	0.035
2-butanone	3.925	3.913	3.915	3.918	0.006	0.164
2-chlorophenol	12.135	12.138	12.140	12.138	0.003	0.021
2-picoline	6.827	6.822	6.815	6.821	0.006	0.088
3-Amino-1-propanol	9.682	9.668	9.663	9.671	0.010	0.102
Acetamide	11.358	11.357	11.362	11.359	0.003	0.023
Acetic Acid	9.142	9.137	9.102	9.127	0.022	0.239
Acetone	3.195	3.195	3.195	3.195	0.000	0.000
Acetophenone	10.635	10.645	10.648	10.643	0.007	0.064

alpha pinene	4.823	4.815	4.812	4.817	0.006	0.118
amyl acetate	6.310	6.310	6.302	6.307	0.005	0.073
Aniline	11.377	11.378	11.382	11.379	0.003	0.023
Benzene	4.013	4.010	4.007	4.010	0.003	0.075
Benzoic Acid	15.733	15.755	15.748	15.745	0.011	0.071
Benzonitrile	10.305	10.307	10.307	10.306	0.001	0.011
Benzyl chloride	9.538	9.537	9.532	9.536	0.003	0.034
biphenyl	12.667	12.663	12.663	12.664	0.002	0.018
Bromobenzene	8.053	8.053	8.057	8.054	0.002	0.029
Chlorobenzene	6.755	6.755	6.755	6.755	0.000	0.000
diiodomethane	7.037	7.048	7.032	7.039	0.008	0.116
Ethanol	3.975	3.977	3.977	3.976	0.001	0.029
Ethyl Acetate	3.592	3.593	3.590	3.592	0.002	0.043
Ethyl benzoate	10.733	10.733	10.737	10.734	0.002	0.022
Ethyl decanoate	10.402	10.417	10.413	10.411	0.008	0.075
formamide	10.085	10.087	10.085	10.086	0.001	0.011
Isoquinoline	13.078	13.092	13.090	13.087	0.008	0.058
lactic acid	7.715	7.708	7.715	7.713	0.004	0.052
Methyl Acetate	3.252	3.255	3.252	3.253	0.002	0.053
Methyl Benzoate	10.413	10.410	10.407	10.410	0.003	0.029
methyl isobutyl ketone	4.607	4.608	4.617	4.611	0.006	0.119
Methylcyclohexane	7.725	7.727	7.730	7.727	0.003	0.033
morpholine	7.110	7.107	7.108	7.108	0.002	0.021
N-propyl alcohol	3.852	3.918	3.940	3.903	0.046	1.173
N,N-Diethylaniline	10.385	10.387	10.380	10.384	0.004	0.035
N,N-Dimethylaniline	9.817	9.815	9.817	9.816	0.001	0.012
N,N-Dimethylformamide	7.935	7.928	7.927	7.930	0.004	0.055
Naphthalene	11.348	11.348	11.352	11.349	0.002	0.020
nitrobenzene	11.327	11.330	11.332	11.330	0.003	0.022
Nonylamine	8.697	8.690	8.702	8.696	0.006	0.069
o-anisaldehyde	12.533	12.545	12.540	12.539	0.006	0.048
Octylamine	7.857	7.842	7.840	7.846	0.009	0.118
pentan-1-ol	7.047	7.050	7.045	7.047	0.003	0.036
phenol	13.317	13.322	13.323	13.321	0.003	0.024
Phenylacetic Acid	15.908	15.900	15.893	15.900	0.008	0.047
Propylene Carbonate	12.072	12.078	12.068	12.073	0.005	0.042
Pyridine	6.455	6.460	6.463	6.459	0.004	0.063
Quinoline	12.787	12.780	12.778	12.782	0.005	0.037
tetrachloroethylene	4.792	4.777	4.775	4.781	0.009	0.194
Tetrahydrofuran	3.467	3.468	3.470	3.468	0.002	0.044
Toluene	4.967	4.952	4.947	4.955	0.010	0.210

N/A: Lidocaine, Cocaine, Morphine, Codeine, 1,2- dichlorobenzene, 1-chloronaphthalene, 1-nitronaphthalene, 2-chlorobenzoic acid, 3-nitrobenzoic acid, 4-nitrophenol, Acenaphthene, Acetamide, Aspirin, Benzophenone, Caffeine, Chloroacetic acid, methyl-4-hydroxybenzoate, m-toluic acid, o-cresol, phenanthrene, resorcinol, vanillin, xanthene do not elute for this column

Table 3.4: Retention Time for Compounds in TG-1301MS (6% cyanopropylphenyl 94% dimethyl polysiloxane) Column

SOLUTE	RUN1	RUN2	RUN3	AVG	SD	RSD
1,3,5-trimethylbenzene	6.577	6.573	6.565	6.572	0.006	0.093
1,2-dichlorobenzene	7.565	7.567	7.563	7.565	0.002	0.026
1,2-dimethyl benzene	5.705	5.718	5.723	5.715	0.009	0.163
1-bromohexane	6.248	6.242	6.243	6.244	0.003	0.051
1-chloronaphthalene	11.177	11.158	11.153	11.163	0.013	0.113
2-acetylpyridine	7.722	7.720	7.725	7.722	0.003	0.033
2-butanone	2.897	2.900	2.898	2.898	0.002	0.053
2-chlorophenol	7.467	7.463	7.470	7.467	0.004	0.047
2-methylcyclohexane	6.762	6.758	6.758	6.759	0.002	0.034
2-octanol	7.265	7.268	7.267	7.267	0.002	0.021
2-picoline	4.872	4.870	4.875	4.872	0.003	0.052
3-amino-1-propanol	5.713	5.732	5.728	5.724	0.010	0.175
acenaphthene	12.003	12.000	11.995	11.999	0.004	0.034
acetic acid	3.442	3.425	3.417	3.428	0.013	0.372
acetophenone	8.240	8.238	8.238	8.239	0.001	0.014
alpha-pinene	5.985	5.980	5.980	5.982	0.003	0.048
amyl acetate	6.105	6.108	6.102	6.105	0.003	0.049
aniline	7.398	7.400	7.403	7.400	0.003	0.034
benzene	3.187	3.187	3.185	3.186	0.001	0.036
benzoic acid	10.032	10.150	10.045	10.076	0.065	0.642
benzonitrile	7.432	7.432	7.430	7.431	0.001	0.016
benzyl chloride	7.408	7.412	7.418	7.413	0.005	0.068
biphenyl	11.038	11.047	11.050	11.045	0.006	0.057
bromobenzene	6.305	6.307	6.308	6.307	0.002	0.024
chlorobenzene	5.175	5.175	5.180	5.177	0.003	0.056
Cocaine	11.548	11.548	11.548	11.548	0.000	0.000
Codeine	15.603	15.607	15.612	15.607	0.005	0.029
ethanol	2.362	2.358	2.360	2.360	0.002	0.085
ethyl acetate	2.902	2.903	2.902	2.902	0.001	0.020
ethyl benzoate	9.115	9.122	9.138	9.125	0.012	0.129
ethyl decanoate	10.952	10.952	10.943	10.949	0.005	0.047
formamide	6.375	6.387	6.376	6.379	0.007	0.104
isoquinoline	10.243	10.252	10.262	10.252	0.010	0.093
lactic acid	4.513	4.505	4.495	4.504	0.009	0.200
Lidocaine	11.452	11.458	11.558	11.489	0.060	0.518
methyl benzoate	8.362	8.360	8.360	8.361	0.001	0.014
methyl isobutyl ketone	4.137	4.132	4.133	4.134	0.003	0.064
Morphine	10.178	10.160	10.123	10.154	0.028	0.276
morpholine	4.912	4.925	4.903	4.913	0.011	0.225
N,N-diethylaniline	9.577	9.593	9.568	9.579	0.013	0.132
N,N-dimethylaniline	8.237	8.233	8.237	8.236	0.002	0.028

N,N-dimethylformamide	5.425	5.395	5.420	5.413	0.016	0.297
naphthalene	9.313	9.320	9.320	9.318	0.004	0.043
nitrobenzene	8.543	8.543	8.538	8.541	0.003	0.034
nonylamine	8.538	8.537	8.542	8.539	0.003	0.031
N-propyl alcohol	2.465	2.465	2.462	2.464	0.002	0.070
o-anisaldehyde	10.675	10.677	10.677	10.676	0.001	0.011
o-cresol	8.512	8.518	8.522	8.517	0.005	0.059
octyl amine	7.430	7.428	7.433	7.430	0.003	0.034
pentan-1-ol	4.580	4.580	4.580	4.580	0.000	0.000
phenol	7.978	7.970	7.963	7.970	0.008	0.094
propylene carbonate	8.608	8.618	8.628	8.618	0.010	0.116
pyridine	4.152	4.147	4.145	4.148	0.004	0.087
quinoline	9.955	9.950	9.958	9.954	0.004	0.041
tetrachloroethylene	4.550	4.542	4.542	4.545	0.005	0.102
tetrahydrofuran	2.972	2.973	2.970	2.972	0.002	0.051
toluene	4.165	4.163	4.163	4.164	0.001	0.028

N/A: 1-nitronaphthalene, 2-chlorobenzoic acid, 3-nitrobenzoic acid, 4-nitrophenol, Acetamide, Acetanilide, Aspirin, Benzophenone, Caffeine, Chloroacetic acid, Diiodomethane, methyl-4-hydroxybenzoate, m-toluic acid, o-cresol, phenanthrene, Phenylacetic acid, resorcinol, vanillin, xanthene do not elute for this column

Table 3.5: Retention Time for Compounds in TG-5MS (5% diphenyl 95% dimethyl polysiloxane) Column

SOLUTE	RUN1	RUN2	RUN3	AVG	SD	RSD
1,3,5-trimethylbenzene	6.403	6.398	6.403	6.401	0.003	0.045
1,2-dichlorobenzene	7.227	7.225	7.232	7.228	0.004	0.050
1,2-dimethyl benzene	5.488	5.488	5.488	5.488	0.000	0.000
1-bromohexane	5.985	5.985	5.985	5.985	0.000	0.000
1-nitronaphthalene	12.502	12.500	12.498	12.500	0.002	0.016
2-acetylpyridine	7.152	7.158	7.153	7.154	0.003	0.045
2-aminophenol	9.062	9.067	9.053	9.061	0.007	0.078
2-butanone	2.562	2.560	2.645	2.589	0.049	1.874
2-chlorobenzoic acid	10.452	10.478	10.462	10.464	0.013	0.125
2-chlorophenol	6.680	6.678	6.673	6.677	0.004	0.054
2-methylcyclohexane	6.177	6.165	6.165	6.169	0.007	0.112
2-octanol	6.753	6.747	6.752	6.751	0.003	0.048
2-picoline	4.452	4.460	4.467	4.460	0.008	0.168
3-amino-1-propanol	4.800	4.737	4.812	4.783	0.040	0.842
3-nitrobenzoic acid	12.155	12.168	12.175	12.166	0.010	0.083
4-nitrophenol	11.752	11.752	11.752	11.752	0.000	0.000
acenaphthene	11.566	11.555	11.552	11.558	0.007	0.064
acetamide	4.677	4.687	4.693	4.686	0.008	0.173
acetanilide	10.537	10.548	10.535	10.540	0.007	0.066

acetic acid	2.678	2.687	2.688	2.684	0.006	0.205
acetone	2.222	2.222	2.220	2.221	0.001	0.052
acetophenone	7.592	7.582	7.580	7.585	0.006	0.085
amyl acetate	5.722	5.717	5.717	5.719	0.003	0.050
aniline	6.552	6.550	6.548	6.550	0.002	0.031
aspirin	9.915	9.932	9.942	9.930	0.014	0.137
benzene	2.987	2.990	2.982	2.986	0.004	0.135
benzoic acid	9.032	9.020	9.070	9.041	0.026	0.289
benzonitrile	6.633	6.640	6.633	6.635	0.004	0.061
benzophenone	12.533	12.650	12.655	12.613	0.069	0.547
benzyl chloride	6.972	6.967	6.967	6.969	0.003	0.041
biphenyl	10.647	10.637	10.637	10.640	0.006	0.054
chloroacetic acid	3.978	3.945	3.990	3.971	0.023	0.587
chlorobenzene	4.893	4.903	4.897	4.898	0.005	0.103
Cocaine	10.072	10.068	10.065	10.068	0.004	0.035
Codeine	18.648	18.655	18.663	18.655	0.008	0.040
decane	6.740	6.740	6.738	6.739	0.001	0.017
ethanol	2.150	2.150	2.155	2.152	0.003	0.134
ethyl acetate	2.648	2.647	2.652	2.649	0.003	0.100
ethyl benzoate	8.638	8.652	8.645	8.645	0.007	0.081
ethyl decanoate	10.603	10.605	10.610	10.606	0.004	0.034
formamide	5.158	5.132	5.115	5.135	0.022	0.422
iso-pentyl acetate	5.293	5.255	5.237	5.262	0.029	0.543
isoquinoline	9.595	9.588	9.582	9.588	0.007	0.068
lactic acid	3.927	3.930	3.883	3.913	0.026	0.672
Lidocaine	11.550	11.555	11.558	11.554	0.004	0.035
methyl acetate	2.317	2.302	2.293	2.304	0.012	0.526
methyl benzoate	7.865	7.857	7.850	7.857	0.008	0.096
methyl isobutyl ketone	3.662	3.680	3.662	3.668	0.010	0.283
methyl-4-hydroxybenzoate	11.133	11.125	11.125	11.128	0.005	0.042
Morphine	11.523	11.522	11.525	11.523	0.002	0.013
morpholine	4.250	4.252	4.245	4.249	0.004	0.085
N,N-diethylaniline	9.172	9.173	9.170	9.172	0.002	0.017
N,N-dimethylaniline	7.842	7.823	7.830	7.832	0.010	0.123
N,N-dimethylformamide	4.468	4.435	4.477	4.460	0.022	0.496
naphthalene	8.838	8.833	8.837	8.836	0.003	0.030
nitrobenzene	7.835	7.825	7.827	7.829	0.005	0.068
nonylamine	8.313	8.307	8.310	8.310	0.003	0.036
N-propyl alcohol	2.223	2.222	2.218	2.221	0.003	0.119
o-anisaldehyde	10.172	10.173	10.172	10.172	0.001	0.006
o-cresol	7.378	7.368	7.375	7.374	0.005	0.070
octyl amine	7.228	7.232	7.230	7.230	0.002	0.028
pentan-1-ol	3.932	3.932	3.930	3.931	0.001	0.029
phenanthrene	13.830	13.825	13.827	13.827	0.003	0.018
phenol	6.530	6.525	6.513	6.523	0.009	0.134

phenylacetic acid	9.440	9.432	9.427	9.433	0.007	0.070
propylene carbonate	7.128	7.102	7.092	7.107	0.019	0.261
pyridine	3.705	3.698	3.698	3.700	0.004	0.109
quinoline	9.367	9.363	9.372	9.367	0.005	0.048
resorcinol	9.578	9.580	9.575	9.578	0.003	0.026
tetrachloroethylene	4.482	4.478	4.475	4.478	0.004	0.078
tetrahydrofuran	2.752	2.752	2.753	2.752	0.001	0.021
toluene	3.977	3.972	3.970	3.973	0.004	0.091
vanillin	10.737	10.730	10.733	10.733	0.004	0.033

Table 3.6: Retention Time for Compounds in ZB-35 (35% phenyl 65% dimethylpolysiloxane) Column

SOLUTE	RUN1	RUN2	RUN3	AVG	SD	RSD
1,3,5-trimethylbenzene	6.920	6.912	6.913	6.915	0.004	0.063
1,2-dichlorobenzene	8.082	8.100	8.087	8.090	0.009	0.115
1,2-dimethyl benzene	6.185	6.183	6.187	6.185	0.002	0.032
1-bromohexane	6.468	6.463	6.458	6.463	0.005	0.077
1-chloronaphthalene	11.783	11.762	11.665	11.737	0.063	0.536
1-nitronaphthalene	13.948	13.948	13.950	13.949	0.001	0.008
2-acetyl pyridine	8.352	8.337	8.328	8.339	0.012	0.145
2-Aminophenol	10.360	10.365	10.360	10.362	0.003	0.028
2-butanone	3.372	3.380	3.380	3.377	0.005	0.137
2-Chlorobenzoic acid	11.548	11.517	11.528	11.531	0.016	0.136
2-chlorophenol	7.588	7.587	7.582	7.586	0.003	0.042
2-methyl cyclohexanone	7.165	7.157	7.165	7.162	0.005	0.064
2-picoline	5.605	5.627	5.618	5.617	0.011	0.197
4-Nitrophenol	13.168	13.167	13.162	13.166	0.003	0.024
acenaphthene	12.698	12.695	12.692	12.695	0.003	0.024
acetanilide	12.018	12.015	12.010	12.014	0.004	0.034
acetic acid	3.438	3.395	3.465	3.433	0.035	1.028
acetone	2.978	2.960	2.952	2.963	0.013	0.449
acetophenone	8.738	8.727	8.740	8.735	0.007	0.080
alpha-pinene	6.138	6.132	6.130	6.133	0.004	0.068
amyl acetate	6.245	6.242	6.233	6.240	0.006	0.100
aniline	7.813	7.828	7.817	7.819	0.008	0.099
Aspirin	10.008	10.008	10.008	10.008	0.000	0.000
benzene	3.767	3.770	3.765	3.767	0.003	0.067
benzoic acid	9.533	9.548	9.508	9.530	0.020	0.212
benzonitrile	7.948	7.948	7.947	7.948	0.001	0.007
benzophenone	13.937	13.938	13.932	13.936	0.003	0.023
benzyl chloride	7.980	7.980	7.988	7.983	0.005	0.058
biphenyl	11.625	11.632	11.630	11.629	0.004	0.031

chlorobenzene	5.730	5.735	5.727	5.731	0.004	0.071
Cocaine	10.305	10.318	10.330	10.318	0.013	0.121
Codeine	14.410	14.807	14.802	14.673	0.228	1.552
Decane	6.365	6.377	6.397	6.380	0.016	0.253
ethyl acetate	3.377	3.377	3.375	3.376	0.001	0.034
ethyl alcohol	2.827	2.833	2.830	2.830	0.003	0.106
ethyl benzoate	9.522	9.527	9.527	9.525	0.003	0.030
ethyl decanoate	10.812	10.815	10.788	10.805	0.015	0.137
formamide	6.693	6.692	6.658	6.681	0.020	0.298
isopentylacetate	5.793	5.782	5.777	5.784	0.008	0.142
isoquinoline	10.858	10.845	10.848	10.850	0.007	0.063
lactic acid	4.527	4.527	4.522	4.525	0.003	0.064
Lidocaine	10.338	10.327	10.328	10.331	0.006	0.059
methyl acetate	3.015	3.017	3.015	3.016	0.001	0.038
methyl benzoate	8.862	8.585	8.863	8.770	0.160	1.827
methyl Isobutyl ketone	4.403	4.410	4.415	4.409	0.006	0.137
methyl-4-hydroxybenzoate	12.380	12.383	12.387	12.383	0.004	0.028
Morphine	10.333	10.333	10.332	10.333	0.001	0.006
morpholine	5.418	5.412	5.425	5.418	0.007	0.120
m-toluic acid	10.405	10.408	10.432	10.415	0.015	0.142
N,N-diethyl aniline	9.940	9.935	9.942	9.939	0.004	0.036
N,N-dimethyl aniline	8.758	8.770	8.765	8.764	0.006	0.069
N,N-dimethyl formamide	5.658	5.682	5.688	5.676	0.016	0.280
naphthalene	9.858	9.858	9.857	9.858	0.001	0.006
nitrobenzene	9.048	9.052	9.048	9.049	0.002	0.026
nonyl amine	8.540	8.537	8.530	8.536	0.005	0.060
n-propyl alcohol	2.918	2.915	2.910	2.914	0.004	0.139
o-anisaldehyde	11.250	11.232	11.228	11.237	0.012	0.104
o-cresol	8.322	8.300	8.312	8.311	0.011	0.133
octylamine	7.507	7.507	7.498	7.504	0.005	0.069
pentane-1-ol	4.578	4.572	4.577	4.576	0.003	0.070
phenanthrene	15.150	15.147	15.145	15.147	0.003	0.017
phenol	7.462	7.472	7.455	7.463	0.009	0.114
Phenylacetic acid	10.375	10.385	10.380	10.380	0.005	0.048
propylene carbonate	8.632	8.618	8.713	8.654	0.051	0.593
pyridine	4.892	4.880	4.877	4.883	0.008	0.163
quinoline	10.642	10.662	10.647	10.650	0.010	0.098
Resorcinol	10.868	10.862	10.860	10.863	0.004	0.038
tetrachloroethylene	5.038	5.042	5.038	5.039	0.002	0.046
tetrahydrofuran	3.527	3.528	3.532	3.529	0.003	0.075
toluene	4.737	4.732	4.730	4.733	0.004	0.076
vanillin	12.137	12.145	12.137	12.140	0.005	0.038
xanthene	14.912	14.915	14.013	14.613	0.520	3.558

#N/A- all the compounds are eluted in this column

The experimental gas-to-liquid partition coefficient data (E, S, A, B, and L) from literature [35-38] are shown in Table 3.7 for the compounds.

Table 3.7: Solute Descriptors for the Chemical Compounds [35-38]

SOLUTE	E	S	A	B	L
1,3,5-trimethylbenzene	0.649	0.520	0.000	0.190	4.344
1,2-Dichlorobenzene	0.872	0.780	0.000	0.040	4.518
1,2-Dimethylbenzene	0.663	0.560	0.000	0.160	3.939
1-bromohexane	0.349	0.400	0.000	0.120	4.130
1-chloronaphthalene	1.417	1.000	0.000	0.140	5.856
1-nitronaphthalene	1.600	1.590	0.000	0.290	7.056
2-acetylpyridine	0.730	1.090	0.000	0.620	4.425
2-butanone	0.166	0.700	0.000	0.510	2.287
2-Chlorobenzoic acid	0.840	1.010	0.680	0.400	4.840
2-chlorophenol	0.853	0.880	0.320	0.310	4.178
2-Methyl-1-propanol	0.217	0.390	0.370	0.480	2.413
2-octanol	0.158	0.360	0.330	0.360	1.295
2-picoline	0.598	0.750	0.000	0.580	3.422
3-Amino-1-propanol	0.465	0.850	0.380	0.950	3.016
3-nitrobenzoic acid	0.990	1.130	0.730	0.530	5.535
4-nitrophenol	1.070	1.720	0.820	0.260	5.876
Acenaphthene	1.604	1.050	0.000	0.220	6.469
Acetamide	0.460	1.300	0.550	0.690	2.990
Acetanilide	0.900	1.370	0.400	0.670	5.570
Acetic Acid	0.265	0.640	0.620	0.440	1.816
Acetone	0.179	0.700	0.040	0.490	1.696
Acetophenone	0.818	1.010	0.000	0.480	4.501
alpha pinene	0.446	0.140	0.000	0.120	4.308
amyl acetate	0.067	0.600	0.000	0.450	3.844
Aniline	0.955	0.960	0.260	0.410	3.934
Aspirin	0.781	1.690	0.710	0.670	6.279
Benzene	0.610	0.520	0.000	0.140	2.786
Benzoic Acid	0.730	0.900	0.590	0.400	4.657
Benzonitrile	0.742	1.110	0.000	0.330	4.039
Benzophenone	1.450	1.500	0.000	0.500	6.852
Benzyl chloride	0.821	0.860	0.000	0.140	4.353
Biphenyl	1.360	0.990	0.000	0.260	6.014
Bromobenzene	0.882	0.730	0.000	0.090	4.041
Caffeine	1.500	1.820	0.080	1.250	7.838
Chloroacetic acid	0.427	1.030	0.790	0.350	2.862
Chlorobenzene	0.718	0.650	0.000	0.070	3.657
Diiodomethane	1.200	0.690	0.050	0.170	3.857
Ethanol	0.246	0.420	0.370	0.480	1.485

Ethyl Acetate	0.106	0.620	0.000	0.450	2.314
Ethyl benzoate	0.689	0.850	0.000	0.460	5.075
Ethyl decanoate	0.013	0.580	0.000	0.450	6.180
Formamide	0.468	1.310	0.640	0.570	2.447
iso-pentyl acetate	0.051	0.570	0.000	0.470	3.740
Isoquinoline	1.211	1.000	0.000	0.540	5.595
lactic acid	0.350	0.860	0.720	0.720	2.874
Methyl Acetate	0.142	0.640	0.000	0.450	1.911
Methyl Benzoate	0.733	0.850	0.000	0.460	4.704
methyl isobutyl ketone	0.111	0.650	0.000	0.510	3.089
methyl-4-hydroxybenzoate	0.900	1.370	0.690	0.450	5.716
Morpholine	0.434	0.790	0.060	0.910	3.289
m-toluic acid	0.730	0.890	0.600	0.400	4.819
N,N-Diethylaniline	0.953	0.800	0.000	0.410	5.287
N,N-Dimethylaniline	0.957	0.810	0.000	0.410	4.701
N,N-Dimethylformamide	0.367	1.310	0.000	0.740	3.173
Naphthalene	1.340	0.920	0.000	0.200	5.161
Nitrobenzene	0.871	1.110	0.000	0.280	4.557
Nonylamine	0.187	0.350	0.160	0.610	5.100
N-propyl alcohol	0.236	0.420	0.370	0.480	2.031
o-anisaldehyde	0.956	1.120	0.000	0.590	5.300
o-cresol	0.840	0.860	0.520	0.300	0.916
Octylamine	0.187	0.350	0.160	0.610	4.600
pentan-1-ol	0.219	0.420	0.370	0.480	3.106
Phenanthrene	2.005	1.290	0.000	0.260	7.632
Phenol	0.805	0.890	0.600	0.300	3.766
Phenylacetic Acid	0.730	1.080	0.660	0.570	4.962
Propylene Carbonate	0.319	1.370	0.000	0.600	3.088
Pyridine	0.631	0.840	0.000	0.520	3.022
Quinoline	1.268	0.970	0.000	0.540	5.457
Resorcinol	0.980	1.110	1.090	0.520	4.618
Tetrachloroethylene	0.640	0.440	0.000	0.000	3.584
Tetrahydrofuran	0.289	0.520	0.000	0.480	2.636
Toluene	0.601	0.520	0.000	0.140	3.325
Vanillin	1.028	1.280	0.330	0.680	5.730
Xanthene	1.502	1.070	0.000	0.230	7.153

With the Statistical Package for the Social Sciences (SPSS) software, the process coefficients (c, e, s, a, b, and l) and R^2 from the experimental data logRT is obtained using multi linear regression analysis (MLRA) method. Using the process co-efficient $logRT_{calc}$ are obtained using the following equation.

$$Log(RT_{calc}) = c + e \cdot \mathbf{E} + s \cdot \mathbf{S} + a \cdot \mathbf{A} + b \cdot \mathbf{B} + l \cdot \mathbf{L}$$

TR-5:

c= 0.178, e= -0.063, s=0.067, a= 0.129, b= -0.085, l= 0.148, R^2= 0.921, F= 142.286, SD= 0.062, N=67;

TR-1MS:

c= 0.439, e= -0.027, s= 0.053, a= 0.083, b= -0.026, l= 0.108, R^2= 0.947, F=203.854, SD= 0.037, N=63;

ZB-WAX Plus:

c= 0.206, e= 0.013, s= 0.274, a= 0.346, b= -0.044, l= 0.117, R^2= 0.866, F= 61.783, SD= 0.072, N=54;

TG-1301MS:

c= 0.367, e= 0.055, s= 0.114, a= 0.138, b= -0.105, l= 0.090, R^2= 0.651, F= 17.537, SD=0.113, N=53;

TG-5MS:

c= 0.371, e= -0.092, s=0.143, a= 0.150, b= -0.166, l= 0.073, R^2= 0.660, F= 24.417, SD= 0.130, N= 69;

ZB-35:

c= 0.266, e= 0.003, s= 0.098, a= 0.061, b= -0.003, l= 0.117, R^2= 0.911, F=127.043, SD= 0.060 N=68

Here R^2 is the correlation coefficient square, F is the Fischer F –statistic, SD is the standard deviation and N is the number of compounds.

Using these co-efficients in the above mention equation the following six equations for each column can be set.

TR-5: c= 0.178, e= -0.063, s=0.067, a= 0.129, b= -0.085, l= 0.148

$$\text{logRT (calculated)} = 0.178 - 0.063E + 0.067S + 0.129A - 0.085B + 0.148L \quad (10)$$

TR-1MS: c= 0.439, e= -0.027, s= 0.053, a= 0.083, b= -0.026, l= 0.108

$$\text{logRT (calculated)} = 0.439 - 0.027E + 0.053S + 0.083A - 0.026B + 0.108L \quad (11)$$

ZB-WAX PLUS: c= 0.206, e= 0.013, s= 0.274, a= 0.346, b= -0.044, l= 0.117

$$\text{logRT(calculated)} = 0.206 + 0.013E + 0.274S + 0.346A - 0.044B + 0.117L \quad (12)$$

TG-1301MS: c= 0.367, e= 0.055, s= 0.114, a= 0.138, b= -0.105, l= 0.090

$$\text{logRT (calculated)} = 0.367 + 0.055E + 0.114S + 0.138A - 0.105B + 0.090L \quad (13)$$

TG-5MS: c= 0.371, e= -0.092, s=0.143, a= 0.150, b= -0.166, l= 0.073

$$\text{logRT (calculated)} = 0.371 - 0.092E + 0.143S + 0.150A - 0.166B + 0.073L \quad (14)$$

ZB-35: c= 0.266, e= 0.003, s= 0.098, a= 0.061, b= -0.003, l= 0.117

$$\text{logRT (calculated)} = 0.266 + 0.0036E + 0.098S + 0.061A - 0.003B + 0.117L \quad (15)$$

The experimental logRT and the calculated logRT of six columns are shown in Tables 3.8 to Table 3.13.

Table 3.8: Experimental logRT and Calculated logRT for Column TG-5MS

Solute	logRT(exp)	logRT(cal)	Solute (cont'd)	logRT(exp)	logRT(cal)
1,2-dichlorobenzene	0.859	0.884	ethyl benzoate*	0.937	0.848
1,2-dimethyl benzene	0.739	0.771	ethyl decanoate*	1.025	0.828
1-bromohexane	0.777	0.740	Formamide*	0.710	0.780
1-nitronaphthalene*	1.097	1.208	iso-pentyl acetate*	0.721	0.650
2-acetylpyridine	0.855	0.812	isoquinoline	0.982	0.941
2-aminophenol	0.957	0.716	lactic acid*	0.592	0.723
2-butanone	0.413	0.587	Mesitylene	0.806	0.789
2-chlorobenzoic acid	1.020	0.979	methyl acetate*	0.363	0.539
2-chlorophenol*	0.825	0.875	methyl benzoate*	0.895	0.825
2-methylcyclohexanone*	0.790	0.643	methyl isobutyl ketone	0.564	0.614
2-octanol*	0.829	0.521	methyl-4-hydroxybenzoate	1.046	1.093
2-picoline	0.649	0.685	Morpholine	0.628	0.620
3-amino-1-propanol	0.680	0.653	N,N-diethylaniline*	0.962	0.888
3-nitrobenzoic acid	1.085	1.046	N,N-dimethylaniline	0.894	0.848
4-nitrophenol*	1.070	0.864	N,N-dimethylformamide	0.649	0.699
Acenaphthene	1.063	1.101	naphthalene	0.946	0.967
acetamide*	0.671	0.784	Nitrobenzene	0.894	0.894
acetanilide	1.023	1.002	Nonylamine*	0.919	0.731
acetic acid*	0.429	0.639	N-propyl alcohol*	0.347	0.576
acetone*	0.347	0.535	o-anisaldehyde*	1.007	0.905
Acetophenone	0.880	0.837	o-cresol*	0.868	0.666
amyl acetate*	0.757	0.667	octyl amine*	0.859	0.695
aniline	0.816	0.852	pentan-1-ol	0.594	0.653
Aspirin*	0.997	0.773	Phenanthrene*	1.141	1.250
Benzene	0.475	0.530	phenol*	0.814	0.886
benzoic acid	0.956	0.927	phenylacetic acid	0.974	0.957
benzonitrile	0.822	0.836	propylene carbonate*	0.851	0.720
Benzophenone	1.101	1.132	pyridine*	0.568	0.682
benzyl chloride	0.843	0.862	Quinoline	0.971	0.932
biphenyl	1.027	1.030	Resorcinol*	0.981	1.032
Chloroacetic acid*	0.599	0.825	tetrachloroethylene*	0.651	0.753
chlorobenzene*	0.690	0.783	tetrahydrofuran*	0.439	0.584
Decane*	0.828	0.482	toluene*	0.599	0.719
ethanol*	0.333	0.538	vanillin	1.030	1.000
ethyl acetate*	0.423	0.562			

*(asterisk) represents compounds that are outliers and not used for the least square method.

Table 3.9: Experimental logRT and Calculated logRT for Column TG-1301MS

Solute	logRT(exp)	logRT(cal)	Solute (cont'd)	logRT(exp)	logRT(cal)
1,2-dichlorobenzene	0.879	0.906	ethyl decanoate*	1.039	0.942
1,2-dimethyl benzene*	0.757	0.805	Formamide	0.805	0.791
1-bromohexane	0.795	0.791	Isoquinoline	1.011	0.994
1-chloronaphthalene	1.048	1.071	lactic acid*	0.653	0.767
2-acetylpyridine	0.888	0.865	mesitylene	0.818	0.833
2-butanone*	0.462	0.608	methyl benzoate	0.922	0.879
2-chlorophenol	0.873	0.902	methyl isobutyl ketone*	0.616	0.672
2-methylcyclohexanone*	0.830	0.686	Morpholine	0.691	0.690
2-octanol	0.861	0.541	N,N-diethylaniline	0.981	0.943
2-picoline	0.688	0.733	N,N-dimethylaniline	0.915	0.892
3-amino-1-propanol	0.758	0.714	N,N-dimethylformamide	0.733	0.744
Acenaphthene	1.079	1.134	Naphthalene	0.969	0.989
acetic acid*	0.535	0.658	nitrobenzene	0.931	0.922
acetophenone	0.916	0.882	Nonylamine*	0.931	0.834
alpha-pinene*	0.777	0.508	N-propyl alcohol*	0.392	0.612
amyl acetate	0.785	0.738	o-anisaldehyde*	1.028	0.962
aniline	0.869	0.876	o-cresol*	0.930	0.634
Benzene	0.503	0.510	octyl amine*	0.871	0.789
benzoic acid	1.003	0.968	pentan-1-ol	0.661	0.707
benzonitrile	0.871	0.863	phenol	0.901	0.903
benzyl chloride	0.870	0.887	propylene carbonate*	0.935	0.756
Biphenyl	1.043	1.068	Pyridine*	0.618	0.715
bromobenzene	0.800	0.853	Quinoline	0.998	0.982
chlorobenzene*	0.714	0.802	Tetrachloroethylene*	0.657	0.775
ethanol*	0.373	0.563	tetrahydrofuran*	0.473	0.629
ethyl acetate*	0.463	0.604	Toluene*	0.619	0.744
ethyl benzoate	0.960	0.910			

*(asterisk) represents compounds that are outliers and not used for the least square method.

Table 3.10: Experimental logRT and Calculated logRT for Column TR-1MS

Solute	logRT(exp)	logRT(cal)	Solute (cont'd)	logRT(exp)	logRT(cal)
1,2-dichlorobenzene	0.961	0.942	isopentylacetate	0.870	0.858
1-bromohexane	0.905	0.892	Isoquinoline	1.056	1.047
1-chloronaphthalene	1.099	1.080	lactic acid*	0.889	0.825
1-nitronaphthalene*	1.154	1.231	mesitylene	0.935	0.911
2-acetyl pyridine	0.954	0.937	methyl acetate	0.628	0.663
2-butanone	0.651	0.704	methyl benzoate	0.988	0.958
2-chlorophenol	0.938	0.931	methyl Isobutyl ketone	0.756	0.789
2-methyl cyclohexanone	0.914	0.894	methyl-4-hydroxybenzoate	1.110	1.147
2-picoline	0.818	0.815	morpholine	0.797	0.804
3-amino-1-propanol	0.809	0.802	N,N-diethyl aniline	1.044	1.014
Acenaphthene	1.127	1.142	N,N-dimethyl aniline	0.987	0.951
Acetanilide	1.089	1.102	N,N-dimethyl formamide	0.786	0.820
acetic acid	0.667	0.700	naphthalene	1.033	1.002
Acetone	0.626	0.644	nitrobenzene	0.984	0.957
acetophenone	0.974	0.942	nonyl amine	1.014	0.999
alpha-pinene	0.922	0.895	n-propyl alcohol*	0.611	0.691
amyl acetate	0.888	0.871	o-anisaldehyde	1.077	1.027
aniline	0.924	0.898	octylamine	0.967	0.945
Benzene	0.701	0.746	pentane-1-ol	0.781	0.808
benzoic acid	1.021	1.006	Phenanthrene*	1.195	1.268
benzonitrile	0.924	0.904	phenol	0.928	0.911
Benzophenone*	1.158	1.203	phenylacetic acid	1.049	1.050
benzyl chloride	0.949	0.927	propylene carbonate*	0.917	0.819
Biphenyl	1.096	1.095	Pyridine	0.758	0.778
bromobenzene	0.911	0.886	Quinoline	1.048	1.029
chlorobenzene	0.845	0.846	Resorcinol	1.056	1.044
Diiodomethane*	0.948	0.858	tetrachloroethylene	0.822	0.831
ethyl acetate	0.660	0.706	tetrahydrofuran	0.694	0.729
ethyl alcohol	0.594	0.632	Toluene	0.785	0.805
ethyl benzoate	1.021	1.000	Vanillin	1.097	1.105
ethyl decanoate	1.097	1.123	Xanthene*	1.168	1.219
Formamide	0.823	0.796			

*(asterisk) represents compounds that are outliers and not used for the least square method.

Table 3.11: Experimental logRT and Calculated logRT for Column TR-5

Solute	logRT(exp)	logRT(calc)	Solute (cont'd)	logRT(exp)	logRT(calc)
1,2-dichlorobenzene	0.863	0.841	ethyl decanoate	1.029	1.093
1,2-dimethyl benzene	0.749	0.744	Formamide	0.694	0.633
1-bromohexane	0.786	0.784	iso-pentyl acetate	0.732	0.727
1-chloronaphthalene	1.032	1.012	isoquinoline	0.985	0.952
1-nitronaphthalene*	1.099	1.205	lactic acid*	0.772	0.671
2-acetylpyridine	0.861	0.808	mesitylene	0.812	0.799
2-butanone*	0.424	0.510	methyl acetate	0.383	0.457
2-chlorobenzoic acid	1.026	0.964	methyl benzoate	0.901	0.847
2-chlorophenol	0.830	0.817	methyl isobutyl ketone	0.574	0.629
2-methylcyclohexanone*	0.797	0.658	methyl-4-hydroxybenzoate	1.050	1.111
2-picoline	0.663	0.648	Morpholine	0.652	0.621
3-amino-1-propanol	0.687	0.621	N,N-diethylaniline	0.966	0.920
3-nitrobenzoic acid	1.089	1.060	N,N-dimethylaniline	0.897	0.834
Acenaphthene	1.065	1.087	N,N-dimethylformamide	0.633	0.650
acetamide	0.649	0.691	naphthalene	0.949	0.903
Acetanilide	1.026	1.033	nitrobenzene	0.900	0.849
acetic acid	0.457	0.516	nonylamine	0.925	0.914
acetone	0.370	0.429	N-propyl alcohol*	0.379	0.499
Acetophenone	0.884	0.820	o-anisaldehyde	0.974	0.928
alpha-pinene	0.788	0.787	octyl amine	0.863	0.840
amyl acetate	0.764	0.745	pentan-1-ol	0.608	0.660
Aniline	0.820	0.764	Phenanthrene*	1.144	1.247
benzoic acid	0.960	0.924	phenol	0.820	0.797
Benzonitrile	0.825	0.776	phenylacetic acid	0.973	0.976
Benzophenone	1.104	1.160	propylene carbonate*	0.832	0.656
benzyl chloride	0.845	0.817	pyridine	0.578	0.598
Biphenyl	1.029	1.028	Quinoline	0.974	0.926
bromobenzene	0.786	0.762	resorcinol	0.986	0.971
Caffeine	1.187	1.271	tetrachloroethylene	0.660	0.698
chloroacetic acid*	0.612	0.716	Tetrahydrofuran*	0.449	0.545
chlorobenzene	0.700	0.712	toluene	0.603	0.656
ethanol	0.358	0.418	Vanillin	1.034	1.033
ethyl acetate*	0.433	0.518	Xanthene	1.113	1.195
ethyl benzoate	0.941	0.904			

*(asterisk) represents compounds that are outliers and not used for the least square method.

Table 3.12: Experimental logRT and Calculated logRT for Column ZB-35

Solute	logRT(exp)	logRT(calc)	Solute (cont'd)	logRT(exp)	logRT(calc)
1,2-dichlorobenzene	0.908	0.872	Formamide*	0.825	0.719
1,2-dimethyl benzene	0.791	0.782	isopentylacetate	0.762	0.758
1-bromohexane	0.810	0.788	Isoquinoline	1.035	1.020
1-chloronaphthalene	1.069	1.052	lactic acid*	0.656	0.729
1-nitronaphthalene*	1.144	1.250	mesitylene	0.840	0.825
2-acetyl pyridine	0.921	0.890	methyl acetate*	0.479	0.551
2-Aminophenol	1.015	1.014	methyl benzoate	0.943	0.900
2-butanone*	0.528	0.601	methyl Isobutyl ketone	0.644	0.690
2-Chlorobenzoic acid*	1.062	0.973	methyl-4-hydroxybenzoate	1.092	1.111
2-chlorophenol	0.880	0.861	morpholine	0.734	0.730
2-methyl cyclohexanone	0.855	0.820	m-toluic acid	1.017	0.954
2-picoline	0.749	0.739	N,N-diethyl aniline	0.997	0.964
4-Nitrophenol	1.119	1.173	N,N-dimethyl aniline	0.943	0.896
Acenaphthene	1.103	1.129	N,N-dimethyl formamide	0.754	0.765
Acetanilide	1.079	1.076	Naphthalene	0.993	0.962
acetic acid	0.535	0.578	nitrobenzene	0.957	0.909
acetone	0.472	0.535	nonyl amine	0.931	0.904
acetophenone	0.941	0.892	n-propyl alcohol*	0.465	0.566
alpha-pinene	0.788	0.784	o-anisaldehyde	1.050	0.996
amyl acetate	0.795	0.773	o-cresol	0.920	0.876
Aniline	0.893	0.837	octylamine	0.875	0.846
Aspirin*	1.000	1.209	pentane-1-ol	0.660	0.692
benzene	0.576	0.644	Phenanthrene*	1.180	1.289
benzoic acid	0.979	0.935	phenol	0.873	0.831
benzonitrile	0.900	0.848	Phenylacetic acid	1.016	0.992
Benzophenone*	1.144	1.216	propylene carbonate*	0.937	0.761
benzyl chloride	0.902	0.861	pyridine	0.689	0.702
Biphenyl	1.066	1.069	Quinoline	1.027	1.000
chlorobenzene	0.758	0.759	Resorcinol	1.036	0.981
Decane	0.805	0.813	tetrachloroethylene	0.702	0.729
ethyl acetate	0.528	0.596	tetrahydrofuran*	0.548	0.624
ethyl alcohol	0.452	0.502	toluene	0.675	0.706
ethyl benzoate	0.979	0.943	Vanillin	1.084	1.082
ethyl decanoate	1.033	1.043	Xanthene	1.165	1.210

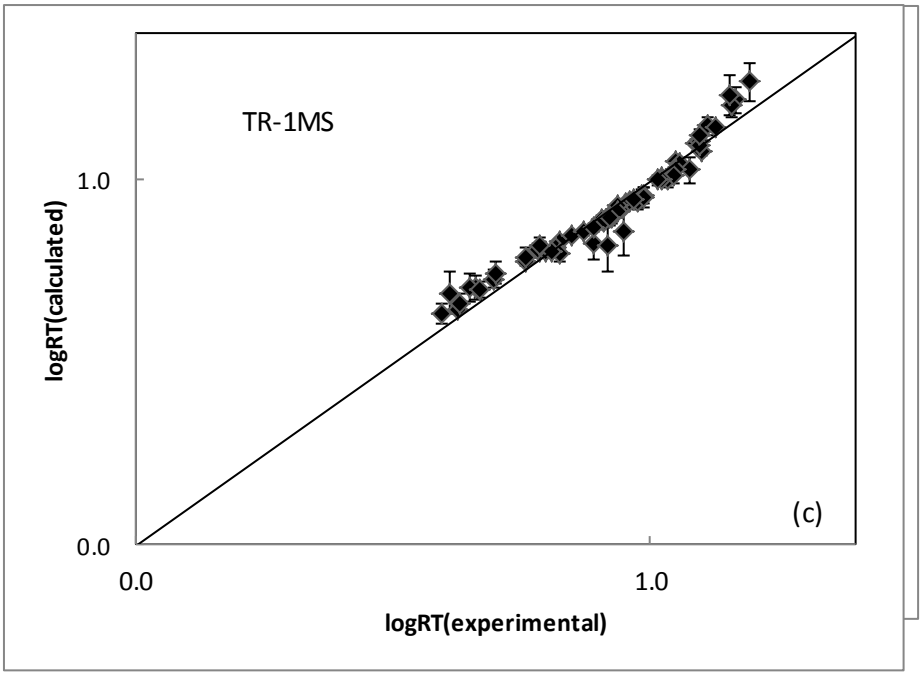
*(asterisk) represents compounds that are outliers and not used for the least square method.

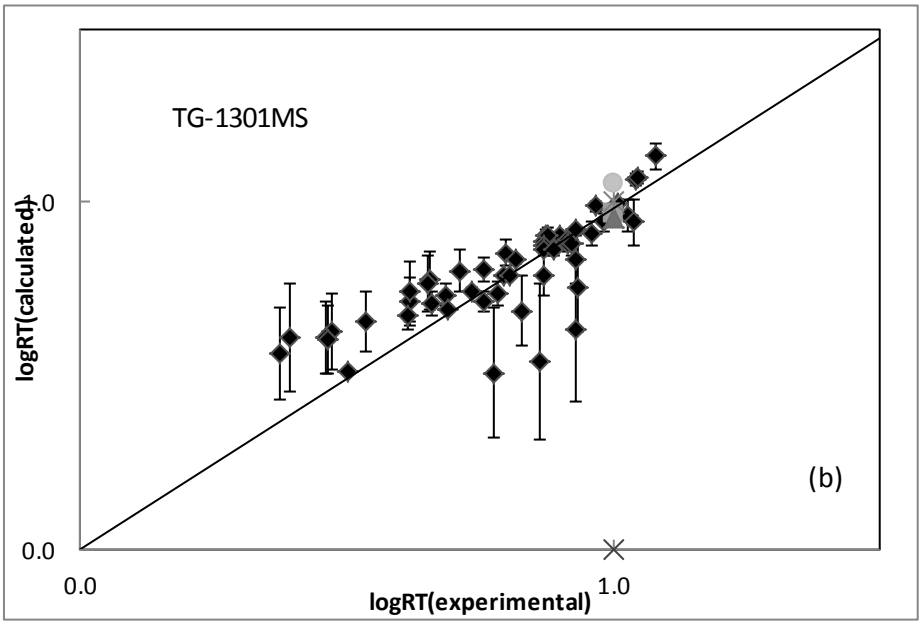
Table 3.13: Experimental logRT and Calculated logRT for Column ZB-WAX PLUS

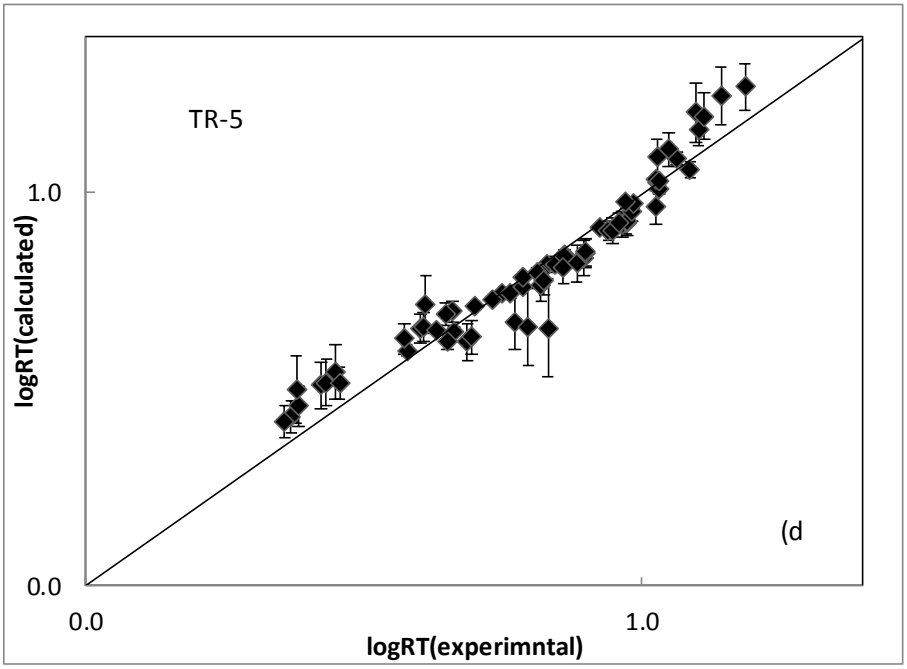
Solute	logRT(exp)	logRT(calc)	Solute (cont'd)	logRT(exp)	logRT(calc)
1,2-Dichlorobenzene	0.970	0.956	Formamide*	1.003	1.052
1,2-Dimethylbenzene	0.812	0.820	Isopentylacetate	0.870	0.858
1-bromohexane	0.786	0.796	Isoquinoline	1.117	1.124
2- methylcyclohexanone*	0.888	0.613	lactic acid*	0.887	0.998
2-acetylpyridine	1.012	1.003	mesitylene	0.850	0.855
2-butanone	0.593	0.644	Methyl Acetate*	0.512	0.586
2-chlorophenol	1.084	1.042	Methyl Benzoate	1.017	0.977
2-picoline	0.834	0.792	methyl isobutyl ketone	0.663	0.723
3-Amino-1-propanol*	0.985	0.886	morpholine	0.851	0.792
Acetamide	1.055	1.076	N,N-Diethylaniline	1.016	1.036
Acetic Acid*	0.960	0.791	N,N-Dimethylaniline	0.992	0.970
Acetone*	0.505	0.589	N,N-Dimethylformamide	0.899	0.906
Acetophenone	1.027	0.997	Naphthalene	1.055	1.069
alpha pinene	0.683	0.747	nitrobenzene	1.054	1.040
amyl acetate	0.800	0.799	Nonylamine	0.939	0.927
Aniline	1.056	1.012	N-propyl alcohol*	0.591	0.667
Benzene*	0.603	0.675	o-anisaldehyde	1.098	1.117
Benzoic Acid	1.197	1.191	Octylamine	0.894	0.869
Benzonitrile	1.013	0.976	pentan-1-ol	0.848	0.793
Benzyl chloride	0.979	0.954	phenol	1.124	1.094
Biphenyl*	1.102	1.185	Phenylacetic Acid*	1.201	1.293
Bromobenzene	0.906	0.884	Propylene Carbonate*	1.082	0.918
Chlorobenzene	0.829	0.817	Pyridine	0.810	0.773
Diiodomethane	0.847	0.870	Quinoline	1.106	1.101
Ethanol	0.599	0.604	tetrachloroethylene*	0.680	0.752
Ethyl Acetate*	0.555	0.627	Tetrahydrofuran*	0.540	0.638
Ethyl benzoate	1.030	1.019	Toluene	0.695	0.738
Ethyl decanoate	1.017	1.066			

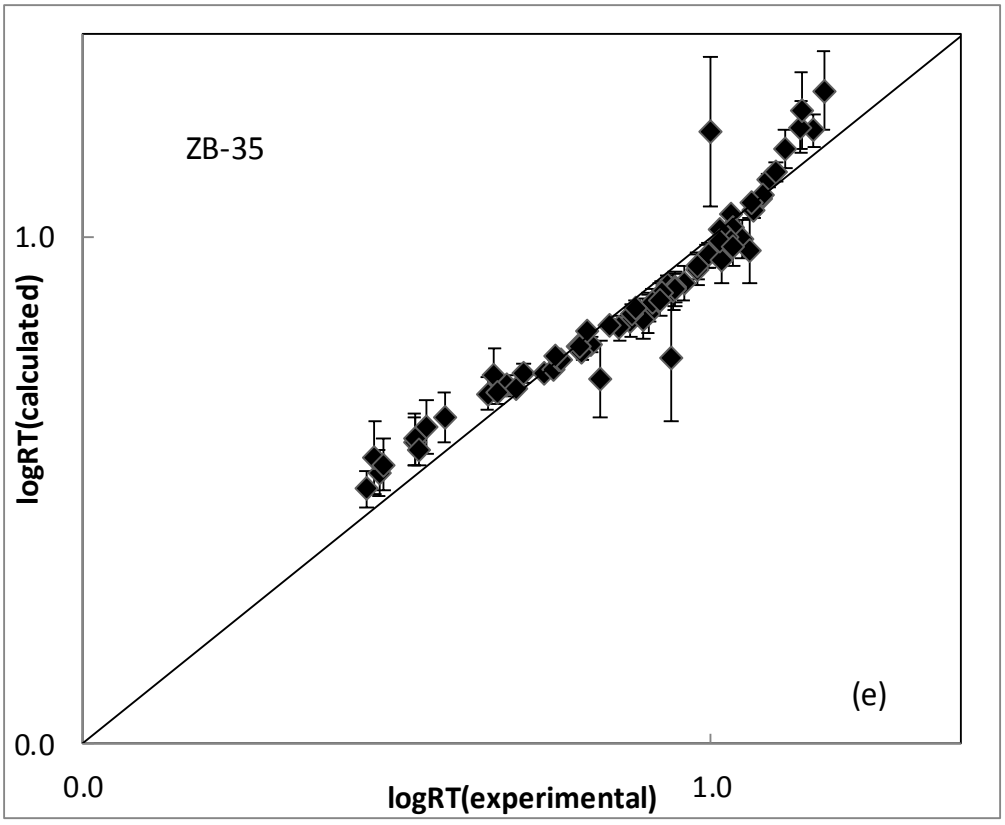
*(asterisk) represents compounds that are outliers and not used for the least square method.

A linear relation between LogRT(calculated) and LogRT(experimental) for the six columns are shown in Figure 3.1.






TR-5
1.0
0.0
logRT(calculated)
(d
0.0
1.0
logRT(experimntal)


ZB-35
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0.0
logRT(calculated)
(e)
0.0
logRT(experimental)
1.0

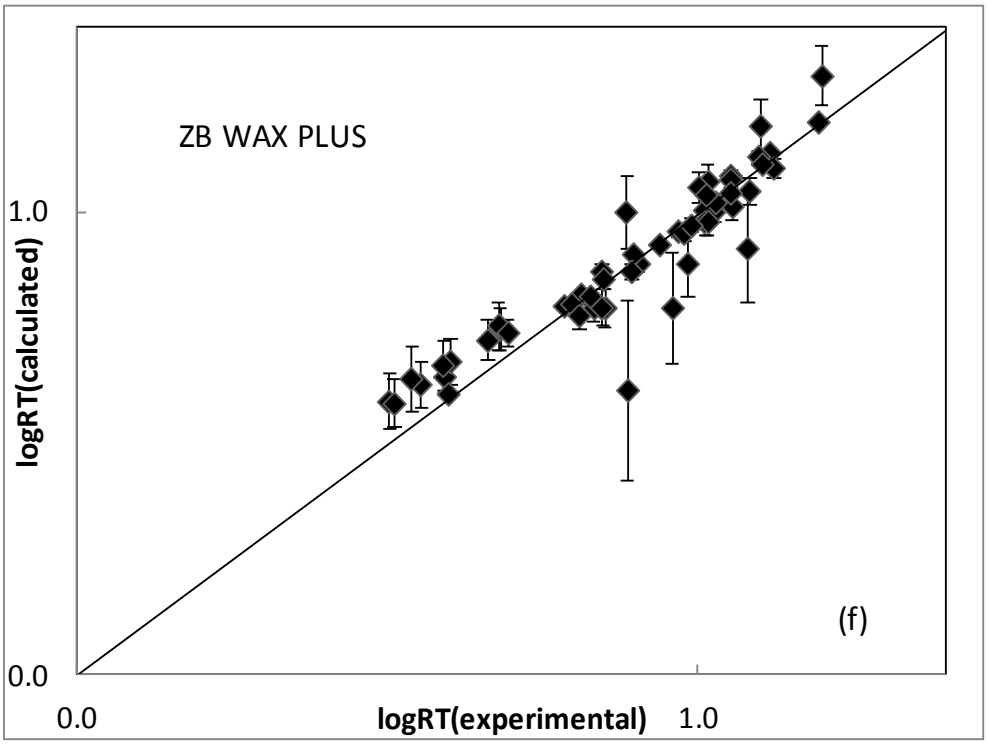
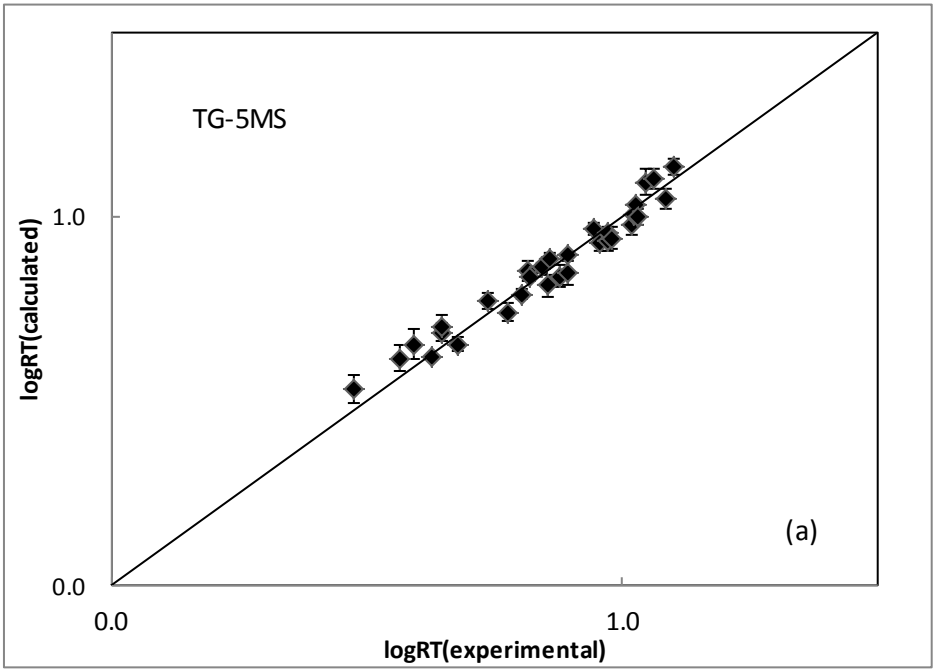


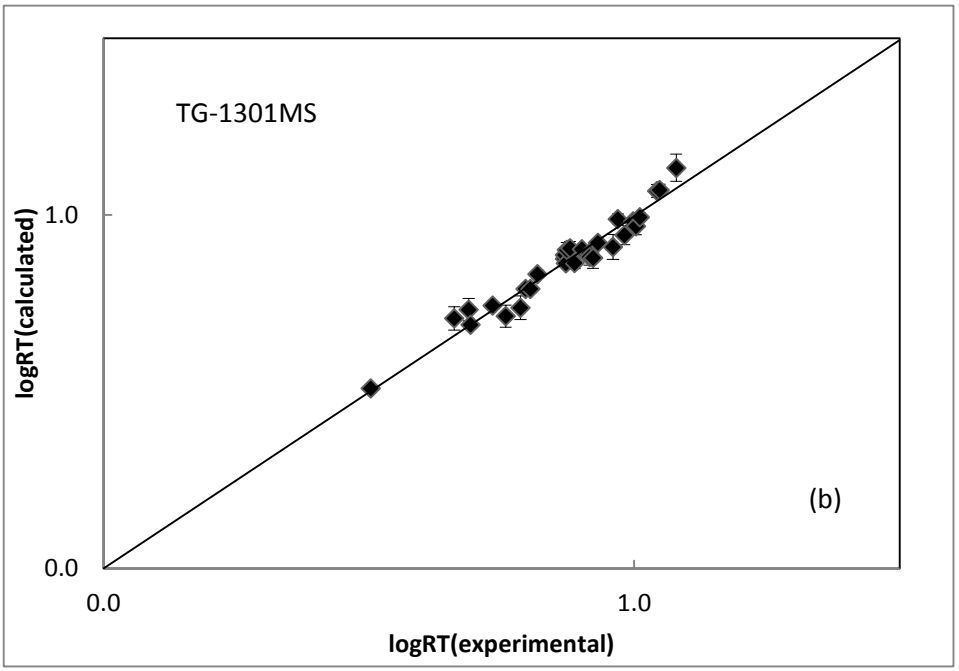
Figure 3.1: Correlation of calculated logRT (calculated) and experimentally observed logRT (experimental) for TG-5MS (a), TG-1301MS (b), TR-1MS (c), TR-5 (d), ZB-35 (e) and ZB WAX PLUS (f) columns

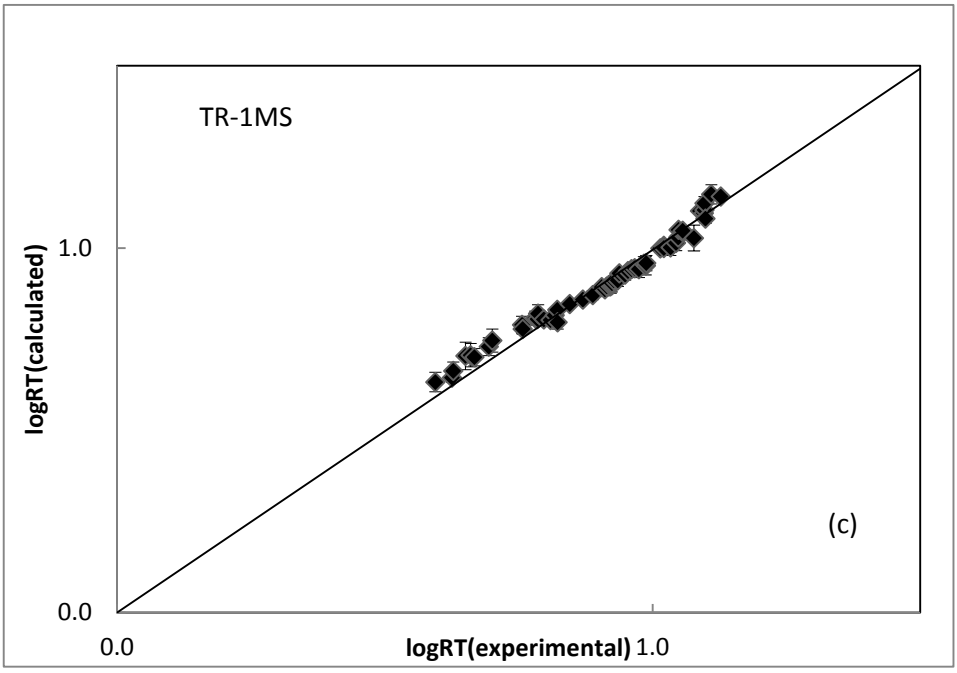
3.2 Discussion

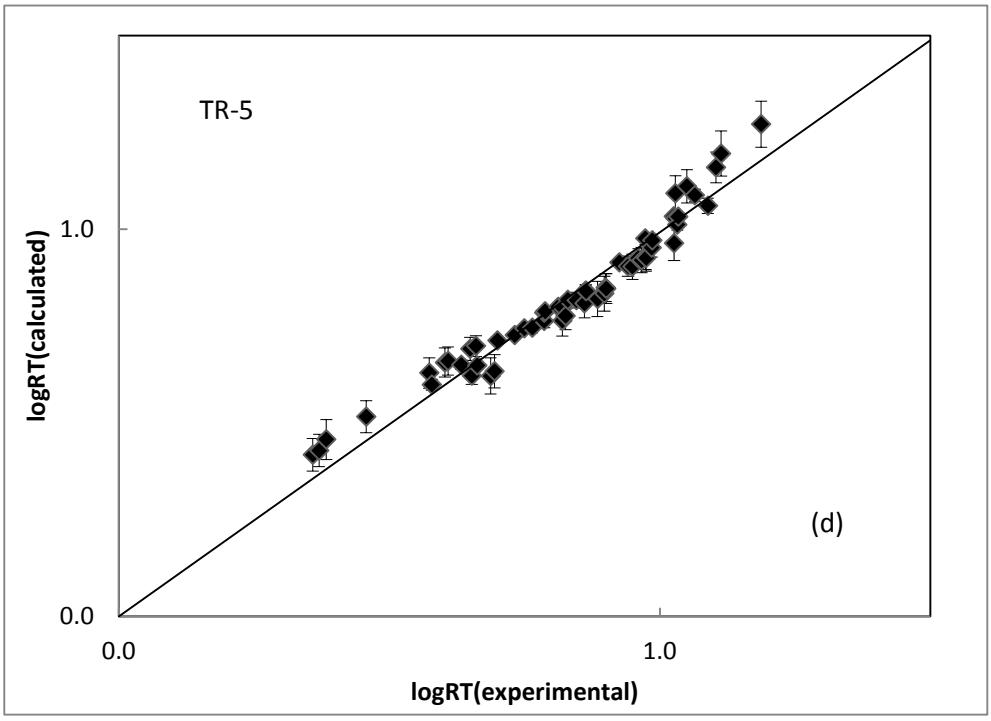
3.2.1 Effective Compounds for Each Column

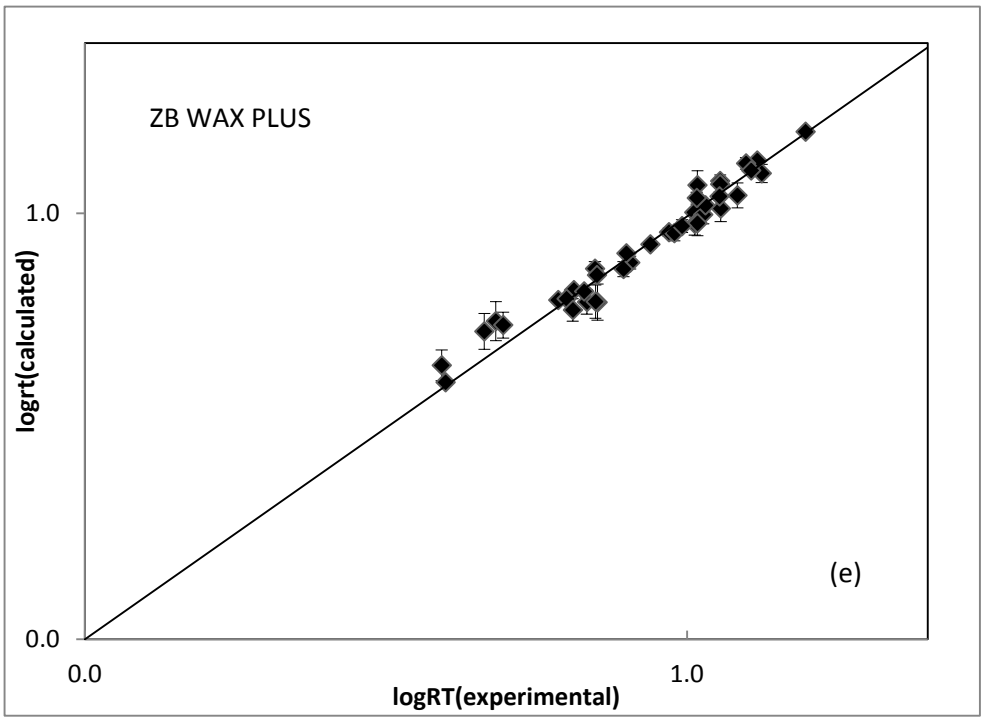
The least squares method is used to describe the linear relationship between the values of logRT (Calculated) and logRT (Experimental) in the experiment. Deviation is the distance between each point and the line in logRT (Calculated). When the sum of the deviation of each point is the smallest, the line is the best fit line. However after the statistical analysis, some outliers are removed. Tables 3.8 to 3.13 show the outliers also. Then the data were replotted as shown in Figure 3.2. The method to remove outliers was to set standard error bars for each of the data point and remove the ones those were not touching the trend line.


TG-5MS
1.0
0.0
logRT(calculated)
0.0
1.0
logRT(experimental)
(a)


TG-1301MS
1.0
0.0
logRT(calculated)
0.0
1.0
logRT(experimental)
(b)


TR-1MS
1.0
0.0
logRT(calculated)
0.0
logRT(experimental)
1.0
(c)


TR-5
1.0
0.0
logRT(calculated)
0.0
1.0
logRT(experimental)
(d)



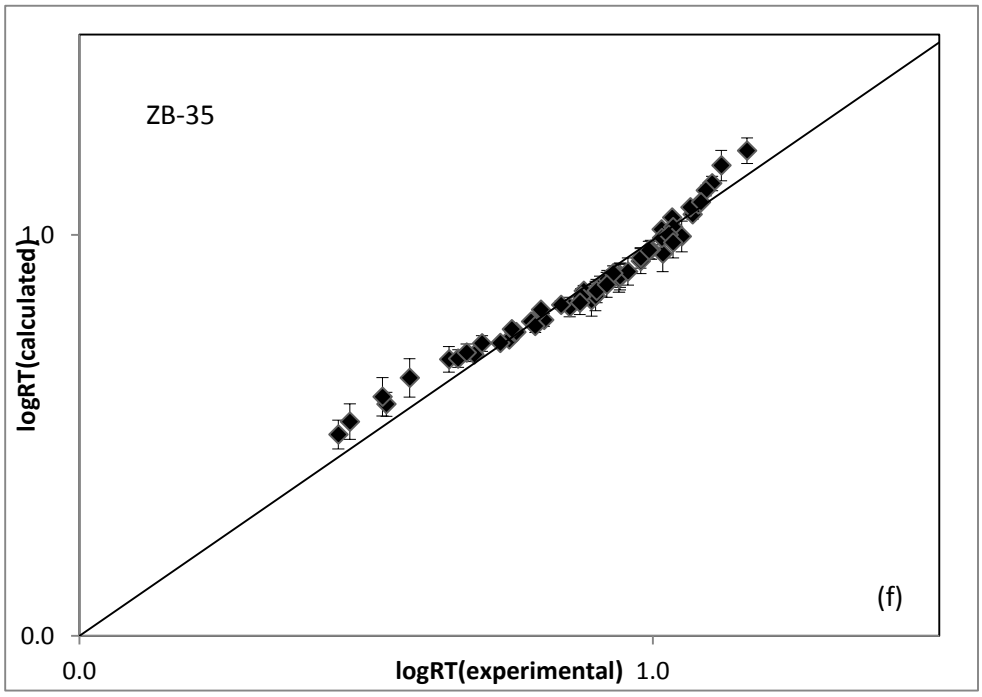


Figure 3.2:Correlation of calculated logRT (calculated) and experimentally observed logRT (experimental) for TG-5MS (a), TG-1301MS (b), TR-1MS (c), TR-5 (d), ZB-WAX PLUS (e) and ZB-35 (f) for effective compounds only

From the linear relationships it can be seen that the R^2 value lies between 0.95-0.98 (Table 3.14) which is very close to 1. This means the experimental value and the calculated value are well correlated for those compounds.

Table 3.14: R^2 values for Six Columns

Column	R^2
TR-1MS	0.973
ZB-Wax Plus	0.965
TR-5	0.953
TG-1301MS	0.962
TG-5MS	0.968
ZB-35	0.965

The list of effective compounds with the calculated logRT and observed logRT are tabulated in Tables 3.8 to 3.13 for six columns.

There are polarity differences among these columns, so not all the compounds are effective on these. The TR-1MS column is non-polar column with 100% dimethyl polysiloxane stationary phase. This column prefers the non-polar functional groups and non-polar compounds. In this case, non-polar and some low-polar functional groups are effective for this column, like benzene, toluene and ester. The TR-5 and TG-5MS column are low polarity columns. The phenyl methyl polyolysiloxane stationary phases prefer the non-polar functional groups and non-polar compounds. The ZB-WAX PLUS column is polar column with 100% polyethylene glycol which prefers the polar compounds. The TG-1301MS is mid-polarity column with 6% cyanopropylphenyl and 95% methyl polysiloxane and ZB-35 is mid polarity column with 35% phenyl and 65% dimethylpolysiloxane preferring both non-polar and polar functional groups and compounds. In addition, the compounds which contain more carbon and hydrogen are more non-polar, and are more effective for these columns except for ZB-WAX PLUS.

After analyzing all the data and determining the effective and ineffective compounds for each column, the process co-efficients can be recalculated only using the effective compounds. Once the new process co-efficients are calculated new sets of Abraham Model equations can be set up.

TR-5:

c=0.187, e=-0.020, s=0.044, a=0.134, b=-0.069, l=0.143, R^2= 0 .953, SD=0.044, F= 206.743, N= 57

$$\text{logRT (calculated)} = 0.187 - 0.020E + 0.044S + 0.134A - 0.069B + 0.143L \quad (16)$$

TR-1MS:

c=0.409, e=-0.007, s=0.042, a=0.077, b=-0.021, l=0.115, R^2= 0.973, SD=0.025, F=359.627, N=56

$$\text{logRT (calculated)} = 0.409 - 0.007E + 0.042S + 0.077A - 0.021B + 0.115L \quad (17)$$

ZB-WAX PLUS:

c=0.187, e=0.048, s=0.269, a=0.379, b=-0.003, l=0.113, R^2= 0.965, SD= 0.031, F= 179.415, N=39

$$\text{logRT(calculated)} = 0.187 + 0.048E + 0.269S + 0.379A - 0.003B + 0.113L \quad (18)$$

TG-1301MS:

c=0.332, e=0.012, s=0.129, a=0.136, b=-0.069, l=0.100, R^2= 0.962, SD= 0.028, F= 121.681, N=30

$$\text{logRT (calculated)} = 0.332 + 0.012E + 0.129S + 0.136A - 0.069B + 0.100L \quad (19)$$

TG-5MS:

c=0.314, e=0.097, s=0.082, a=0.165, b=-0.097, l=0.809, R^2=0.968, SD=0.033, F= 151.285, N=31

$$\text{logRT (calculated)} = 0.314 + 0.097E + 0.082S + 0.165A - 0.097B + 0.809L \quad (20)$$

ZB-35:

c=0.224, e=0.022, s=0.078, a=0.065, b=0.034, l=0.126, R^2= 0.965, SD= 0.034, F=272.517, N=56

$$\text{logRT (calculated)} = 0.224 + 0.022E + 0.078S + 0.065A + 0.034B + 0.126L \quad (21)$$

The molecular descriptors for the drug compounds can be predicted from the equation by simply measuring the retention time in GC-FID and plug it into these equations.

3.2.2 Process Co-Efficients

The process co-efficients reflects the solvent interaction with the solute. Positive value means that the solute is more preferred by the condensed phase and the negative value means that the solute is more preferred to the gas phase phase. From our calculated values, the various coefficients c, e, s, a, b and l are statistically significant and can be interpreted. The **s** increases as the phase becomes more polar. Among the six columns the ZB WAX PLUS is the most polar and has the highest value for coefficient **s** (= 0.269). The **a** coefficients for TR-5, TG-5MS, TR-1MS, TG-1301MS and ZB-35 are less than that of the ZB WAX PLUS since the functional groups in those phases are weak acceptors of hydrogen bond. The **a** coefficients for the TG-1301MS is higher among these weaker hybond acceptor because of the cyano functional group. ZB WAX PLUS is the most acidic (=0.379). The negative value for **b** coefficient shows that the solute hydrogen bond basicity prefers to the gas phase. It is predicted that the ZB WAX PLUS should have a higher **b** coefficient value than the other five column since it is the most polar column among the six columns. But here we have a exception of ZB-35 and TR-1MS. The negative sign of **e** coefficients shows that the solute with larger value of excess molar co-efficients prefers to the gas phase.

3.2.3 Molecular Solute Descriptors for Lidocaine, Cocaine, Codeine and Morphine

Molecular descriptors for lidocaine, cocaine, codeine and morphine are determined by converting the average retention time into calculated logRT values. The calculated logRT value

can be compared with the experimentally determined values. Once logRT is calculated Microsoft solver is used to minimize the sum of squares on the set of described system equations. System equation contains of a set of equations with known process coefficients (*c,e,s,a,b,v* and *l*) which is calculated using the multi linear regression (MLRA) method. The overall sums of squares are set at a minimum to fit the targeted cells S, A and B [45].

The retention time of these drugs are measured by gas chromatography shown in Tables 3.1 to 3.6. Since ZB-WAX PLUS is highly polar column, the non-polar drugs are not retained by the wax stationary phase. The average retention time is then plugged into equations to calculate logRT for each column. Retention time of these drugs could have errors that should be considered, since these are semi-volatile and also heat labile.

Partition coefficient for six chromatographic column TR-1MS, TR-5, TG-5MS, TG-1301MS, ZB-WAX PLUS and ZB-35 were calculated by MLRA method in SPSS software and six equations were established (eqn. 16 to 21). The excess molar refraction descriptor, E ; the Oswald solubility descriptor, L and the McGowan volume, V were retrieved from the literature as discussed before [35-38]. Microsoft Solver was employed to yield the numerical values of the remaining solute descriptors that give the best fit of experimental and calculated logRT values. Since there are only few retention data points for each of the drug compounds, a good correlation is not expected. Octanol/water partition coefficient is added to it to add up one more data point to the set. This logP can be found in literature since it's been well established. Since octanol/water is a condensed to condensed phase transfer, the McGowan volume needs to be considered. The Abraham model equation for octanol/water is as follows:

Octanol/water: c=0.088, e=0.562, s=-1.054, a=0.034, b=-3.460, v=3.814

$$\text{LogP(calculated)} = 0.088 + 0.562E - 1.054S + 0.034A - 3.460B + 3.814V \qquad (22)$$

Equation (22) is then combined with the other six equations (eqn 16 to eqn. 21) to predict the descriptor for the targeted drug compound.

3.2.3.1 Lidocaine

Calculated retention data for lidocaine is obtained from equation 16 to equation 22 (Table 3.15).

Table 3.15: Observed and Calculated Retention Data for Lidocaine

Phase	Experimental LogRT	Calculated LogRT
TR-1MS	1.214	1.312
TR-5	1.199	1.229
TG-1301MS	1.060	0.964
TG-5MS	1.063	0.947
ZB-WAX PLUS	--	--
ZB-35	1.014	1.325
Octanol	2.196	2.203

The numerical values of the solute descriptors for Lidocaine are: S = -1.039, A = 0.420, B = 2.158 with E= 1.100, L = 8.448 and V= 2.059 can be obtained as the best fit values (Table 3.16).

Table 3.16: Calculated Molecular Descriptors for Lidocaine

Descriptors	Value
E	1.110
S	-1.039
A	0.420
B	2.158
L	8.448
V	2.059

The molecular descriptors reproduce the experimental logRT for lidocaine within an overall standard deviation of 0.180 log unit. From the vast literature review it has been established that the A, B, S and E are all zero for the saturated hydrocarbons. So the properties of

test compounds are referenced to that of the saturated hydrocarbons. From the structure of lidocaine (Figure 3.3) it can be seen that it has one hydrogen atom attached to the nitrogen that can be donated to form hydrogen bond. A=0.420 is quite reasonable. The lone pair on the nitrogen molecules may exhibit the basic nature of lidocaine indicating that B= 2.158 is quite reasonable. It is always hard to encode the solubility nature of the molecule from the numerical values. The negative sign of S shows that the solute is less polar and more hydrophobic in nature than the corresponding hydrocarbons [74]. *S* has dipolarity and polarizability information. It can be influenced by the steric hindrance of the fully substituted N-atom that has the ability to accept hydrogen bonding and possibilities of resonance conjugation [75]. It is difficult to separate the exact distribution of polarity, dispersion, and induction effects from the numerical value of the parameter. The actual interaction information can be found in the intercept of the LFER equations which is very difficult to interpret [72]. Also it can be seen that for most of the coefficients the value is very small, it is not useful to calculate the descriptors appropriately. There are too few experimental data points (Table 3.15) to draw any real conclusion due to broad minimum.

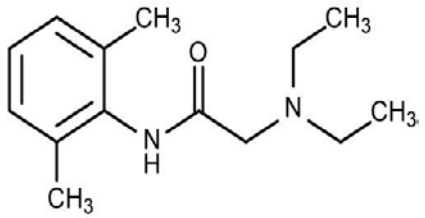


Figure 3.3: Structure of lidocaine

3.2.3.2 Cocaine

Calculated retention data for cocaine is obtained from equation 16 to equation 22 (Table 3.17).

Table 3.17: Observed and Calculated Retention Data for Cocaine

Phase	Experimental logRT	Calculated logRT
TR-1MS	1.078	1.408
TR-5	0.998	1.307
TG-1301MS	1.063	0.776
TG-5MS	1.003	0.821
ZB-WAX PLUS	--	--
ZB-35	1.013	1.429
Octanol	2.275	2.282

The numerical values of the solute descriptors for Cocaine are: S = -3.193, A = 0.000, B = 3.092 with E= 1.355, L = 10.530 and V= 2.298 can be obtained as the best fit values (Table 3.18).

Table 3.18: Calculated Molecular Descriptors for Cocaine

Descriptors	Value
E	1.355
S	-3.193
A	0.000
B	3.092
L	10.530
V	2.298

The molecular descriptors reproduce the experimental logRT for cocaine within an overall standard deviation of 0.3510 log unit. From the structure of cocaine (Figure 3.4) it can be seen that it has no hydrogen atom available for hydrogen bond formation with the stationary phases. The A=0.000 value is quite reasonable. The lone pair on the nitrogen and oxygen molecules may exhibit the basic nature of cocaine indicating that B= 3.092 is quite reasonable. It is always hard to encode the solubility nature of the molecule from the numerical values. The negative sign of S shows that the solute is less polar and more hydrophobic in nature than the corresponding hydrocarbons [74]. *S* has dipolarity and polarizability information. It can be influenced by the steric hindrance of the fully substituted N-atom that has the ability to accept

hydrogen bonding and possibilities of resonance conjugation [75]. During the experiment, the temperature ramp may cause conformational change in the molecule, which may cause not to form hydrogen bonding with phase. It is difficult to separate the exact distribution of polarity, dispersion, and induction effects from the numerical value of the parameter. The actual interaction information can be found in the intercept of the LFER equations which is very difficult to interpret [72]. Also it can be seen that for most of the coefficients the value is very small and close enough. It means that there is not much difference in column phases, so it might not be useful to calculate the descriptors appropriately. There are too few experimental data points (Table 3.17) to draw any real conclusion due to broad minimum.

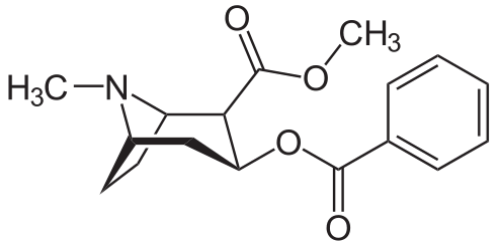


Figure 3.4: Structure of cocaine

3.2.3.3 Morphine

Calculated retention data for morphine is obtained from equation 16 to equation 22 (Table 3.19).

Table 3.19: Observed and Calculated Retention Data for Morphine

Phase	Experimental logRT	Calculated logRT
TR-1MS	1.078	1.364
TR-5	0.998	1.24
TG-1301MS	1.007	0.773
TG-5MS	1.061	0.874
ZB-WAX PLUS	--	--
ZB-35	1.014	1.415
Octanol	1.394	1.401

The numerical values of the solute descriptors for Morphine are: S = -2.947, A = 0.000, B = 3.139 with E= 2.120, L = 10.120 and V= 2.065 can be obtained as the best fit values (Table 3.20).

Table 3.20: Calculated Molecular Descriptors for Morphine

Descriptors	Value
E	2.120
S	-2.947
A	0.000
B	3.139
L	10.120
V	2.065

The molecular descriptors reproduce the experimental logRT for morphine within an overall standard deviation of 0.3129 log unit. From the structure of morphine (Figure 3.5) it can be seen that it has hydrogen molecule available for hydrogen bond formation with the stationary phases. But because of the orientation of the molecule the interaction with the stationary phase may be less. The tendency to form hydrogen bond may lose due to the change in molecular conformation of morphine as the temperature increases during the experiment. A=0.000 is quite reasonable. The lone pair on the nitrogen and oxygen molecules may exhibit the basic nature of morphine indicating that B= 3.139 is quite reasonable. It is always hard to encode the solubility nature of the molecule from the numerical values. The negative sign of S shows that the solute is less polar and more hydrophobic in nature than the corresponding hydrocarbons [74]. It is difficult to separate the exact distribution of polarity, dispersion, and induction effects from the numerical value of the parameter. The actual interaction information can be found in the intercept of the LFER equations which is very difficult to interpret [72]. Also it can be seen in that for most of the coefficients the value is very small and close enough. It means that there is not much difference in column phases, so it might not be useful to calculate the descriptors

appropriately. There are too few experimental data points (Table 3.19) to draw any real conclusion due to broad minimum.

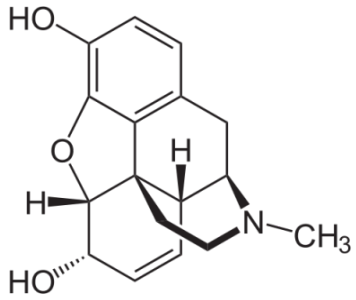


Figure 3.5: Structure of morphine

3.2.3.4 Codeine

Calculated retention data for codeine is obtained from equation 16 to equation 22 (Table 3.21).

Table 3.21: Observed and Calculated Retention Data for Codeine

Phase	Experimental logRT	Calculated logRT
TR-1MS	1.261	1.520
TR-5	1.261	1.428
TG-1301MS	1.193	1.014
TG-5MS	1.271	1.040
ZB-WAX PLUS	--	--
ZB-35	1.166	1.612
Octanol	0.872	0.882

The numerical values of the solute descriptors for Codeine are: S =-1.814, A = 0.000, B = 3.073 with E= 1.960, L = 11.04 and V= 2.206 can be obtained as the best fit values (Table 3.22).

Table 3.22: Calculated Molecular Descriptors for Codeine

Descriptors	Value
E	1.960
S	-1.814
A	0.000
B	3.073
L	11.040
V	2.206

The molecular descriptors reproduce the experimental logRT for codeine to within an overall standard deviation of 0.3077 log unit. Looking at codeine structure (Figure 3.6) it can be seen that it has one hydrogen atom available for hydrogen bond formation with the stationary phases. But because of the orientation of the molecule the interaction with the stationary phase may be less. Also the tendency to form hydrogen bond may lose because of the high temperature condition of the experiment. The value of A=0.000 is quite reasonable. The lone pair on the nitrogen and oxygen molecules may exhibit the basic nature of codeine indicating that B= 3.073 is quite reasonable. It is always hard to encode the solubility nature of the molecule from the numerical values. The negative sign of S shows that the solute is less polar and more hydrophobic in nature than the corresponding hydrocarbons [74]. It is difficult to separate the exact distribution of polarity, dispersion, and induction effects from the numerical value of the parameter. The actual interaction information can be found in the intercept of the LFER equations which is very difficult to interpret [72]. Also it can be seen in that for most of the coefficients the value is very small and close enough. It means that there is not much difference in column phases, so it might not be useful to calculate the descriptors appropriately. There are too few experimental data points (Table 3.21) to draw any real conclusion due to broad minimum.

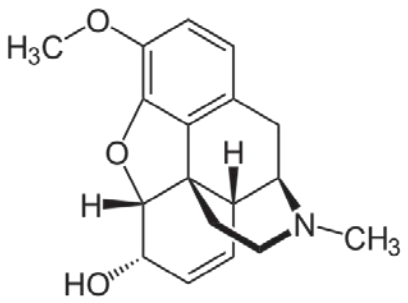


Figure 3.6: Structure of codeine

The calculated descriptors for the drugs are in the question of whether or not the calculated values reflect the chemical properties of the drug molecule. The drugs are somehow semi-volatile and also non-polar it is understandable that they may not cover the range of appropriate column chemistry.

Table 3.23: Predicted Molecular Descriptors for Lidocaine, Cocaine, Morphine and Codeine

DRUGS	E	S	A	B	L	V
Lidocaine	1.110	-1.039	0.420	2.158	8.448	2.059
Cocaine	1.355	-3.193	0.000	3.092	10.530	2.298
Morphine	2.120	-2.947	0.000	3.139	10.120	2.065
Codeine	1.960	-1.814	0.000	3.073	11.040	2.206

3.3 Conclusion

The Abraham solvation parameter model provides a fairly accurate description of the drug molecule's partitioning behavior of many biological systems. Mathematical correlations between the logarithm of retention time of illegal drugs with GC system and the solute molecular descriptor from the Abraham model can be developed through this experiment. Gas Chromatography is an easy technique to analyze illegal drugs. Abraham solvation parameter model is used to calculate and analyze the sorption coefficient of illegal drugs. Comparison of the experimental data and calculated data shows that the Abraham linear free energy relationship (LFER) model predicts retention behavior reasonably well for most compounds. The Abraham model could predict more accurate results by increasing the samples with effective functional groups. It can calculate the solute descriptors of illegal drugs from the retention time of GC system.

Molecular descriptors for the drug compounds need to be estimate to define the properties of the drug molecules that is its basicity, acidity, polarity and so on. Based on these properties we can predict how it will interact with different stationary phases which can give us

some idea about its interaction with the biological barriers. More literature survey is needed to establish this prediction. To predict well it is better to have more data points for the drug compounds. If more new GC columns are used in this project, it would be helpful to solve or predict the descriptors for the drug compounds. However, some illegal drugs lack volatility and are not ideal for GC analysis. HPLC is the optimal instrument and could be used for future work.

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