49. Solubility of Organic Solvents. I. Gas Chromatographic Determination of Olive Oil-Gas Partition Coefficients

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(29.XII.76)

Summary

A gas chromatographic method of measuring the olive oil-gas partition coefficients is described. It is based on the relationship existing between the retention time of each substance and its solubility in olive oil used as a stationary liquid phase. The validity of this method has been tested by varying the length of the column, the percentage of liquid phase and the flow rate of the carrier gas. Using this technique, the partition coefficients of 24 hydrocarbons, 8 aliphatic, 6 aromatic and 10 chlorinated, have been determined (see Table 4).

Introduction. - The solubility of organic solvents in the blood and in the different body tissues is a determining factor in the understanding of their absorption, distribution and excretion in the organism [1]. In fact, these substances are distributed in the body according to their affinity for the principal biological materials, such as water, proteins and lipids. Moreover, it is generally agreed that the greater the solubility of a vapour solvent in the blood and tissues, the more rapidly it will be absorbed and the less rapidly the saturation point of the blood and tissues is reached by the organism. Furthermore, the degree to which a biological system responds to the action of a toxic agent is in many cases influenced by the rate of the absorption since it determines the concentration of the solvent at the receptor.

Although the physico-chemical properties of some anaesthetic gases have been studied [2] [3], the characteristics of most industrial solvents are still little known. Several studies have been made during the past few years on the solubility of some aromatic and halogenated hydrocarbons [4] [7], but the data obtained are still too fragmentary or approximative to be used in pharmacokinetic studies.

This study presents the results obtained in the determination of the partition coefficients between olive oil (satisfying model of human fats [3]) and a gas, for a series of organic solvents frequently used in industry. The gas chromatographic method described here, is based on the relationship existing between the retention time of a product and its solubility in olive oil used as the liquid phase of the column. It has been successfully applied by several authors [2] [8] [9] and appears to be particularly adequate for determining the lipid-gas or oil-gas partition coeffi-

cients of apolar products. The validity of this technique is first tested on different chromatographic columns, then the partition coefficients of three series of hydrocarbons (aliphatic, aromatic, chlorinated) are determined.

Experimental Part

Apparatus. The measurements have been taken on a *Perkin-Elmer* F11 gas chromatograph fitted with an FID detector and a 1 ml gas sampling valve thermostatized at 37.0±0.1°. The nitrogen used as the carrier gas was preheated through a copper coil maintained in a thermostat at the same temperature as the column (37.0±0.05°). The pressure at the column inlet was measured using a mercury manometer fixed to the liquid injection block; the column outlet was at ambient pressure. The flow rate of the carrier gas was regulated by a fine needle valve, and measured by a bubble meter at the column outlet before and after each series of measurements. In addition, a precision rotameter, placed before the needle valve, allowed the stability of the nitrogen flow rate to be controlled during the determinations. The column holdup time was determined by the *Peterson & Hirsch* method [10] by extrapolating the retention times of three homologous compounds (hexane, heptane, octane). All retention times were measured using a *Perkin-Elmer* 56 recorder.

Products. Olive oil, quality Ph. H. VI, was obtained from *Siegfried* AG, Zofingen, Switzerland. Before being used it was vacuum treated (15 Torr) at 25° for 15 h in order to eliminate eventual volatile compounds, and was subsequently characterized by the determination of its fatty acid content [11]. The results obtained are given in Table 1. The density of the olive oil was measured at 22°

Table 1. *Fatty acid content of olive oil (Ph. H.VI, Siegfried AG)*

Acids	Percentages	Acids	Percentages
Palmitic	8.2	Linoleic	5.1
Palmitoleic	0.5	Arachidic	0.5
Stearic	3.4	Linolenic	1.0
Oleic	81.3		

(0.9059) and recalculated at 37° (0.8980) [12]. All solvents used were *puriss p.a.* quality (*Fluka*, Buchs, Switzerland or *Merck*, Darmstadt, West Germany) except for cyclohexane (puriss, *Fluka*), isooctane, 1,1-dichloroethane, 1,1,2-trichloroethane, 1,1,2,2-tetrachloroethane (purum, *Fluka*), styrene (stabilized, *Siegfried*), tetrachloroethylene (very pure, *Merck*) and 1,1,1-trichloroethane (non-stabilized, *Dow Chemical Europe*, Zurich, Switzerland).

Columns. The olive oil was deposited on the Gas-Chrom Q support (100–120 mesh, *Applied Sciences Laboratories Inc.*) by batch coating [13]. The exact percentage of liquid phase fixed on to the support was determined by the weight difference before and after extraction of the olive oil by toluene. The results obtained differed by not more than 1% from the percentages expected. In addition, the olive oil coating was controlled by the same method at the end of each series of measurements; the bleeding thus registered did not exceed 2%. Four glass columns (⌀3.2 mm) of varying lengths and different phase percentages were prepared. The physical properties of the columns are given in Table 2. A fifth column 65 cm long was prepared without any olive oil so that the interactions of the injected products with the support could be estimated.

Table 2. *Physical properties of the chromatographic columns*

Column	Length [cm]	Coating [%]	Weight of olive oil [g]
A	110	16.33	0.533
B	110	9.51	0.379
C	110	5.14	0.209
D	65	16.03	0.242

Procedure. In order to prevent the apparition of diffused edges due to insufficiently instantaneous vaporisation during the introduction of the sample, the solvents were injected by means of the gas sampling valve, as an air-vapour mixture prepared beforehand in a 50 l container. The injected concentrations were approximately 200 ppm, but tests with concentrations ten times smaller or ten times greater did not modify the retention times. Moreover, all the chromatograms obtained were gaussian in shape indicating that the isotherms governing the phase equilibria were linear and that equilibrium was achieved throughout the column.

Results and discussion. – Using the basic relationships of gas chromatography [13], the olive oil-gas partition coefficients were calculated from the retention times, carrier gas flow rates and pressure gradients through the column. In Table 3 the

Table 3. *Partition coefficients of 9 organic solvents determined with 4 different chromatographic columns*

Products	Columns			
	A	B	C	D
Trichloroethylene	766	762	765	758
1,1,1-Trichloroethane	373	378	375	367
Tetrachloroethylene	2085	2068	2081	2047
Chloroform	427	431	422	416
Carbon tetrachloride	438	435	432	424
Benzene	502	503	493	489
Toluene	1460	1465	1475	1438
m-Xylene	4285	4337	4380	4307
Styrene	5860	5808	5903	5768

results obtained for 9 solvents on 4 columns of varying lengths and olive oil coatings are compared. These values are the averages of 2 to 4 determinations carried out with varying carrier gas flow rates from 10 to 50 ml/min. There is no systematic variation in the partition coefficients as a function of the olive oil coatings or column lengths. Moreover, the partition coefficients obtained at different flow rates proved to be coherent. Measurements taken on a column containing only the support revealed no important solvent retention on Gas-Chrom Q. Consequently the gas-support and gas-liquid surface absorption processes can be considered as being negligeable [8]. The partition coefficients thus obtained correspond to the olive oil-gas equilibrium only.

The partition coefficients of 24 aliphatic, aromatic and chlorinated hydrocarbons have been determined. The results obtained as well as the standard deviations and the number of measurements taken are given in Table 4. The values obtained in this study for trichloroethylene (763), benzene (498), toluene (1460) and *m*-xylene (4321) agree with those recently published by *Sherwood* [9]. On the other hand, the styrene coefficient is significantly greater than the value estimated (4160) by *van Rees* [7]. A comparison of our results with those obtained with human fats for benzene (406), toluene (1296) and *m*-xylene (3605) by *Sato et al.* [6] indicates that olive oil can be used as a satisfactory model for studying the behaviour of solvents in the fatty tissues of the organism. An identical statement can be made with respect to chloroform (424) if the values found by *Lowe & Hagler* are taken into account (340 and 394) [2].

Table 4 shows that, for the *n*-alcanes, the partition coefficients increase gradually with the molecular weight. The cyclisation or the introduction of a double bond enhances their solubility even more. It is interesting to note that in the case of aromatic solvents, the partition coefficients of the isomers of xylene differ from each other (*o*-xylene > *m*-xylene > *p*-xylene). With regard to chlorinated hydrocarbons, it can also be noted that the partition coefficients of the geometric isomers differ considerably: in fact 1,2-dichloroethane is twice as soluble as 1,1-dichloroethane, whilst 1,1,2-trichloroethane is five times more soluble than 1,1,1-trichloroethane. 1,1,2,2-tetrachloroethane is the most soluble product (11543) studied here. This partition coefficient could possibly be related to the high toxicological risk of an exposure to this solvent by inhalation (TVL 5 ppm). In fact, with equal toxicity, the most liposoluble substances present the greater risks.

In conclusion, the chromatographic method presented in this study enabled the olive oil-gas partition coefficients of three series of solvents, 8 aliphatic, 6 aromatic and 10 chlorinated, to be determined in a simple and rapid way. The measurements

Table 4. *Olive oil-gas partition coefficients of 24 organic solvents at 37.0°*

	λ_{oil}	Variability coefficient [%]	Number of determinations
Aliphatic hydrocarbons			
Pentane	62	3.22	3
Hexane	178	2.32	15
Heptane	496	1.69	15
Octane	1381	1.56	15
Isooctane	418	0.86	3
Cyclohexane	351	1.57	3
Methylcyclohexane	657	1.60	3
Cyclohexene	454	1.67	3
Aromatic hydrocarbons			
Benzene	498	1.33	10
Toluene	1460	1.51	9
o-Xylene	5354	0.58[a])	2
m-Xylene	4321	1.59	8
p-Xylene	4161	2.17	3
Styrene	5838	1.70	9
Chlorinated hydrocarbons			
Methylene chloride	157	0.00	3
Chloroform	424	1.72	9
Carbon tetrachloride	433	1.85	9
1,1-Dichloroethane	214	0.97	3
1,2-Dichloroethane	503	1.15	3
1,1,1-Trichloroethane	373	1.61	9
1,1,2-Trichloroethane	2113	0.51	3
1,1,2,2-Tetrachloroethane	11543	-	1
Trichloroethylene	763	1.78	10
Tetrachloroethylene	2072	1.38	9

[a]) Deviation from the mean in percent.

were taken on a commercial gas chromatograph without having to make any important technical modifications. The precision obtained is characterized by an average standard deviation of 1.6%. The method can be adapted for polar products such as alcohols, esters, ketones, *etc.* For the latter, however, gas-support and gas-liquid surface interactions would probably occur. In addition, the absorption isotherms would no longer be linear for the concentrations considered. Different methods from those used in this work would therefore have to be used to overcome these undesirable processes [14].

We are grateful to the *Fonds National Suisse pour la Recherche Scientifique* for its financial support and to Mrs. *A. A. Humbert, Interfood* SA, Neuchâtel, Switzerland, for determining the fatty acid content of the olive oil.

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