Pflügers Arch. 384, 131 – 134 (1980)

Pflügers Archiv
European Journal of Physiology

Solubility of Inert Gases in Dog Blood and Skeletal Muscle*

M. Meyer, U. Tebbe, and J. Piiper

Abteilung Physiologie, Max-Planck-Institut für experimentelle Medizin, Hermann-Rein-Strasse 3, D-3400 Göttingen, Federal Republic of Germany

Abstract. Solubility of H_2, Ar, CH_4 and SF_6 was determined at 310 K (37°C) in water, in saline (0.154 mol NaCl/l H_2O), in plasma and whole blood of dogs, and in homogenates of the dog gastrocnemius muscle. The liquids were equilibrated with pure gases, and the dissolved gases were extracted and measured by gas chromatography as described previously (Meyer, M.: Pflügers Arch. 375, 161 – 165, 1978). In saline, the solubilities were 4% (SF_6) to 15% (Ar) lower than in water. For dog blood the following mean values for the solubility coefficient (in $\mu mol \cdot l^{-1} \cdot kPa^{-1}$) were found: for H_2, 6.44; for Ar, 9.94; for CH_4, 11.44; for SF_6, 2.62. The red cell/plasma and the muscle/blood solubility ratios were near unity for H_2, Ar and CH_4 (ranging from 0.9 to 1.3); for SF_6, however, they were much higher (about 2.1), apparently due to the high solubility of SF_6 in hydrophobic substances (lipids).

Key words: Blood – Inert gases – Partition coefficient – Plasma – Solubility.

Introduction

Inert gases have been shown to be useful for quantitative analysis of gas exchange both in lungs (e.g. Farhi, 1967; Farhi and Yokoyama, 1967; Wagner et al., 1975; Cerretelli et al., 1974) and in tissues (Piiper et al., 1962; Ohta et al., 1978; Meyer, 1978). The solubility of the gases in the media concerned (blood, tissue) is the important gas property in such applications. Using a modified technique for determination of solubility in liquids (Meyer, 1978), the solubilities of some frequently employed inert gases were measured in blood and in skeletal muscle and, for standardization purposes, in water and saline.

Send offprint requests to M. Meyer at the above address

* Supported by the Deutsche Forschungsgemeinschaft (SFB 89, Kardiologie Göttingen)

Methods

Measurements were made in distilled water, normal saline (0.154 mol NaCl/1 H_2O), blood, plasma and muscle homogenates of the dog.

For measurement of solubility coefficients a technique described earlier in detail (Meyer, 1978) was followed. The essence of the procedure is equilibration of the test solvent with humidified pure test gases at 310 K (37°C) and atmospheric pressure, and the estimation of the amount of gas dissolved in a 2.5 ml sample of the test solvent using an equilibration technique for partial extraction of gases from the solvent. Quantitative analysis of gases released from solvents was performed by gas chromatography.

Heparinized blood samples (1 mg heparin per ml blood) were collected from mongrel dogs (body weight 22 – 28 kg) that were fasting for about 16 h. Plasma was obtained by centrifugation of whole blood. No visible sign of hemolysis was present. Solubility in red cells was calculated from the values for whole blood and plasma of the same animal by volume-weighted subtraction, using the individual hematocrit values. Hemoglobin, plasma proteins, total lipids, triglycerides and cholesterol were determined by standard spectrophotometric methods. Mean values are presented in Table 1.

The gastrocnemius muscle was excised from dogs, which had been anesthetized for about 6 – 8 h with chloralose (80 mg/kg) and urethane (250 mg/kg), and killed by bleeding after having been used for other experimental purposes. The blood was allowed to drain from the major vessels, however, no effort was made to squeeze out residual blood manually. Multiple muscle samples, about 5 g each, were excised avoiding larger vessels and excluding the tendinous areas. The muscle samples were frozen in liquid nitrogen, homogenized and diluted with four times their weight of normal saline, whereby a suspension suitable for equilibration was obtained. A microscopic examination revealed that the cells were disrupted. The solubility in muscle was calculated from the inert gas content, the dilution ratio and the solubility in saline.

The reproducibility of the method is shown in Table 2 as the coefficient of variation (= SD/mean value) of multiple measurements performed on samples of identical origin.

Results

The solubility coefficients in normal saline, whole blood, plasma and dog gastrocnemius muscle for H_2, Ar, CH_4 and SF_6 are summarized in Table 3. Data are expressed in $\mu mol \cdot l^{-1} \cdot kPa^{-1}$. To facilitate comparison with literature values the solubility coefficients are also reported in the conventional units of the Bunsen

0031-6768/80/0384/0131/$01.00

Table 1. Composition of dog blood used for measurements of solubility in whole blood and plasma. Mean values ± SD

Hematocrit (%)	45 ± 4.5
Hemoglobin (g/100 ml blood)	16.9 ± 1.6
Plasma protein (g/100 ml plasma)	6.2 ± 0.5
Total lipids (mg/100 ml plasma)	519 ± 118
Triglycerides (mg/100 ml plasma)	108 ± 82
Cholesterol (mg/100 ml plasma)	202 ± 68

Table 2. Accuracy of methods. Mean coefficients of variation (= SD/mean value), in per cent. Blood, plasma and muscle: mean value of the coefficients of variation for multiple determinations on material from one animal. For number of measurements, see Table 3

	H_2	Ar	CH_4	SF_6
Water, saline	0.5	1.9	1.6	1.5
Blood	1.5	2.5	2.5	2.3
Plasma	1.5	2.6	2.9	2.3
Muscle	3.5	4.7	4.8	4.9

Table 3. Solubility of H_2, Ar, Ch_4 and SF_6 in various media. Mean values ± SE, in $\mu mol \cdot l^{-1} \cdot kPa^{-1}$ [in parentheses, in ml (STPD) $\cdot$ $ml^{-1} \cdot atm^{-1}$]. *n*, Number of determinations; *m*, number of dogs

	H_2	Ar	CH_4	SF_6
Water ($n = 12$)	7.21 ± 0.01 (0.0164)	11.46 ± 0.06 (0.0260)	11.47 ± 0.09 (0.0260)	1.60 ± 0.01 (0.0036)
0.9% NaCl ($n = 10$)	6.90 ± 0.02 (0.0157)	9.71 ± 0.06 (0.0221)	10.20 ± 0.10 (0.0232)	1.54 ± 0.002 (0.0035)
Blood ($n = 50$; $m = 10$)	6.44 ± 0.08 (0.0146)	9.94 ± 0.31 (0.0226)	11.44 ± 0.30 (0.0260)	2.62 ± 0.05 (0.0059)
Plasma ($n = 30$; $m = 10$)	6.44 ± 0.05 (0.0146)	9.37 ± 0.13 (0.0213)	9.99 ± 0.21 (0.0227)	1.73 ± 0.03 (0.0039)
Red cells ($m = 10$)	6.44 ± 0.15 (0.0146)	10.62 ± 0.67 (0.024)	13.21 ± 0.47 (0.0300)	3.70 ± 0.09 (0.0084)
Muscle ($n = 39$; $m = 13$)	6.80 ± 0.021 (0.0155)	8.88 ± 0.31 (0.0202)	11.95 ± 0.40 (0.0271)	5.52 ± 0.23 (0.0125)

Table 4. Partition coefficients (dimensionless) of H_2, Ar, CH_4 and SF_6 at 310 K (37°C). Mean values ± SE

	H_2	Ar	CH_4	SF_6
Water/Gas	$1.859 \cdot 10^{-2}$ ($\pm 0.002 \cdot 10^{-2}$)	$2.96 \cdot 10^{-2}$ ($\pm 0.02 \cdot 10^{-2}$)	$2.96 \cdot 10^{-2}$ ($\pm 0.02 \cdot 10^{-2}$)	$0.412 \cdot 10^{-2}$ ($\pm 0.002 \cdot 10^{-2}$)
Blood/Gas	$1.662 \cdot 10^{-2}$ ($\pm 0.002 \cdot 10^{-2}$)	$2.56 \cdot 10^{-2}$ ($\pm 0.08 \cdot 10^{-2}$)	$2.95 \cdot 10^{-2}$ ($\pm 0.08 \cdot 10^{-2}$)	$0.675 \cdot 10^{-2}$ ($\pm 0.013 \cdot 10^{-2}$)
Saline/Water	0.957 (±0.002)	0.848 (±0.007)	0.889 (±0.001)	0.962 (±0.006)
Plasma/Water	0.894 (±0.006)	0.819 (±0.012)	0.871 (±0.002)	1.085 (±0.018)
Blood/Water	0.894 (±0.011)	0.87 (±0.03)	1.00 (±0.03)	1.64 (±0.03)
Muscle/Water	0.94 (±0.03)	0.78 (±0.03)	1.04 (±0.04)	3.45 (±0.14)
Red cells/Plasma	1.00 (±0.03)	1.13 (±0.07)	1.32 (±0.05)	2.13 (±0.06)
Muscle/Blood	1.06 (±0.04)	0.89 (±0.04)	1.05 (±0.05)	2.11 (±0.10)
Oil/Water	3.0[a]	5.3[b]	10[c]	66[a]

[a] After Power and Stegall (1970)
[b] After Lawrence et al. (1946)
[c] After Campos Carles et al. (1975)

absorption coefficient, ml gas (STPD) $\cdot$ $ml^{-1} \cdot atm^{-1}$. In Table 4 the solubilities in various media are compared as partition coefficients (= ratio of solubilities in two media). In order to describe the interindividual variability of solubility coefficients, the coefficients of variation for the mean values of individual animals are presented in Table 5.

Discussion

Physiological Interindividual Variability

As shown by Tables 5 and 2, the interindividual variation of the solubilities in blood, plasma and muscle tissue is larger than the accuracy of a single determination, and is much larger when it is considered

that in all cases multiple measurements were performed.

It is of interest to notice that SF_6, which has a high oil/water partition coefficient (see below), shows essentially the same variability as the other gases. This probably reflects the relatively constant plasma and muscle fat content due to uniform experimental conditions (fasting, prolonged anesthesia). In other conditions larger deviations are expected to occur.

Solubility in the Various Media

The following trends and relationships may be discerned upon inspection of the values of Tables 3 and 4.

(1) The depression of solubility by addition of NaCl to water (termed "salting-out effect") is quite different for the individual gas species, amounting from 4% (SF_6) to 15% (Ar).

(2) For three gases solubility in plasma is lower than in saline; only for (the extremely lipophilic) SF_6 it is higher.

Table 5. Biological variability of solubilities in blood, plasma and muscle. Coefficient of variation, in percent, of mean values determined for each individual animal (= SD/overall mean)

	H_2	Ar	CH_4	SF_6
Blood	3.8	9.9	8.4	6.1
Plasma	2.2	4.5	6.5	4.9
Muscle	11	12	12	15

(3) With the exception of H_2, the solubility in red cells is higher than in plasma.

(4) Tissue/water coefficients for the two tissues tested, blood and skeletal muscle, show a relationship to the oil/water partition coefficient ranging from below unity, for the relatively little lipid soluble H_2 and Ar, to higher than 2, for the extremely lipophilic SF_6.

(5) The muscle/blood partition coefficients, important for analysis of tissue perfusion and diffusion, are variable and, except for SF_6, show no clear relationship to oil/water partition coefficients.

Comparison with Literature Data: Blood

Literature values for solubility of inert gas in water have been reviewed in a previous paper (Meyer, 1978). In Table 6 literature data have been compiled for solubilities in blood. Considerable discrepancies are evident. In particular, the present value for CH_4 is considerably lower when compared to previous findings. Also for Ar and SF_6 our values are lower than the average literature values. It is relevant to note that our water solubility values for all these four gases, including CH_4, are in good agreement with literature values (Meyer, 1978). From the higher oil/water partition coefficients of CH_4 and SF_6 one would expect that variations in plasma fat content modify the solubility in whole blood. Part of the differences of CH_4 and SF_6 solubilities in the present study as compared to the data by Wagner et al. (1974) and Young and Wagner (1979) may therefore be attributed to the slightly lower content of plasma lipids in our dogs (cf. Table 1). Furthermore the solubility may not be identical for all types of lipids.

Table 6. Solubility of H_2, Ar, CH_4 and SF_6 in blood at 310 K (37°C): comparison with literature values

Gas	Animal	Authors	Solubility coefficient	
			$\left(\frac{\mu mol}{l \cdot kPa}\right)$	$\left(\frac{ml\,(STPD)}{ml \cdot atm}\right)$
H_2	ox[a]	Van Slyke and Sendroy (1928)	6.60	0.0150
	dog	Present study	6.44	0.0146
Ar	rabbit	Ohta et al. (1979)	11.85	0.0269
	dog	Present study	9.94	0.0226
CH_4	man	Wagner et al. (1974)[b]	14.74	0.0335
	dog[a]	Wagner et al. (1974)[b]	15.85	0.0360
	rabbit	Ohta et al. (1979)	14.70	0.0334
	dog	Present study	11.44	0.0260
SF_6	man	Longo et al. (1970)	2.96	0.0067
	man	Wagner et al. (1974)[b]	2.32	0.0053
	dog[a]	Wagner et al. (1974)[b]	3.45	0.0078
	rabbit	Ohta et al. (1979)	3.15	0.0072
	dog	Young and Wagner (1979)[b]	3.57	0.0081
	dog	Present study	2.62	0.0059

[a] 311 K (38°C)

[b] These authors apparently have used ml BTPS as unit for amount of gas. We converted their values to ml STPD using as factor (V STPD/V BTPS) 0.826 for 310 K and 0.824 for 311 K (obtained assuming P_B = 1.0 atm in La Jolla, CA, near sea)

It should be noticed that in the studies of Wagner et al. (1974) and Young and Wagner (1979) very low partial pressures were used in equilibration (about 10^{-5} atm) whereas in all other investigations the partial pressure range was about 0.1 to 1 atm since the equilibrations were performed with pure gases or mixtures containing the test gases in high concentrations. It is possible that the solubility varies with the partial pressure range. However, the values of Table 6 show no clear correlation with the partial pressure range.

Solubility in Tissues

For technical reasons muscle tissue had to be homogenized for measurement of solubilities. To our knowledge all measurements of solubility in tissues and organs have been performed on homogenized material, with the exception of Campos Carles et al. (1975) who used excised, but intact, rat abdominal muscle which could be equilibrated by diffusion within a reasonable time, due to their small thickness. The values found by Campos Carles et al. (1975) in muscle differ largely from the values reported in this study: the solubility of H_2 was 25% and that of CH_4 60% higher, that of SF_6 was 24% lower than the corresponding values for muscle from the present study. It is quite possible that destruction of structures by homogenization affects the overall solubility. A convincing proof, however, has not yet been provided, since the discrepancies between the results of this study and those published by Campos Carles et al. (1975) may be sought in differences in species, muscle and techniques.

References

Campos Carles, A., Kawashiro, T., Piiper, J.: Solubility of various inert gases in rat skeletal muscle. Pflügers Arch. **359**, 209–218 (1975)

Cerretelli, P., Veicsteinas, A., Teichmann, J., Magnussen, H., Piiper, J.: Estimation by a rebreathing method of pulmonary O_2 diffusing capacity in man. J. Appl. Physiol. **37**, 526–532 (1974)

Farhi, L. E.: Elimination of inert gas by the lung. Respir. Physiol. **3**, 1–11 (1967)

Farhi, L. E., Yokoyama, T.: Effects of ventilation-perfusion inequality on elimination of inert gases. Respir. Physiol. **3**, 12–20 (1967)

Lawrence, J. H., Loomis, W. F., Tobias, C. A.: Preliminary observations on the narcotic effect of xenon with a review of values for solubilities of gases in water and oils. J. Physiol. (London) **105**, 197–204 (1946)

Longo, L. D., Delivoria-Papadopoulos, M., Power, G. G., Hill, E. P., Forster, R. E.: Diffusion equilibration of inert gases between maternal and fetal placental capillaries. Am. J. Physiol. **219**, 561–569 (1970)

Meyer, M.: Technique for measurement of inert gases in liquids by gas chromatography. Pflügers Arch. **375**, 161–165 (1978)

Ohta, Y., Ar, A., Farhi, L. E.: Solubility and partition coefficients for gases in rabbit brain and blood. J. Appl. Physiol. **46**, 1169–1170 (1979)

Ohta, Y., Song, S. H., Groom, A. C., Farhi, L. E.: Is inert gas washout from tissues limited by diffusion? J. Appl. Physiol. **45**, 903–907 (1978)

Piiper, J., Canfield, R. E., Rahn, H.: Absorption of various inert gases from subcutaneous gas pockets in rats. J. Appl. Physiol. **17**, 268–274 (1962)

Power, G. G., Stegall, H.: Solubility of gases in human red blood cell ghosts. J. Appl. Physiol. **29**, 145–149 (1970)

Van Slyke, D. D., Sendroy, J., Jr.: Studies of gas and electrolyte equilibria in blood. XI. The solubility of hydrogen at 38° in blood serum and cells. J. Biol. Chem. **78**, 801–805 (1928)

Wagner, P. D., Neumann, P. F., Laravuso, R. B.: Simultaneous measurement of eight foreign gases in blood by gas chromatography. J. Appl. Physiol. **36**, 600–605 (1974)

Wagner, P. D., Laravuso, R. B., Goldzimmer, E., Naumann, P. F., West, J. B.: Distributions of ventilation-perfusion ratios in dogs with normal and abnormal lungs. J. Appl. Physiol. **38**, 1099–1109 (1975)

Young, I. H., Wagner, P. D.: Solubility of inert gases in homogenates of canine lung tissue. J. Appl. Physiol. **46**, 1207–1210 (1979)

Received October 8, 1979 / Accepted January 9, 1980