Technical Report

In-vitro dissolution rate of mineral fibres at pH 4.5 and 7.4 – A new mathematical tool to evaluate the dependency on composition

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Useful mathematical models for the compositional dependency of the dissolution rate in flow-through measurements are presented. The rate of dissolution K_{dis}(Si) was determined for 81 different compositions at pH 4.5 and 7.4, respectively. A high degree of correlation to composition was found at both pH regimes.

In this work, the commonly used regression equation: $K_{dis} = K_0 \exp(S)$ or $\ln K_{dis} = \ln K_0 + S$ has been replaced by: $K_{dis} = K_\infty \exp(S)/(\exp(S)+1)$, where $S \equiv \Sigma C_i X_i$ is a linear combination ("index") of oxide contents. K_0 and K_∞ are constants, the latter is a limiting dissolution rate for $S \rightarrow \infty$. At the other extreme $S \rightarrow -\infty$, K_{dis} tends to zero. This feature of the new regression equation improves the correlation for the data sets applied and allows it to cover wider ranges of compositions.

The coefficients in $\Sigma C_i X_i$ are clearly different in the two regimes (pH 4.5 and 7.4). The most important difference is between the coefficients of alumina. At pH 4.5, it is highly positive, and at pH 7.4, it is highly negative.

1. Introduction

The classification of fibres with respect to health hazard is based on in-vivo studies. Bio-solubility of fibres measured in vivo has been shown to correlate with the tendency to cause damage to the lung or even lung cancer. The bio-solubility depends on the cooperative roles played by the two different regimes found in the lung: pH 4.5 (macrophages) and 7.4 (lung fluid). The bio-solubility is therefore simulated in vitro by measuring the dissolution rates at pH 4.5 and 7.4. The two dissolution rates are often mutually exclusive, i.e., compositions with a high dissolution rate at pH 4.5 have a low dissolution rate at pH 7.4, and vice versa. Yet, fibres with a high dissolution rate at either pH and with highly different compositions have been exonerated by in-vivo studies. This underlines the importance of both of these pH regimes for bio-solubility and the importance of an accurate mathematical modelling of in-vitro dissolution rates for the relevant composition space.

The development and introduction of bio-soluble fibres have resulted in various compliance schemes, such as the German RAL [1] and the European EUCEB [2]. Both schemes rely on controlling the chemical composition of the fibres. Fibres within a certain allowed range of the chemical composition of an in-vivo exonerated fibre are regarded as having equivalent or sufficiently close bio-solubility.

The importance of the different oxides with respect to bio-solubility has been accounted for differently in the two systems (RAL/EUCEB). A close analysis of the effect of the different oxides in in-vitro experiments may suggest relevant modifications in the existing compliance schemes.

Therefore the need for a uniform and accurate mathematical tool to predict in-vitro behaviour of mineral fibres at both pH 4.5 and 7.4 has long been apparent. The present paper is an attempt to meet this need.

1.1 Present state

Earlier attempts to correlate the glass composition with the rate of dissolution of amorphous fibres at pH = 4.5 have focused on structural parameters found by others to efficiently characterize the glass network: the molar ratio Al/(Si+Al) [3] and the molar ratio of Si–O–Si linkages [4]. Both of these parameters provide a fair accuracy in prediction of dissolution rates. In the present work, we have abandoned structural parameters and included the effect of all oxide components in the index S. This has improved the correlation and given a more straightforward modelling of the effect of each oxide component.

As early as 1991, an investigation of the dissolution rate of glass fibres at pH 7.4 concluded on the qualitative influence of the main oxides [5]: Al_2O_3 decreases the dissolution by double the factor of B_2O_3, BaO, Na_2O, CaO, and MgO. All the latter oxides increase the dissolution rate. This relation was later adapted and used in the so-called "Kanzerogenitätsindex" KI introduced in the German classification of fibres in 1994 [6].

Regression analyses on the same data [5] and additional measurements on glass fibres using the same protocol estab-

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Table 1. Chemical oxide compositions in wt%, in-vitro dissolution rates K_{dis}(Si) at pH 4.5 in ng/(cm^2 h) of the new fibres tested

SiO_2	Al_2O_3	TiO_2	FeO	CaO	MgO	Na_2O	K_2O	P_2O_5	K_{dis}(Si)
41.4	17.9	1.6	4.5	16.4	9.4	1.3	0.6	5.9	226
41.4	18.3	1.7	3.8	18.8	9.7	1.6	0.7	2.7	341
41.6	18.9	1.9	5.1	17.6	9.7	1.9	0.7	0.5	378
38.4	17.5	1.9	6.0	21.0	9.8	1.5	0.7	0.7	546
41.0	14.6	1.6	4.1	19.1	9.5	1.6	0.7	6.0	133
39.9	15.0	1.6	5.6	21.1	9.5	1.7	0.7	3.3	219
38.5	14.0	1.7	6.4	24.2	9.7	1.5	0.7	1.2	300
44.2	18.4	1.7	2.9	13.2	9.2	2.0	0.7	6.1	144
40.6	20.8	1.6	7.1	13.6	11.4	1.6	0.8	0.3	616
41.7	15.1	1.3	6.1	22.0	9.6	1.6	1.0	0.3	327
42.1	15.0	1.4	6.3	18.7	12.5	1.6	0.9	0.3	265
41.8	16.7	1.5	6.3	20.2	9.3	1.7	1.1	0.3	323
41.5	16.4	1.5	6.7	20.0	9.0	1.6	1.1	0.3	341
41.9	14.3	1.3	6.2	19.7	12.0	1.5	0.9	0.3	275
41.4	16.7	1.4	6.4	19.9	9.3	1.6	1.0	0.3	462
40.6	20.8	1.6	7.1	13.6	1.4	1.6	0.8	0.3	635
41.7	15.1	1.3	6.1	22.0	9.6	1.6	0.8	0.3	287
42.1	15.0	1.4	6.3	18.7	12.5	1.6	0.9	0.3	220
41.8	16.7	1.5	6.3	20.2	9.3	1.7	1.1	0.3	304
41.9	14.7	1.4	6.4	18.5	12.2	1.6	0.9	0.3	232
40.5	21.8	0.3	0.9	29.5	4.5	1.7	0.3	0.3	677
39.6	15.9	1.3	6.4	19.8	12.4	1.9	0.6	0.2	395
40.0	13.3	1.3	6.1	17.3	17.5	2.0	0.6	0.3	266
40.1	13.0	1.3	6.6	17.4	17.4	2.0	0.6	0.3	245
41.7	16.1	1.8	6.0	20.2	9.2	2.5	0.7	0.3	354
39.9	13.0	1.3	6.6	22.1	12.2	1.9	0.6	0.3	220
41.9	12.6	1.9	5.5	23.5	9.2	2.6	0.8	0.4	139
40.9	20.7	0.4	1.0	31.8	2.4	1.4	0.4	0.1	639
40.6	16.4	1.8	6.7	20.2	8.9	2.6	0.7	0.3	509
42.6	18.8	1.8	6.2	13.4	9.5	2.0	0.7	3.1	344

Table 2. Results of the regression calculation for in-vitro tests at pH 4.5, chemical oxide composition in wt% and K_∞ in ng/(cm^2 h)

	SiO_2	Al_2O_3	TiO_2	FeO	CaO	MgO	Na_2O	K_2O	P_2O_5	K_∞
minimum	32.4	11.6	0.3	0.9	10.1	2.4	0.7	0.3	0	
maximum	47.7	23.3	2.8	8.6	31.8	17.5	7.2	2.3	6.1	
C_{mol} in mol%	−0.178	0.536	−0.89	0.14	0.069	0.032	0.15	0.37	−0.225	725
C_V in %	−15	13	−30	46	22	40	32	53	−51	4
C_{wt} in wt%	−0.184	0.333	−0.68	0.12	0.078	0.049	0.15	0.24	−0.107	727
C_V in %	−14	12	−25	26	26	51	31	27	−29	4

Note: K_∞ is extremely well determined, in agreement with the improved correlation obtained with the new regression equation. Data are equally well fitted when concentrations are in wt% or mol%, with R^2 = 0.90 and residual root mean square deviation = 61 ng/(cm^2 h).

Table 3. Results of the regression calculation for in-vitro tests at pH 7.4, reported in [8]; K_∞ in ng/(cm^2 h)

	SiO_2	Al_2O_3	Fe_2O_3	RO	R_2O	P_2O_5	B_2O_3	ZrO_2	K_∞
C_{mol} in mol%	−0.065	−1.14	−0.272	0.117	0.04	0.489	0.454	−0.349	1047
C_V in %	−14	−10	−18	15	51	47	23	−25	19
C_{wt} in wt%	−0.064	−0.678	−0.222	0.124	0.034	0.206	0.390	−0.169	1043
C_V in %	−25	−21	−31	30	70	68	41	−27	17

Note: wt% and mol% fit equally well with R^2 = 0.91 and residual root mean square deviation = 81 in ng/(cm^2 h).

lished a linear correlation between lg K_{dis} and $\Sigma C_i W_i$, where C_i are the coefficients reflecting the influence of the individual oxides, and W_i the wt% of these [7]. A set of coefficients was found which was not very different from those found by Potter [5], only, they included fluorine. R^2 for the correlation was 0.96.

The authors of [5 and 7] correctly emphasize the limitations imposed by the linear form of the regression equation and the corresponding limited compositional range. The nonlinear equation used in the present article does not suffer from this limitation, and a much wider compositional range can thus be modelled.

Table 4. Chemical oxide compositions in wt%, in-vitro dissolution rates K_{dis}(Si) in ng/(cm^2 h) at pH 7.4

SiO_2	Al_2O_3	TiO_2	FeO	CaO	MgO	Na_2O	K_2O	P_2O_5	B_2O_3	K_{dis}(Si)
44.2	15.6	1.2	4.7	17.5	11.6	3.2	0.6	0.1	0.0	30.4
39.4	11.4	1.0	3.2	24.5	17.3	1.9	0.2	0.1	0.0	43.7
42.0	15.7	1.2	7.7	19.4	7.8	3.6	0.6	0.2	0.0	48.9
44.2	15.5	1.8	7.9	16.5	8.6	2.0	0.9	0.3	0.0	42.5
42.9	18.8	1.6	6.3	18.4	7.8	1.6	0.9	0.2	0.0	38.6
44.3	19.1	1.7	6.7	15.6	8.0	1.7	0.9	0.2	0.0	25.6
46.1	13.2	2.8	6.3	16.6	9.3	2.6	1.3	0.0	0.0	38.3
42.6	13.8	0.0	0.0	33.9	5.1	0.7	1.5	0.0	0.0	15.9
45.1	12.7	0.0	0.0	30.1	6.3	1.2	0.5	0.0	0.0	6.4
41.5	12.4	1.3	4.3	23.5	13.0	2.3	0.7	0.0	0.0	27.5
41.3	15.6	0.8	4.7	20.5	12.0	3.1	0.2	0.0	0.0	35.6
42.7	12.4	0.5	0.6	37.7	2.9	0.3	0.5	0.1	0.0	15.4
46.8	9.4	0.7	0.2	29.9	10.1	0.2	0.6	0.0	0.0	21.0
64.8	0.3	0.1	0.1	15.5	11.1	0.1	0.1	0.1	0.0	170.7
62.9	0.7	0.1	0.1	30.6	3.8	0.1	0.1	0.1	0.0	1200.4
67.4	0.2	0.1	0.1	30.2	0.1	0.1	0.1	0.1	0.0	572.0
43.5	10.1	0.4	0.5	37.7	6.5	0.3	0.4	0.1	0.0	21.5
35.7	20.7	1.0	8.6	18.0	9.5	2.2	2.1	0.2	0.0	65.0
56.9	2.1	0.2	8.3	18.3	6.7	2.8	0.3	0.9	0.0	174.3
41.1	17.8	0.6	2.6	15.6	16.2	4.5	0.4	0.1	0.0	24.5
32.6	20.9	0.8	9.4	20.0	8.9	2.6	2.6	0.2	0.0	94.0
31.4	21.8	0.7	9.4	20.6	8.2	2.7	2.9	0.1	0.0	116.4
38.7	22.6	1.4	3.7	11.2	15.6	4.8	0.6	0.2	0.0	67.4
42.4	19.2	1.6	4.6	15.3	9.3	3.4	0.7	1.3	0.0	46.2
58.2	1.5	0.1	7.5	8.4	16.3	3.7	0.4	0.9	0.0	347.1
57.3	1.5	0.1	3.9	13.3	16.7	2.8	0.3	0.8	0.0	924.8
56.5	1.7	0.3	5.9	19.8	7.4	2.8	0.4	1.2	0.0	450.3
43.9	11.6	2.1	5.2	24.3	8.0	1.9	0.5	0.0	0.0	33.3
50.5	2.9	0.1	9.0	15.2	14.2	0.1	0.4	4.5	0.0	563.6
36.6	21.1	1.4	5.4	18.5	10.4	4.1	0.7	0.2	0.0	75.1
57.4	1.3	0.1	6.3	12.0	13.8	3.8	0.3	1.5	0.0	569.7
43.2	23.2	1.7	6.1	15.0	5.1	2.9	0.6	0.2	0.0	32.2
36.6	22.8	1.8	4.8	20.6	8.8	1.9	0.7	0.4	0.0	76.0
36.7	20.5	1.5	5.8	18.3	10.6	4.0	0.7	0.2	0.0	79.8
57.0	1.3	0.1	2.9	23.0	8.8	4.1	0.4	0.1	0.0	906.5
49.4	3.0	0.2	5.8	18.1	14.9	0.2	0.5	5.3	0.0	1093.2
39.6	21.5	2.0	6.4	15.4	10.7	1.2	0.8	0.0	0.0	47.2
36.7	20.5	1.5	5.8	18.3	10.6	4.0	0.7	0.2	0.0	77.5
56.5	1.9	0.0	7.1	17.1	9.3	1.4	0.1	3.2	0.0	670.5
34.4	21.4	1.8	5.5	23.1	8.8	1.8	1.6	0.4	0.0	106.8
32.4	22.1	1.8	3.1	27.0	8.7	1.9	1.4	0.4	0.0	119.2
41.2	19.7	1.1	3.4	17.4	9.6	2.0	0.6	2.4	0.0	32.3

Other glass parameters such as nonbridging oxygen (NBO), optical basicity (OB), free energy of hydration (ΔG_0), and the *KI* index have been investigated [8]; it was found that none of these can be used to reliably predict the in-vitro dissolution rate at pH 7.4. The *KI* index was found to give a fair prediction in a limited compositional range. As demonstrated later in this article, the whole compositional range can be modelled with high accuracy when using the nonlinear model applied by us.

The molar ratio Al/(Al+Si), which has been found useful at pH 4.5 is also seen to correlate with the in-vitro dissolution rate at pH 7.4 for low-alumina glasses [3].

2. Method of calculation

At pH 4.5, Gambles liquid is active mainly due to complex-binding of alumina by citric and tartaric acid [9]. The concentration of these acids and the flow rate in the cell set a limit to the rate of dissolution. At the "saturation" limit, the concentration at the outlet does not increase with increasing amounts of sample. This prompted the introduction of the new regression equation:

$$K_{dis} \equiv K_\infty \exp(S)/(\exp(S)+1),$$

where $S = \Sigma C_i X_i$ is a linear combination of oxide contents. This equation has a limit in dissolution rate at K_∞. Contrary to the more commonly used equation:

$$K_{dis} \equiv K_0 \exp(S), \text{ or}$$

$$\ln K_{dis} \equiv \ln K_0 + S,$$

it cannot be linearized by taking the logarithm on both sides. Nonlinear regression calculations have to be applied. We have chosen to use the random perturbation method.

2.1 Random perturbation calculations

The random perturbation calculation changes all adjustable parameters in a random way until best fit. Each time a

Table 4. Continued

SiO_2	Al_2O_3	TiO_2	FeO	CaO	MgO	Na_2O	K_2O	P_2O_5	B_2O_3	K_{dis}(Si)
37.2	20.6	1.2	3.7	22.9	10.0	2.5	0.3	0.1	0.0	79.8
38.8	11.3	0.5	0.3	39.6	7.6	0.3	0.4	0.1	0.0	41.2
42.8	10.2	0.4	0.4	31.0	11.9	0.6	0.6	0.1	0.0	26.1
45.8	14.9	1.6	7.6	14.3	10.9	2.0	1.0	0.4	0.0	21.1
64.1	3.1	0.1	0.1	7.7	3.0	15.9	1.3	0.1	3.5	209.0
62.8	0.9	0.1	0.1	7.2	2.9	15.4	0.3	1.1	8.1	2319.8
40.6	20.8	1.6	7.1	13.6	11.4	1.6	0.8	0.3	0.0	47.0
40.8	17.9	1.2	5.4	16.7	13.2	2.3	0.5	0.2	0.0	47.8
42.3	20.4	1.1	5.6	16.2	10.1	1.0	1.6	0.1	0.0	26.8
41.1	19.9	1.3	7.2	15.2	10.2	2.7	0.7	0.3	0.0	36.2
41.3	19.9	1.0	3.2	16.8	12.7	2.6	0.9	0.2	0.0	639.3
42.0	18.0	1.6	4.0	10.1	16.8	4.4	1.4	0.1	0.0	24.3
41.3	13.3	0.7	6.3	23.6	9.7	2.7	0.4	0.2	0.0	25.2
39.6	20.0	1.9	7.9	17.5	7.9	2.5	1.1	0.4	0.0	34.4
64.8	1.7	0.1	0.1	7.3	3.0	16.7	0.6	0.1	4.0	648.9
65.0	1.9	0.1	0.4	7.5	2.3	16.5	0.4	0.1	4.5	319.2
64.8	1.7	0.1	0.1	7.3	3.0	16.7	0.6	0.1	4.0	648.9
64.1	3.1	0.1	0.1	7.7	3.0	15.9	1.3	0.1	3.5	241.5
65.0	1.9	0.1	0.4	7.5	2.3	16.5	0.4	0.1	4.5	344.4
62.8	0.9	0.1	0.1	7.2	2.9	15.4	0.3	0.1	8.1	2292.7
62.8	0.9	0.1	0.1	7.2	2.9	15.4	0.3	0.1	8.1	2710.4
64.1	3.1	0.1	0.1	7.7	3.0	15.9	1.3	0.1	3.5	367.5
40.6	20.8	1.6	7.1	13.6	11.4	1.6	0.8	0.3	0.0	35.3
41.7	15.1	1.3	6.1	22.0	9.6	1.6	1.0	0.3	0.0	29.7
42.1	15.0	1.4	6.3	18.7	12.5	1.6	0.9	0.3	0.0	22.6
41.8	16.7	1.5	6.3	20.2	9.3	1.7	1.1	0.3	0.0	27.2
39.6	15.9	1.3	6.4	19.8	12.4	1.9	0.6	0.2	0.0	37.2
39.9	13.0	1.3	6.6	22.1	12.2	1.9	0.6	0.3	0.0	32.6
40.1	13.0	1.3	6.6	17.4	17.4	2.0	0.6	0.3	0.0	36.3
40.6	16.4	1.8	6.7	20.2	8.9	2.6	0.7	0.3	0.0	47.7
42.6	18.8	1.8	6.2	13.4	9.5	2.0	0.7	3.1	0.0	42.9
39.3	22.6	2.0	6.9	14.7	10.5	1.7	0.8	0.3	0.0	73.1
42.5	23.3	2.2	5.9	15.2	5.5	1.6	0.5	0.0	0.0	42.7
40.4	20.7	1.3	6.3	17.2	10.3	0.7	1.4	0.0	0.0	60.1
40.8	20.2	1.9	4.9	15.9	11.1	1.2	0.7	0.0	0.0	46.8
39.0	22.6	2.1	4.6	17.2	10.3	1.3	0.9	0.0	0.0	67.9
40.7	22.9	1.4	7.0	15.1	7.5	1.7	0.5	0.0	0.0	46.8
42.9	21.8	1.7	5.6	16.9	6.0	2.1	0.7	0.0	0.0	42.9
41.4	21.3	2.0	7.6	16.2	6.2	1.9	0.9	0.6	0.0	44.5

perturbation has been performed, its implication on the criterion function will be checked. If improvement is found, the set will be used for the next trial. The criterion function has been constructed to serve the special purpose of the calculation. In our case, the sum of square deviations between measured and calculated values: $\Sigma[K_{dis}(meas)-K_{dis}(calc)]^2$ has been used. A minimization of this criterion function depends on the assumption of a normal distribution of errors (least square deviation method).

The success of this method depends, to some degree, on a proper starting approximation and on the size of the perturbation. Step size 0.001 was chosen, meaning that a perturbation consisted of the transformation: $C_{new} = C_{old}[1+0.001(^1/_2\text{-RND})]$, where RND stands for a random number between 0 and 1. When a sufficiently good first guess has been obtained, good convergence can be achieved with less than 100 000 trials, requiring only a few minutes' calculation.

The big advantage of the random perturbation scheme is the freedom to choose the regression function. Even the powers of the oxide molar ratios may be treated as adjustable parameters. Some improvement of correlations can be obtained in this way. We have chosen to maintain linear indices in this work, mostly for the sake of clarity. Linear indices give a more direct conception of the effect of the different oxides.

Confidence limits for the estimated model parameters were found by repeated generations (10 times) of normally distributed "fictitious" values of K_{dis} around the regression line, and repeated calculation of the coefficients by the random perturbation method [10]. The resulting ten different values of each single coefficient were used to calculate an estimate of its standard deviation and, based on this, the coefficients of variation, C_V, stated in tables 2, 3, 5, and 7.

3. Results and discussions

3.1 Dissolution rate at pH 4.5

In this work, data have supplemented previously published data [4]. The compositions in wt% of the 30 new in-vitro studies are shown in table 1. The K_{dis} calculated for these data were for Si in the period of one to four days, the same as done previously in [4].

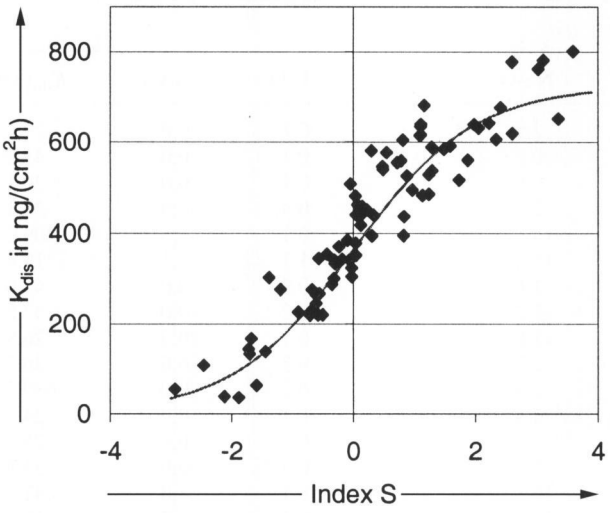

Figure 1. 81 measured values of K_{dis}(Si) at pH 4.5 plotted as a function of the linear composition index S. The sigmoidal form of the regression equation is borne out well by the data points.

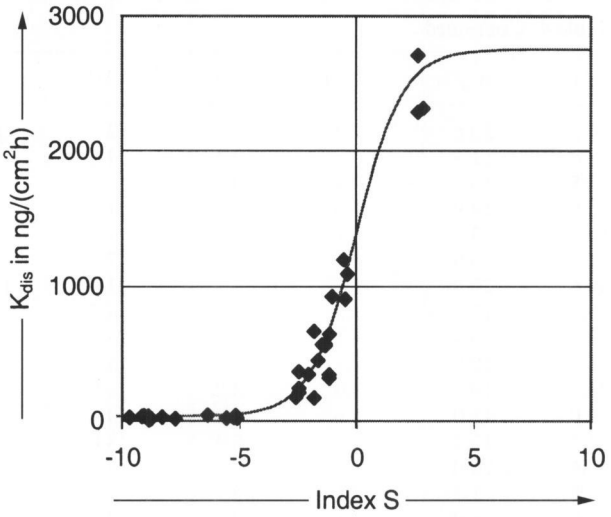

Figure 2. Measured values of K_{dis}(Si) at pH 7.4 plotted as a function of the linear index S. 54 data points randomly spread around the value 45 ng/(cm² h) with values of S between −10 and −20 have been left out of the plot.

The coefficients C_i in $S \equiv \Sigma C_i X_i$ can be seen in table 2. Confidence limits for the coefficients are given as coefficients of variation (C_V), the ratio between standard deviation and mean. The first two rows show the ranges scanned by the data set. The accuracy of fit with these coefficients is shown in figure 1.

3.2 Transformations of the regression equation and the coefficients C_i

When comparing indices of the kind $S \equiv \Sigma C_i X_i$ used with different regression equations, it is important to realize the degree of arbitrariness in the values of coefficients. Comparing coefficients directly is only meaningful if the same regression equation has been applied. It may easily be verified that a different choice of regression equation, say:

$$K_{dis} \equiv K_\infty \exp(S'/F)/(\exp(S'/F) + \exp(C_0/F))$$

would alter the coefficients by $C' \equiv F(C+C_0)$. The choice of regression equation can change both the sign and the size of a coefficient. The only constants of transformation are the ratios of differences:

$$(C_i'-C_j')/(C_g'-C_h') \equiv [F(C_i + C_0) - F(C_j + C_0)]/[F(C_g + C_0) - F(C_h + C_0)] \equiv (C_i-C_j)/(C_g-C_h).$$

The conclusion from this is twofold. Firstly, a change in composition must change at least the amounts of two oxides. Thus an increase of say 2 % of Al_2O_3 could be counteracted by a decrease of 2 % of SiO_2 or a decrease of 2 % of CaO. These two alternatives would give totally different results. An increase of the oxide Al_2O_3 will always increase the dissolution rate at pH 4.5. For SiO_2, the opposite is the case, except when the other oxide involved is TiO_2 or P_2O_5. This is in accordance with the earlier attempts to correlate the dissolution rate to the composition, where especially these two oxides were found to be important [4]. Secondly, a comparison to other sources of indices should be made only after an appropriate transformation has been applied to the coefficients.

The second point may be illustrated by an example: the coefficients in table 3 (C_{wt}, pH 7.4) may be changed by the transformation $C_i' \equiv 3.95(C_i + 0.172)$. This would alter the coefficients of Al_2O_3, RO, R_2O, and B_2O_3 from −0.678, 0.124, 0.034, and 0.390 to −2.00, 1.17, 0.81, and 2.20. Perhaps with the exception of boron, these transformed coef-

Table 5. Results of the regression calculation for Rockwool International's in-vitro tests at pH 7.4, chemical oxide composition in wt% and K_∞ in ng/(cm² h)

	SiO_2	Al_2O_3	TiO_2	FeO	CaO	MgO	Na_2O	K_2O	P_2O_5	B_2O_3	K_∞
minimum	31.4	0.2	0.3	0	7.2	0	0	0.05	0	0	
maximum	67.7	23.3	2.8	9.4	39.6	17.4	16.7	2.9	5.3	8.1	
C_{mol} in mol%	−0.101	−1.57	−3.95	−0.017	0.184	0.128	0.072	1.46	0.511	0.885	2626
C_V in%	−6	−16	−34	−73	8	11	58	30	29	19	10
C_{wt} in wt%	−0.102	−0.924	−3.04	−0.018	0.199	0.198	0.072	0.872	0.212	0.765	2642
C_V in%	−10	−23	−32	−19	13	18	40	39	32	20	13

Note: The negative value of the coefficient to alumina is contrary to the positive sign for pH 4.5. This negative value is so dominating, that for all compositions in this data set, as little as 5 wt% alumina in the fibre completely nullifies K_{dis}. Concentrations in wt% and mol% fit equally well with $R^2 = 0.98$ and residual root mean square deviation = 75 ng/(cm² h).

Table 6. Chemical compositions in wt%, in-vitro dissolution rates K_{dis}(Si) in ng/(cm^2 h) at pH 7.4; complete data for 36 fibres from [8]

code	SiO_2	Al_2O_3	TiO_2	Fe_2O_3	CaO	MgO	Na_2O	K_2O	P_2O_5	B_2O_3	ZrO_2	K_{dis}(Si)
1	58.4	5.95	0.013	0.049	1.77	0.182	9.6	3.03	0.015	11.04	0.031	17
3	65	3.2	0.02	0.14	7.4	3.03	15.5	1.3	0	4.4	0	56
4	64.6	3.7	0.019	0.1	7.9	2.98	14.4	0.77	0.05	4.4	0	52
5	65	0.5	0.05	0.15	30	3.3	0.14	0.11	0.03	0	0	453
6	67.3	0.7	0.06	0.16	12.9	10.9	0.16	0.05	0.03	0	7	109
7	63.3	2.07	0	0.12	7.05	3.16	15	1.15	0	8.2	0	450
8	64.4	2.8	0.03	0.19	7	3.18	14.4	1.07	0	6.7	0	110
9	65.1	2	0.038	0.07	7.9	2.4	16.5	0.8	0.67	4.4	0	172
11	65.1	2	0	0.1	7.5	2.5	16.2	0.7	1.1	4.5	0	118
12	61.2	0.46	0.01	0.06	16.4	2.9	15.1	0.32	0.02	3.5	0	580
13	65.4	0.93	0.02	0.06	7.4	3.2	15.7	0.37	1	6.1	0	610
14	61.5	0.9	0	0.1	7.4	2.8	15.5	0.5	1.1	10.2	0	970
15	57.9	0.4	0	0.1	8.4	3.4	17.9	0.3	0	11.9	0	1033
22	52	47	0.05	0.18	0.1	0.05	0.25	0.05	0	0	0	7
23	56.5	24	0.05	0.15	0.1	0.05	0.2	0.05	0	0	19	0
24	58.4	0.44	0.06	0.3	0.8	39.9	0.08	0.04	0.02	0	0	940
25	38	0.46	0.09	0.35	0.8	45	0.06	0.03	0.04	0	15	630
26	57.46	5.08	0.007	0.05	7.69	4.15	14.9	1.06	0	8.6	0.029	340
27	45.9	13.75	2.97	6.9	17	9.5	2.46	1.26	0.26	0	0.037	17
28	38.4	10.6	0.5	0.3	38	9.9	0.4	0.5	0	0	0	35
29	47.7	48	2.05	0.97	0.07	0.98	0.54	0.16	0	0	0.11	19
30	51.25	45.5	1.84	0.89	0.082	0.058	0.04	0.118	0	0	0.038	11
33	>99.9	0	0	0	0	0	0	0	0	0	0	11
42	56.3	3.15	0.1	0.25	26.1	6.4	3.2	0.65	2.9	0	0	241
43	60.6	0.4	0	6.2	19	8.4	5.4	0	0	0	0	132
44	60.23	1.05	0.04	5.45	19.3	8.8	4.6	0.4	0.04	0	0	120
45	57.2	3.9	0.09	0.28	25.15	9.85	0.17	0.1	2.85	0	0	220
46	58.7	1.5	0.02	0.09	39	0.51	0.2	0.3	0	0	0	358
47	50	6.55	0.31	6	25.5	5.1	1.35	0.18	4.25	0	0	17
53	50.3	2.9	0.1	0.4	31.3	10.3	4.7	0.2	0	0	0	523
54	53.8	1.77	0.06	0.87	29	9.2	4.5	0.43	0	0	0.01	681
55	52.8	3.7	0.4	2.5	26.3	9.2	4.2	0.6	0.1	0	0	86
56	53.2	3	0.3	1.9	27.4	9.2	4.3	0.5	0.1	0	0	331
57	53.6	2.28	0.179	1.4	28.2	9.2	4.37	0.47	0.1	0	0	629
58	50.8	6.3	1.01	5.4	21.6	9.3	3.8	0.85	0.2	0	0	17
59	52.3	4.1	0.54	3.2	25.3	9.3	4.1	0.64	0	0	0	60

Table 7. Results of the regression calculation for in-vitro tests at pH 7. 4 [8], chemical oxide composition in wt% and K_∞ in ng/(cm^2 h)

	SiO_2	Al_2O_3	TiO_2	Fe_2O_3	CaO	MgO	Na_2O	K_2O	P_2O_5	B_2O_3	ZrO_2	K_∞
minimum	38	0	0	0	0	0	0	0	0	0	0	
maximum	100	48	3.0	6.9	39	45	17	3	4.25	11.9	19	
C_{mol} in mol%	−0.077	−1.74	−0.118	−0.966	0.126	0.210	0.021	0.061	0.551	0.675	−1.39	949
C_V in %	−18	−13	−12	−24	19	14	100	226	46	18	−18	4
C_{wt} in wt%	−0.076	−1.04	−0.077	−0.355	0.135	0.315	0.018	0.045	0.250	0.585	−0.688	948
C_V in %	−14	−11	−14	−15	17	14	85	165	43	19	−17	4

Note: Coefficients corresponding to concentrations in wt% and in mol% fit equally well with $R^2 = 0.96$, and root mean square deviation = 58 ng/(cm^2 h). The high values of C_V for the coefficients to Na_2O and K_2O show clearly that they are virtually zero.

ficients are close to those of the carcinogenicity index *KI*, where the coefficients are −2,1,1, and 1 [8 and 6].

3.3 Dissolution rate at pH 7.4

The data set used here consists of 81 in-vitro studies performed in the laboratory of Rockwool International A/S according to the Eurima guidelines [11]. The results used are the dissolution rates over the one to four days of the experiment. The compositions and the rate of dissolution can be seen in table 4. The model fit to these data is presented in figure 2.

Table 5 displays the coefficients C_i in $S = \Sigma C_i X_i$ and the statistical results. In this case, the regression equation has been changed slightly by adding a constant 45 ng/(cm^2 h):

$$K_{dis} = K_\infty \exp(S)/(\exp(S)+1) + 45 \text{ ng/(cm}^2 \text{ h)}.$$

In their work, Meringo et al. [8] did not try to improve the coefficients of the index *KI* to fit their data. Furthermore,

they only measured the degree of correlation by linear regression. They found a linear correlation coefficient $R^2 = 0.78$ when leaving out 20 observations with $KI < 15$. We have adjusted the coefficients to fit their data by the method presented here and improved the correlation. The results of this regression calculation can be seen in table 3.

Meringo et al. have made their complete chemical analyses for 36 of the fibres from [8] available to us, see table 6. The regression analysis provides the results shown in table 7. The increased degree of correlation indicates the importance of including all oxide species.

4. Conclusion

The results of a nonlinear regression analysis of in-vitro rates of dissolution on chemical composition were presented. Large data sets for pH 4.5 (81) and pH 7.4 (81) were employed, and high degrees of correlations were found. Two distinctly different indices were found to account for dissolution rates in the two pH regimes. Regression analysis of earlier work by Meringo et. al. [8] along the lines presented here improved the correlation substantially.

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