Modeling the retention behavior of analytes in RPLC with mixed solvent mobile phases using Jouyban-Acree and Abraham models

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An extension to the Jouyban-Acree model was proposed to calculate the retention factor of analytes in RPLC with hydro-organic solvent mixtures as mobile phase by using the Abraham solvent coefficients and Abraham solute parameters. The accuracy of the proposed method was checked by computing the mean percentage deviation as a criterion. The proposed method provides an *ab initio* prediction (without employing any experimental retention data of an analyte) method with an acceptable prediction error for the retention data of various analytes based on their chemical structures. The accuracy of the proposed method was also compared with that of a previously reported model and provided comparable results with the advantage of modeling the effects of various organic modifiers using a single equation.

1. Introduction

Reverse phase liquid chromatography (*RPLC*) is the most widely used separation technique in pharmaceutical/chemical analysis. Despite of this wide range of applications, separations are still being developed using a non-systematic manner (trial and error) which is time consuming and leads to non-optimum conditions. In an attempt to overcome this problem many efforts have been made in order to predict the retention factor as the most important variables governing the separations, and some models were developed.[1–11] Among these, the models which are based on linear free energy relationships (*LFER*) have been used over two decades to study solute retention in *RPLC*. Vitha and Carr[12] reviewed the applications of these models and evaluated the different chemical interactions which affect the retention and selectivity in chromatographic separations. Torres-Lapasio and co-workers[13] compared a number of models predicting the retention factor as a function of solvation parameters and mobile phase composition. They used a set of 146 organic compounds of diverse nature, eluted with methanol and acetonitrile as organic modifier, and concluded that the poor quality of the general solvation parameter models should be improved and tend to target the prediction quality of individual models. The main limitation of the Torres-Lapasio model is that it treats each solvent composition as a separate system and this may cause trouble in predicting the retention behavior by interpolation techniques.

In the previous studies,[14–16] the Jouyban-Acree models were developed to represent the retention factor of analytes in binary,[15] ternary[16] and quaternary[14] mobile phases as a function of the mobile phase compositions. Using this model, it is possible to optimize the concentration of organic modifier of the mobile phase for each analyte, however, the generated model is valid for only one analyte. The general form of the Jouyban-Acree model for representing the retention factor of analytes in a binary solvent mobile phase is:

$$\log k_m = f_1 \log k_1 + f_2 \log k_2 + f_1 f_2 \sum_{j=0}^{2} B_j(f_1 - f_2)^j \qquad (1)$$

where k is the retention factor of the analyte, f denotes the volume fraction of the solvent in the binary solvent mobile phase, subscripts m, 1 and 2 are the mixed solvent mobile phase, components 1 and 2, respectively, B_j is the model constant which represents various solvent–solvent and analyte–solvent interactions and is calculated by using a no intercept least square analysis for each analyte separately.[15] The model produced reasonably accurate predictions after training by a minimum number of experimental data points. The required retention data in mixed solvent mobile phases (even a minimum number of experimental data) to train the Jouyban-Acree model is a limitation for the model and any attempt to overcome this limitation could improve its practical applicability. The aim of this work is to provide a model to simulate the retention data of analytes in hydro-organic mobile phases using the Abraham solvation parameters of the analytes and the solvents. Using such models, one is able to predict the retention data of an analyte employing the computed chemical descriptors. The models could provide rational starting conditions considering the solvent composition of the mobile phase and save time and cost of method development.

2. Experimental

2.1. Experimental data

The details of the experimental data sets collected from the literature including names of analytes, organic modifiers, number of data points in each set, the references and the mean percentage deviations are listed in Table 1. All data were obtained using

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Table 1 Details of experimental data of analytes, the organic modifier, the references, the number of data points in each set (*NDP*) and the mean percentage deviation (*MPD*)

Analyte	Organic modifier	NDP	Reference	MPD[a]	MPD[b]	MPD[c]	MPD[d]
1-Bromo-2-nitrobenzene	Acetonitrile	4	1	18.0	10.2	18.2	22.1
1-Bromo-2-nitrobenzene	Methanol	4	1	38.7	38.9	24.3	25.9
1-Phenyl-1-propanol	Acetonitrile	6	5	13.9	21.9	15.3	15.4
1-Phenyl-1-propanol	Methanol	5	5	10.1	12.7	13.7	5.4
1-Phenyl-1-propene	Acetonitrile	6	5	13.2	15.0	16.1	33.2
1-Phenyl-1-propene	Methanol	5	5	16.4	18.5	15.5	25.8
1-Phenyl-2-butanone	Acetonitrile	6	3	18.9	17.1	16.0	17.5
1-Phenyl-2-butanone	Methanol	5	3	8.5	8.5	7.2	5.7
1,2-Dihydroxybenzene	Acetonitrile	6	6	21.6	39.9	24.8	50.0
1,2-Dihydroxybenzene	Methanol	5	6	6.2	15.1	20.9	38.3
1,2-Dimethylbenzene	Acetonitrile	6	6	9.2	5.5	7.3	19.6
1,2-Dimethylbenzene	Methanol	5	6	6.0	13.3	10.8	19.4
1,3-Dihydroxybenzene	Acetonitrile	6	6	23.2	41.7	24.0	52.2
1,3-Dihydroxybenzene	Methanol	3	6	3.8	—[e]	—[e]	—[e]
1,3-Dimethylbenzene	Acetonitrile	6	6	5.2	6.7	12.3	19.9
1,3-Dimethylbenzene	Methanol	5	6	13.0	19.6	16.8	23.5
1,4-Dihydroxybenzene	Acetonitrile	6	6	19.8	38.3	20.9	69.3
1,4-Dihydroxybenzene	Methanol	3	6	28.6	18.9	10.7	88.9
1,4-Dimethylbenzene	Acetonitrile	6	6	4.7	—[e]	—[e]	—[e]
1,4-Dimethylbenzene	Methanol	5	6	15.8	22.2	19.4	25.0
2-Aminophenol	Acetonitrile	6	6	30.2	47.6	30.6	50.3
2-Aminophenol	Methanol	5	6	21.4	10.3	8.7	46.5
2-Bromoaniline	Acetonitrile	4	1	11.9	18.7	12.4	20.2
2-Bromoaniline	Methanol	3	1	14.7	10.3	5.9	6.4
2-Bromophenol	Acetonitrile	6	6	65.0	—[f]	—[f]	—[f]
2-Bromophenol	Methanol	5	6	88.8	—[f]	—[f]	—[f]
2-Bromotoluene	Acetonitrile	6	6	9.8	5.9	9.8	23.0
2-Bromotoluene	Methanol	5	6	8.9	14.5	12.9	26.3
2-Chlorophenol	Acetonitrile	6	6	55.3	30.9	40.2	40.2
2-Chlorophenol	Methanol	5	6	75.4	—[f]	—[f]	—[f]
2-Chlorotoluene	Acetonitrile	6	6	13.3	7.2	7.5	22.3
2-Chlorotoluene	Methanol	5	6	5.3	13.9	11.2	24.6
2-Hydroxyacetophenone	Acetonitrile	6	6	34.5	27.2	29.6	22.7
2-Hydroxyacetophenone	Methanol	5	6	41.9	36.6	24.7	23.5
2-Hydroxybenzaldehyde	Acetonitrile	6	6	15.0	16.0	10.1	13.9
2-Hydroxybenzaldehyde	Methanol	5	6	80.5	—[f]	—[f]	—[f]
2-Hydroxybenzamide	Acetonitrile	6	6	16.0	15.4	15.3	34.0
2-Hydroxybenzamide	Methanol	5	6	23.2	24.1	17.2	27.9
2-Hydroxybenzonitrile	Acetonitrile	6	6	27.4	16.2	22.2	36.2
2-Hydroxybenzonitrile	Methanol	3	6	58.0	54.6	63.9	92.5
2-Methoxyphenol	Acetonitrile	6	6	42.3	20.3	33.8	39.3
2-Methoxyphenol	Methanol	5	6	93.8	—[f]	—[f]	—[f]
2-Methylacetophenone	Acetonitrile	6	6	7.3	6.8	4.1	2.5
2-Methylacetophenone	Methanol	5	6	15.7	18.8	14.3	10.2
2-Methylanisole	Acetonitrile	6	6	7.9	12.4	15.7	17.1
2-Methylanisole	Methanol	5	6	5.4	8.7	9.1	12.5
2-Methylphenol	Acetonitrile	6	6	34.9	16.7	24.3	24.2
2-Methylphenol	Methanol	5	6	38.8	29.2	30.6	29.2
2-Nitroaniline	Acetonitrile	4	1	4.4	—[e]	—[e]	—[e]
2-Nitroaniline	Methanol	3	1	14.9	11.7	3.8	8.4
2-Nitrotoluene	Acetonitrile	6	6	16.3	13.9	11.4	14.7
2-Nitrotoluene	Methanol	5	6	17.4	10.2	5.8	4.5
2-Phenyl-2-propanol	Acetonitrile	6	5	34.2	45.7	39.2	33.2
2-Phenyl-2-propanol	Methanol	5	5	21.8	30.4	31.6	24.7
2-Phenylethanol	Acetonitrile	6	3	21.4	14.5	18.9	38.2
2-Phenylethanol	Methanol	5	3	6.2	5.0	8.2	17.0
2-Phenylethyl bromide	Acetonitrile	6	3	10.3	11.0	11.3	24.3
2-Phenylethyl bromide	Methanol	5	3	16.1	14.8	12.7	27.5
2-Phenylethyl chloride	Acetonitrile	6	3	7.7	5.0	3.6	24.1
2-Phenylethyl chloride	Methanol	5	3	4.4	—[e]	—[e]	—[e]
2-Phenylphenol	Acetonitrile	6	6	25.9	15.4	9.6	24.4
2-Phenylphenol	Methanol	5	6	29.3	11.7	7.6	22.3
2-Phenyltoluene	Acetonitrile	5	6	8.4	37.2	19.6	63.8
2-Phenyltoluene	Methanol	4	6	16.4	20.2	23.2	64.6
2-Tolualdehyde	Acetonitrile	6	6	16.8	10.9	8.3	7.4
2-Tolualdehyde	Methanol	5	6	39.0	27.9	16.3	14.2
2-Toluamide	Acetonitrile	6	6	16.1	18.6	10.1	39.6
2-Toluamide	Methanol	5	6	23.7	19.5	24.7	31.5
2-Toluidine	Acetonitrile	6	6	13.5	27.6	13.8	19.2
2-Toluidine	Methanol	5	6	36.9	24.6	9.5	24.9

Table 1 (*Contd.*)

Analyte	Organic modifier	NDP	Reference	MPD^a	MPD^b	MPD^c	MPD^d
2-Tolunitrile	Acetonitrile	6	6	34.4	26.1	21.4	20.0
2-Tolunitrile	Methanol	5	6	46.4	35.5	29.8	27.6
2,4-Dimethylphenol	Acetonitrile	4	1	19.8	27.6	15.7	11.0
2,4-Dimethylphenol	Methanol	4	1	12.6	16.2	18.9	14.6
2,5-Dimethylphenol	Acetonitrile	4	1	13.6	21.8	9.3	8.9
2,5-Dimethylphenol	Methanol	3	1	17.6	22.0	25.4	20.8
2,6-Dimethyl-4-nitrophenol	Acetonitrile	4	1	29.7	65.4	31.3	33.5
2,6-Dimethyl-4-nitrophenol	Methanol	3	1	64.5	114.0	129.8	139.3
3-Aminophenol	Acetonitrile	6	6	25.4	44.7	23.5	49.2
3-Aminophenol	Methanol	3	6	55.3	37.2	6.5	86.6
3-Bromoaniline	Acetonitrile	4	1	5.6	12.8	6.3	13.6
3-Bromoaniline	Methanol	3	1	19.2	16.0	9.6	4.7
3-Bromophenol	Acetonitrile	6	6	11.4	7.5	7.9	5.4
3-Bromophenol	Methanol	5	6	13.1	15.3	10.1	11.5
3-Bromotoluene	Acetonitrile	6	6	5.9	4.1	8.7	23.9
3-Bromotoluene	Methanol	5	6	16.1	21.1	19.4	29.7
3-Chlorophenol	Acetonitrile	6	6	14.5	8.9	6.2	8.7
3-Chlorophenol	Methanol	5	6	7.1	12.0	6.5	6.8
3-Chlorotoluene	Acetonitrile	6	6	10.6	6.5	7.6	22.9
3-Chlorotoluene	Methanol	4	6	8.2	16.6	14.2	20.1
3-Hydroxyacetophenone	Acetonitrile	6	6	11.4	13.1	13.4	28.8
3-Hydroxyacetophenone	Methanol	5	6	11.3	8.2	5.9	25.9
3-Hydroxybenzaldehyde	Acetonitrile	5	6	5.1	—^{e}	—^{e}	—^{e}
3-Hydroxybenzaldehyde	Methanol	5	6	4.7	—^{e}	—^{e}	—^{e}
3-Hydroxybenzonitrile	Acetonitrile	6	6	12.1	15.3	16.0	22.6
3-Hydroxybenzonitrile	Methanol	5	6	20.1	20.6	13.7	18.2
3-Methoxyphenol	Acetonitrile	6	6	22.5	12.2	17.8	25.9
3-Methoxyphenol	Methanol	5	6	29.7	27.0	29.2	34.5
3-Methylacetophenone	Acetonitrile	6	6	9.7	8.8	7.5	4.4
3-Methylacetophenone	Methanol	5	6	16.5	19.3	14.3	10.8
3-Methylanisole	Acetonitrile	6	6	7.0	4.4	4.7	13.3
3-Methylanisole	Methanol	5	6	6.7	6.0	6.9	4.9
3-Methylphenol	Acetonitrile	6	6	33.1	18.9	23.5	21.6
3-Methylphenol	Methanol	5	6	19.6	12.0	13.2	16.4
3-Nitroaniline	Acetonitrile	4	1	20.3	25.3	19.5	31.5
3-Nitroaniline	Methanol	3	1	11.3	12.2	19.1	26.1
3-Nitrobenzyl alcohol	Acetonitrile	4	1	15.6	16.3	10.7	30.2
3-Nitrobenzyl alcohol	Methanol	3	1	14.0	13.8	15.6	32.4
3-Nitrophenol	Acetonitrile	6	6	16.0	18.1	18.0	20.0
3-Nitrophenol	Methanol	5	6	26.0	25.1	20.6	18.5
3-Nitrotoluene	Acetonitrile	6	6	14.2	12.7	9.2	15.7
3-Nitrotoluene	Methanol	4	6	7.6	4.9	4.3	3.8
3-Phenyl-1-propanol	Acetonitrile	6	5	22.5	31.8	26.1	20.9
3-Phenyl-1-propanol	Methanol	5	5	9.6	12.0	12.4	5.4
3-Phenyl-1-propene	Acetonitrile	6	5	10.9	12.1	16.8	31.2
3-Phenyl-1-propene	Methanol	5	5	10.3	14.0	7.2	23.7
3-Phenyl-1-propionamide	Acetonitrile	6	3	22.9	16.3	14.9	32.9
3-Phenyl-1-propionamide	Methanol	5	3	52.9	50.8	45.4	44.5
3-Phenyl-1-propionitrile	Acetonitrile	6	3	7.8	11.7	7.4	10.0
3-Phenyl-1-propionitrile	Methanol	5	3	21.6	12.5	19.4	18.1
3-Phenyl-1-propyl bromide	Acetonitrile	5	3	16.3	10.2	14.9	25.1
3-Phenyl-1-propyl bromide	Methanol	5	3	33.9	26.6	20.1	37.2
3-Phenyl-1-propyl chloride	Acetonitrile	6	3	7.4	4.8	9.4	33.7
3-Phenyl-1-propyl chloride	Methanol	5	3	26.6	23.2	9.6	34.3
3-Phenylphenol	Acetonitrile	6	6	13.1	14.7	10.8	24.3
3-Phenylphenol	Methanol	5	6	26.8	9.7	6.0	24.2
3-Phenyltoluene	Acetonitrile	5	6	4.3	—^{e}	—^{e}	—^{e}
3-Phenyltoluene	Methanol	4	6	25.5	15.1	6.5	50.1
3-Tolualdehyde	Acetonitrile	6	6	10.4	14.6	9.3	8.5
3-Tolualdehyde	Methanol	5	6	25.7	15.7	6.9	7.1
3-Toluamide	Acetonitrile	6	6	10.0	8.2	10.2	38.2
3-Toluamide	Methanol	5	6	21.8	17.7	21.3	21.7
3-Toluidine	Acetonitrile	6	6	7.3	20.8	7.9	18.2
3-Toluidine	Methanol	5	6	42.0	29.4	12.7	25.2
3-Tolunitrile	Acetonitrile	6	6	10.4	5.6	3.1	2.7
3-Tolunitrile	Methanol	5	6	23.9	14.5	9.1	7.6
4-Aminophenol	Acetonitrile	6	6	14.6	37.4	12.1	63.7
4-Aminophenol	Methanol	3	6	70.2	—^{f}	—^{f}	—^{f}
4-Bromophenol	Acetonitrile	6	6	5.1	5.3	2.9	4.2
4-Bromophenol	Methanol	5	6	17.6	20.2	16.1	18.7

Table 1 (*Contd.*)

Analyte	Organic modifier	NDP	Reference	MPD^a	MPD^b	MPD^c	MPD^d
4-Bromotoluene	Acetonitrile	6	6	6.3	4.3	8.5	24.1
4-Bromotoluene	Methanol	5	6	14.6	19.7	17.6	28.9
4-Chlorophenol	Acetonitrile	6	6	7.9	7.1	4.5	5.6
4-Chlorophenol	Methanol	5	6	14.4	19.7	15.5	16.5
4-Chlorotoluene	Acetonitrile	6	6	7.9	6.5	9.1	22.8
4-Chlorotoluene	Methanol	5	6	13.6	21.2	17.4	26.3
4-Hydroxyacetophenone	Acetonitrile	6	6	10.7	10.2	14.2	43.4
4-Hydroxyacetophenone	Methanol	5	6	6.4	5.0	4.6	23.4
4-Hydroxybenzaldehyde	Acetonitrile	5	6	6.5	6.6	4.9	37.9
4-Hydroxybenzaldehyde	Methanol	3	6	32.9	31.8	36.0	68.0
4-Hydroxybenzonitrile	Acetonitrile	6	6	7.0	10.1	10.2	27.7
4-Hydroxybenzonitrile	Methanol	4	6	9.2	7.9	6.2	14.2
4-Methoxyphenol	Acetonitrile	6	6	15.3	5.9	12.0	30.3
4-Methoxyphenol	Methanol	5	6	30.3	26.8	23.8	39.0
4-Methylacetophenone	Acetonitrile	6	6	11.0	9.2	9.5	5.7
4-Methylacetophenone	Methanol	5	6	17.8	20.6	14.4	10.5
4-Methylphenol	Acetonitrile	6	6	44.2	29.1	33.4	30.8
4-Methylphenol	Methanol	5	6	27.5	19.4	22.0	21.4
4-Nitrobenzyl alcohol	Acetonitrile	4	1	8.2	8.6	6.0	26.7
4-Nitrobenzyl alcohol	Methanol	3	1	9.0	8.3	10.5	27.0
4-Nitrophenol	Acetonitrile	6	6	16.8	14.7	12.1	19.8
4-Nitrophenol	Methanol	4	6	27.5	27.5	24.8	14.7
4-Nitrotoluene	Acetonitrile	6	6	10.6	8.5	6.1	10.9
4-Nitrotoluene	Methanol	5	6	5.5	6.6	5.5	7.3
4-Phenyl-1-butanol	Acetonitrile	4	1	8.3	27.9	13.6	11.8
4-Phenyl-1-butanol	Methanol	3	1	15.1	10.1	13.9	9.9
4-Phenyl-1-butyronitrile	Acetonitrile	6	3	11.0	8.8	8.4	11.5
4-Phenyl-1-butyronitrile	Methanol	5	3	8.6	9.1	8.7	11.0
4-Phenyl-2-butanone	Acetonitrile	6	3	15.5	14.1	8.7	9.3
4-Phenyl-2-butanone	Methanol	5	3	6.2	5.4	14.5	9.9
4-Phenylphenol	Acetonitrile	6	6	16.3	10.8	7.3	20.2
4-Phenylphenol	Methanol	5	6	30.3	10.6	6.0	20.7
4-Phenyltoluene	Acetonitrile	5	6	10.4	14.2	6.8	49.2
4-Phenyltoluene	Methanol	4	6	32.0	15.9	10.0	52.6
4-Tolualdehyde	Acetonitrile	4	6	12.4	15.0	6.6	6.5
4-Tolualdehyde	Methanol	3	6	19.2	26.0	12.7	12.1
4-Toluamide	Acetonitrile	6	6	10.5	12.5	7.6	32.2
4-Toluamide	Methanol	5	6	37.3	21.2	25.1	23.3
4-Toluidine	Acetonitrile	6	6	11.9	14.5	3.1	18.8
4-Toluidine	Methanol	5	6	25.0	33.4	18.1	25.3
4-Tolunitrile	Acetonitrile	6	6	5.9	6.7	4.0	3.2
4-Tolunitrile	Methanol	5	6	46.2	11.4	7.0	5.3
4-*t*-Butylphenol	Acetonitrile	6	1	12.9	48.5	11.9	25.2
4-*t*-Butylphenol	Methanol	5	1	20.4	10.1	11.2	34.3
5-Phenyl-1-pentanol	Acetonitrile	4	1	14.6	44.1	16.7	17.9
5-Phenyl-1-pentanol	Methanol	3	1	74.2	—^{f}	—^{f}	—^{f}
Acetophenone	Acetonitrile	7	2	32.5	16.1	22.7	24.7
Acetophenone	Methanol	6	2	38.5	37.0	17.4	19.5
α-4-Dibromoacetophenone	Acetonitrile	4	1	12.2	8.2	10.7	9.8
α-4-Dibromoacetophenone	Methanol	4	1	19.2	16.5	13.1	14.7
Aniline	Acetonitrile	7	2	7.7	20.1	10.9	32.8
Aniline	Methanol	6	2	62.0	47.0	17.9	45.0
Anisole	Acetonitrile	6	2	20.1	8.7	3.5	4.3
Anisole	Methanol	5	2	39.2	26.8	12.3	12.5
Benzaldehyde	Acetonitrile	6	2	22.4	10.4	6.6	15.3
Benzaldehyde	Methanol	5	2	59.2	41.4	13.8	25.5
Benzamide	Acetonitrile	7	2	14.3	20.8	13.5	50.6
Benzamide	Methanol	6	2	23.2	23.5	35.0	41.4
Benzene	Acetonitrile	7	2	30.5	18.3	2.8	11.1
Benzene	Methanol	6	2	44.0	24.0	5.9	11.7
Benzonitrile	Acetonitrile	7	2	15.7	12.0	4.5	14.0
Benzonitrile	Methanol	6	2	35.9	24.0	8.9	18.6
Benzyl acetate	Acetonitrile	5	6	17.8	17.8	16.5	18.7
Benzyl acetate	Methanol	5	6	12.8	12.7	13.2	15.5
Benzyl alcohol	Acetonitrile	7	2	24.7	14.6	14.3	47.1
Benzyl alcohol	Methanol	6	2	26.2	21.7	10.4	35.8
Benzylbromide	Acetonitrile	7	2	15.0	9.4	10.9	22.5
Benzylbromide	Methanol	6	2	22.6	30.4	14.5	25.7
Benzylchloride	Acetonitrile	7	2	14.6	26.6	21.0	26.7
Benzylchloride	Methanol	6	2	6.3	15.5	19.1	23.2

Table 1 (*Contd.*)

Analyte	Organic modifier	NDP	Reference	MPD[a]	MPD[b]	MPD[c]	MPD[d]
Benzylcyanide	Acetonitrile	7	2	12.8	7.7	5.0	9.0
Benzylcyanide	Methanol	6	2	60.0	58.6	36.1	32.9
Biphenyl	Acetonitrile	6	2	6.3	6.9	7.3	42.4
Biphenyl	Methanol	5	2	14.7	9.5	7.7	39.4
Bromobenzene	Acetonitrile	7	2	18.5	14.5	7.5	21.3
Bromobenzene	Methanol	6	2	15.3	8.3	11.0	18.3
Butyrophenone	Acetonitrile	7	2	9.5	17.6	9.8	19.5
Butyrophenone	Methanol	6	2	8.4	29.1	18.6	31.8
Chlorobenzene	Acetonitrile	7	2	25.7	13.9	5.1	21.3
Chlorobenzene	Methanol	6	2	21.7	10.9	6.7	14.0
Dimethyl phthalate	Acetonitrile	4	1	7.3	7.0	1.9	13.5
Dimethyl phthalate	Methanol	3	1	6.1	13.8	19.2	12.9
Ethyl-3-phenylpropionate	Acetonitrile	5	1	16.0	11.1	16.4	18.1
Ethyl-3-phenylpropionate	Methanol	3	1	35.1	20.9	13.8	9.7
Ethyl benzoate	Acetonitrile	4	1	7.9	7.2	9.9	10.0
Ethyl benzoate	Methanol	4	1	2.8	—[e]	—[e]	—[e]
Ethylphenylacetate	Acetonitrile	4	1	18.3	32.8	17.5	25.0
Ethylphenylacetate	Methanol	4	1	18.6	30.8	41.6	44.9
Ethylbenzene	Acetonitrile	6	3	3.2	—[e]	—[e]	—[e]
Ethylbenzene	Methanol	5	3	6.4	14.8	10.0	21.4
Heptanophenone	Acetonitrile	7	2	20.9	29.5	12.1	62.5
Heptanophenone	Methanol	6	2	43.4	67.5	6.8	102.5
Hexanophenone	Acetonitrile	7	2	13.2	25.6	4.9	48.3
Hexanophenone	Methanol	6	2	32.1	52.8	4.1	75.8
Isobutylbenzene	Acetonitrile	6	5	18.4	14.2	23.7	37.6
Isobutylbenzene	Methanol	4	5	33.7	30.5	15.1	44.6
Isopropylbenzene	Acetonitrile	6	5	47.8	49.4	33.8	42.4
Isopropylbenzene	Methanol	5	5	14.3	16.4	6.6	32.1
Methyl-2-hydroxybenzoate	Acetonitrile	6	6	16.1	11.0	13.3	8.1
Methyl-2-hydroxybenzoate	Methanol	5	6	5.2	7.8	5.4	5.9
Methyl-2-Methylbenzoate	Acetonitrile	6	6	26.6	31.4	23.7	26.9
Methyl-2-Methylbenzoate	Methanol	5	6	14.5	22.1	24.5	21.5
Methyl-3-hydroxybenzoate	Acetonitrile	6	6	10.5	14.6	13.5	22.4
Methyl-3-hydroxybenzoate	Methanol	5	6	16.1	7.7	6.0	10.5
Methyl-3-Methylbenzoate	Acetonitrile	6	6	13.9	14.7	8.8	13.8
Methyl-3-Methylbenzoate	Methanol	5	6	9.2	5.1	3.5	14.1
Methyl-3-phenylpropionate	Acetonitrile	6	3	13.8	8.5	11.7	14.6
Methyl-3-phenylpropionate	Methanol	5	3	30.5	29.2	14.2	16.8
Methyl-4-hydroxybenzoate	Acetonitrile	6	6	19.5	24.5	23.5	31.5
Methyl-4-hydroxybenzoate	Methanol	5	6	13.0	8.5	17.0	14.5
Methyl-4-methylbenzoate	Acetonitrile	6	6	13.6	14.5	8.2	13.2
Methyl-4-methylbenzoate	Methanol	5	6	10.3	6.2	3.5	14.0
Methyl-4-phenylbutyrate	Acetonitrile	6	3	18.0	9.5	12.0	17.6
Methyl-4-phenylbutyrate	Methanol	5	3	43.9	38.3	16.9	25.8
Methylphenylacetate	Acetonitrile	7	3	18.3	5.8	3.9	6.5
Methylphenylacetate	Methanol	6	3	16.0	8.7	14.0	4.9
Methylbenzoate	Acetonitrile	6	2	5.6	19.8	7.8	14.1
Methylbenzoate	Methanol	5	2	4.7	—[e]	—[e]	—[e]
n-Butylbenzene	Acetonitrile	6	3	22.2	15.5	26.8	37.2
n-Butylbenzene	Methanol	5	3	43.5	40.1	23.7	48.0
N-Ethylaniline	Acetonitrile	4	1	15.6	19.3	15.0	20.9
N-Ethylaniline	Methanol	4	1	24.5	23.0	16.8	16.6
N-Methylbenzamide	Acetonitrile	5	1	12.8	12.8	8.2	33.7
N-Methylbenzamide	Methanol	5	1	8.7	8.6	12.3	32.6
n-Propylbenzene	Acetonitrile	3	5	20.4	10.4	19.9	29.0
n-Propylbenzene	Methanol	5	5	34.8	27.8	15.4	35.6
n-Propyl-4-hydroxybenzoate	Acetonitrile	6	1	11.1	73.7	28.7	23.4
n-Propyl-4-hydroxybenzoate	Methanol	5	1	26.1	10.5	11.1	25.5
N,N-Dimethylbenzamide	Acetonitrile	5	1	12.4	15.1	3.9	30.9
N,N-Dimethylbenzamide	Methanol	5	1	12.1	12.5	20.5	23.1
Nitrobenzene	Acetonitrile	7	2	14.1	11.1	3.5	9.2
Nitrobenzene	Methanol	6	2	22.1	10.7	9.3	15.2
Phenacyl bromide	Acetonitrile	4	1	10.1	9.2	6.5	5.9
Phenacyl bromide	Methanol	4	1	30.7	37.1	28.6	28.4
Phenol	Acetonitrile	7	2	18.1	6.3	9.9	25.9
Phenol	Methanol	6	2	33.3	21.4	12.2	34.3
Phenylacetaldehyde	Acetonitrile	6	3	17.9	12.1	9.5	20.1
Phenylacetaldehyde	Methanol	5	3	93.0	—[e]	—[e]	—[e]
Phenylacetamide	Acetonitrile	6	3	12.9	14.5	8.8	46.5
Phenylacetamide	Methanol	5	3	22.7	25.7	29.6	33.2

Table 1   (*Contd.*)

Analyte	Organic modifier	NDP	Reference	MPD[a]	MPD[b]	MPD[c]	MPD[d]
Propiophenone	Acetonitrile	7	2	16.4	10.8	12.9	10.8
Propiophenone	Methanol	6	2	18.2	29.6	16.1	13.3
s-Butylbenzene	Acetonitrile	6	5	14.1	12.8	17.5	39.6
s-Butylbenzene	Methanol	4	5	24.4	20.8	6.5	44.0
t-Butylbenzene	Acetonitrile	6	5	93.1	—[f]	—[f]	—[f]
t-Butylbenzene	Methanol	4	5	92.7	—[f]	—[f]	—[f]
Thymol	Acetonitrile	5	1	7.2	28.5	5.1	14.9
Thymol	Methanol	5	1	26.8	17.5	18.2	32.0
Toluene	Acetonitrile	7	2	14.1	18.5	8.8	16.6
Toluene	Methanol	6	2	16.3	5.1	9.2	8.9
Valerophenone	Acetonitrile	7	2	9.3	26.3	8.7	36.4
Valerophenone	Methanol	6	2	15.7	33.7	16.9	56.5

[a] The *MPDs* calculated for back-calculated data sets using eqn (7). [b] The *MPDs* calculated for predicted data sets using the trained eqn (4) by experimental data of five references and one reference left out method. [c] The *MPDs* calculated for predicted data sets using eqn (8) or (9). [d] The *MPDs* calculated for predicted data sets using eqn (10) or (11). [e] The excluded data sets with the lowest *MPD*. [f] The excluded data sets with the highest *MPD*. [g] All data were obtained using a 100 × 5 mm I.D., column packed with Spherisorb ODS 5-μm.

Table 2   The Abraham solvent coefficients used in this work taken from a ref.[17]

Solvent	c	e	s	a	b	v
Acetonitrile	0.413	0.077	0.326	−1.566	−4.391	3.364
Methanol	0.329	0.299	−0.671	0.08	−3.389	3.512
Water	−0.994	0.577	2.549	3.813	4.841	−0.869

a 100 × 5 mm I.D., column packed with Spherisorb ODS 5-μm. The Abraham solvent coefficients of water, acetonitrile and methanol are listed in Table 2. The Abraham solvation parameters of the analytes are reported in Table 3. In addition to the experimentally derived solvation parameters, descriptors can be computed using Pharma-Algorithms web-based software,[19] this makes predictive procedures presented in this study more feasible.

2.2.   Computational methods

As noted above, the B_j constants are functions of an analyte's physico-chemical properties and the separation system under investigation. Analytes interact with the stationary and mobile phases through various dipole–dipole and hydrogen-bonding interactions. These interactions can be mathematically described using the Abraham solvation model. The basic model for solute transfer between two condensed phases is:

$$log k = c + eE + sS + aA + bB + vV \qquad (2)$$

where k is the retention factor, E is the excess molar refraction, S is dipolarity/polarizability of solute, A denotes the solute's hydrogen-bond acidity, B stands for the solute's hydrogen-bond basicity and V is the McGowan volume of the solute. In eqn (2) the coefficients c, e, s, a, b and v are the model constants (*i.e.* solvent's coefficients), which depend upon the solvent system under consideration. Numerical values of these coefficients have been reported for several water-to-organic solvent partition systems.[17] Eqn (2) was used for representing the retention factor of analytes in RPLC with a given solvent composition (monosolvents or mixed solvents) as:

$$log k = c' + e'E + s'S + a'A + b'B + v'V \qquad (3)$$

in which the regressed parameters (*i.e.* c', e', s', a', b' and v') refer to the differences of stationary and mobile phases, e' refer to the capability of interacting with analyte π and n-electron pairs, s' dipolarity/polarizability, a' hydrogen-bond basicity (an acidic analyte interacts with basic phase), b' hydrogen-bond acidity and v' hydrophobicity.[12]

The model constants of the Jouyban-Acree model could be correlated with the Abraham solvation parameters (of analytes and solvents) for building a generally trained version of the Jouyban-Acree model for predicting the retention factor of analytes in mixed solvent mobile phases. There are 2 kinds of model constants:

1) α_i and β_i, which denote the differences in the mobile phases (containing pure solvents) and solvated stationary phase capabilities to interact with the analyte, the larger the coefficient resulted from the linear regression, the larger the difference between the mobile and stationary phases with respect to the particular interactions. Also one can consider the first line of eqn (4) as modifier selector part of the model and the second line as solute behavior in pure aqueous mobile phase.

2) W_i, W_i and W_i' constants arising from the nature of the analytes and mobile phases of the analytical systems under investigation which is our main hypothesis. Another independent variable affecting these constants could be the nature of the solvated stationary phase, however we considered this variable as a constant since all data were collected using a single stationary phase. Therefore, the Jouyban-Acree model could be represented as eqn (4) in which α, β and W terms are the model constants. The numerical values of these terms could be computed by regressing $log k_m$ against f_1c_1, f_1e_1E, f_1s_1S, f_1a_1A, f_1b_1B, f_1v_1V, f_2c_2, f_2e_2E, f_2s_2S, f_2a_2A, f_2b_2B, f_2v_2V, f_1f_2, $f_1f_2(c_1-c_2)^2$, $f_1f_2E(e_1-e_2)^2$, $f_1f_2S(s_1-s_2)^2$, $f_1f_2A(a_1-a_2)^2$, $f_1f_2B(b_1-b_2)^2$, $f_1f_2V(v_1-v_2)^2$, $f_1f_2(f_1-f_2)$, $f_1f_2(f_1-f_2)[(c_1-c_2)^2]$, $f_1f_2(f_1-f_2)[E(e_1-e_2)^2]$, $f_1f_2(f_1-f_2)[S(s_1-s_2)^2]$, $f_1f_2(f_1-f_2)[A(a_1-a_2)^2]$, $f_1f_2(f_1-f_2)[B(b_1-b_2)^2]$, $f_1f_2(f_1-f_2)[V(v_1-v_2)^2]$, $f_1f_2(f_1-f_2)^2$, $f_1f_2(f_1-f_2)^2[(c_1-c_2)^2]$, $f_1f_2(f_1-f_2)^2[E(e_1-e_2)^2]$, $f_1f_2(f_1-f_2)^2[S(s_1-s_2)^2]$, $f_1f_2(f_1-f_2)^2[A(a_1-a_2)^2]$, $f_1f_2(f_1-f_2)^2[B(b_1-b_2)^2]$ and $f_1f_2(f_1-f_2)^2[V(v_1-v_2)^2]$, using a no intercept least square analysis. It should be noted that the Abraham solvent coefficients

$$\begin{aligned}
\log k_m = & f_1\{\alpha_0 c_1 + \alpha_1 e_1 E + \alpha_2 s_1 S + \alpha_3 a_1 A + \alpha_4 b_1 B + \alpha_5 v_1 V\} \\
& + f_2\{\beta_0 c_2 + \beta_1 e_2 E + \beta_2 s_2 S + \beta_3 a_2 A + \beta_4 b_2 B + \beta_5 v_2 V\} \\
& + f_1 f_2 \left\{ \begin{array}{l} W_1 + W_2[(c_1-c_2)^2] + W_3[E(e_1-e_2)^2] + W_4[S(s_1-s_2)^2] \\ + W_5[A(a_1-a_2)^2] + W_6[B(b_1-b_2)^2] + W_7[V(v_1-v_2)^2] \end{array} \right\} \\
& + f_1 f_2 (f_1 - f_2) \left\{ \begin{array}{l} W_1' + W_2'[(c_1-c_2)^2] + W_3'[E(e_1-e_2)^2] + W_4'[S(s_1-s_2)^2] \\ + W_5'[A(a_1-a_2)^2] + W_6'[B(b_1-b_2)^2] + W_7'[V(v_1-v_2)^2] \end{array} \right\} \\
& + f_1 f_2 (f_1 - f_2)^2 \left\{ \begin{array}{l} W_1'' + W_2''[(c_1-c_2)^2] + W_3''[E(e_1-e_2)^2] + W_4''[S(s_1-s_2)^2] \\ + W_5''[A(a_1-a_2)^2] + W_6''[B(b_1-b_2)^2] + W_7''[V(v_1-v_2)^2] \end{array} \right\}
\end{aligned} \tag{4}$$

used in our computations were taken from regression analysis of solubility data and infinite dilution activity coefficient data. The solvent coefficients represent only the mobile phase properties and no experimental chromatographic data are needed to compute these coefficients.

The predictive ability of the model was assessed in terms of the mean percentage deviation (MPD) of observed ($(k_m)_{obs.}$) and calculated ($(k_m)_{cal.}$) retention factors, defined by:

$$MPD = \frac{100}{NDP} \sum \frac{|(k_m)_{cal.} - (k_m)_{obs.}|}{(k_m)_{obs.}} \tag{5}$$

where NDP is the number of data points. In addition, we also calculated the individual percentage deviation (IPD):

$$IPD = 100 \left\{ \frac{|(k_m)_{cal.} - (k_m)_{obs.}|}{(k_m)_{obs.}} \right\} \tag{6}$$

for each retention factor data point.

3. Results and discussion

The available experimental k_m values collected from the literature were fitted to the proposed model and the constants with probability of < 0.05 were included in the model (eqn (7)).

This correlation was significant at $p < 0.0005$, the F value of 1407 and the number of data points (NDP) fitted to the model was 1539. Solutes studied included both polar and nonpolar aromatic compounds, as well as aromatic compounds capable of hydrogen-bond formation. The solute descriptor range defined by the compounds studied would be: $E = 0.58$–1.55, $S = 0.47$–1.72, $A = 0.00$–1.16, $B = 0.07$–0.98 and $V = 0.83$–1.72.

The back-calculated k_m values were used to compute the $MPDs$ and standard deviation values for the studied datasets. The details of the values were listed in Table 1 (see column 5). The overall MPD ($\pm SD$) was 20.9 (± 16.7) % and the number of data sets (NDS) was 292. When these values were analyzed

considering a given organic modifier, the values were 16.5 ($\pm$ 11.7) % and 25.3 ($\pm$ 19.7) %, respectively for acetonitrile and methanol. Careful examination of the results revealed that a number of data sets produced very large MPD values and appeared to be possible outliers. We excluded the 10 data sets having the largest $MPDs$ from the computations and in order to avoid any bias, the 10 data sets with the least $MPDs$ were also excluded. The obtained overall $MPDs$ for the back-calculated data using eqn (7) for remaining data sets was 19.2 ($\pm$ 11.9) % ($NDS = 272$). The corresponding values for acetonitrile and methanol were 16.1 ($\pm$ 8.8) % ($NDS = 139$) and 22.6 ($\pm$ 13.6) % ($NDS = 133$), respectively. These MPD values are relatively high when compared with the corresponding values of the trained versions of the model for each analyte (8.1%) reported in a previous work.[15] However, considering the proposed *ab initio* prediction method (without employing any experimental retention data of an analyte), the accuracy of the predictions could be considered acceptable. As it is evident from eqn (4) or (7), there is not an independent variable representing the properties of the stationary phases. Therefore, the model constants should be computed when other types of stationary phases are considered in the computations. As a more evident, eqn (4) was fitted to the k_m data of a number of analytes measured on five different stationary phases with aqueous mobile phases containing acetonitrile and methanol as organic modifiers.[8] The obtained overall $MPDs$ for these stationary phases were 26.1 ($\pm$ 21.2) %, 20.6 ($\pm$ 17.6) %, 29.1 ($\pm$ 22.2) %, 20.3 ($\pm$ 18.4) % and 18.4 ($\pm$ 16.7) %, respectively for LiChrospher 100 RP-18e, LiChrospher 100 RP-8, Purospher RP-18e, SymmetryShield RP-C$_{18}$ and SymmeteryShield RP-C$_8$ columns. Careful examination of these $MPDs$ revealed that the proposed model could provide acceptable calculations for other types of stationary phases as the average of overall $MPDs$ of these columns was 22.9%.

Fig. (1) shows the relative frequency of $IPDs$ of the calculated k_m data listed in Table 1, sorted into four subgroups,

$$\begin{aligned}
\log k_m = & f_1\{ -5.308 c_1 - 0.264 a_1 A + 0.254 v_1 V\} \\
& + f_2\{ -2.136 c_2 + 2.340 e_2 E - 0.210 s_2 S - 0.365 a_2 A - 0.791 b_2 B + 1.889 v_2 V\} \\
& + f_1 f_2 \left\{ \begin{array}{l} -8.049[E(e_1-e_2)^2] - 0.180[S(s_1-s_2)^2] \\ +0.027[B(b_1-b_2)^2] + 0.392[V(v_1-v_2)^2] \end{array} \right\} \\
& + f_1 f_2 (f_1 - f_2) \left\{ \begin{array}{l} 6.910 + 7.027[E(e_1-e_2)^2] - 0.079[A(a_1-a_2)^2] \\ -0.035[B(b_1-b_2)^2] - 0.632[V(v_1-v_2)^2] \end{array} \right\} \\
& + f_1 f_2 (f_1 - f_2)^2 \left\{ \begin{array}{l} -19.428 + 13.237[(c_1-c_2)^2] - 0.208[S(s_1-s_2)^2] \\ -0.126[A(a_1-a_2)^2] + 0.239[V(v_1-v_2)^2] \end{array} \right\}
\end{aligned} \tag{7}$$

Table 3 The Abraham solute parameters of the analytes investigated in this work taken from a ref.[18]

Analyte	E	S	A	B	V
1-Bromo-2-nitrobenzene	1.18	1.32	0.00	0.26	1.07
1-Phenyl-1-propanol	0.78	0.83	0.30	0.66	1.20
1-Phenyl-1-propene	0.91	0.72	0.00	0.18	1.10
1-Phenyl-2-butanone	0.75	1.14	0.00	0.66	1.30
1,2-Dihydroxybenze	0.97	1.07	0.85	0.52	0.83
1,2-Dimethylbenzene	0.66	0.56	0.00	0.16	1.00
1,3-Dihydroxybenze	0.98	1.00	1.10	0.58	0.83
1,3-Dimethylbenzene	0.62	0.52	0.00	0.16	1.00
1,4-Dihydroxybenzene	1.00	1.00	1.16	0.60	0.83
1,4-Dimethylbenzene	0.61	0.52	0.00	0.16	1.00
2-Aminophenol	1.11	1.10	0.60	0.66	0.88
2-Bromoaniline	1.07	0.98	0.31	0.39	0.99
2-Bromophenol	1.04	0.90	0.35	0.31	0.95
2-Bromotoluene	0.92	0.72	0.00	0.09	1.03
2-Chlorophenol	0.85	0.88	0.32	0.31	0.90
2-Chlorotoluene	0.76	0.65	0.00	0.07	0.98
2-Hydroxyacetophenone	0.95	1.14	0.00	0.42	1.07
2-Hydroxybenzaldehyde	0.96	1.15	0.11	0.31	0.93
2-Hydroxybenzamide	1.14	1.50	0.59	0.53	1.03
2-Hydroxybenzonitrile	0.92	1.33	0.78	0.34	0.93
2-Methoxyphenol	0.84	0.91	0.22	0.52	0.98
2-Methylacetophenone	0.78	1.00	0.00	0.51	1.16
2-Methylanisole	0.73	0.75	0.00	0.30	1.06
2-Methylphenol	0.84	0.86	0.52	0.30	0.92
2-Nitroaniline	1.18	1.37	0.30	0.36	0.99
2-Nitrotoluene	0.87	1.11	0.00	0.28	1.03
2-Phenyl-2-propanol	0.85	0.85	0.32	0.65	1.20
2-Phenylethanol	0.81	0.91	0.30	0.64	1.06
2-Phenylethyl bromide	0.97	0.94	0.00	0.30	1.17
2-Phenylethyl chloride	0.80	0.90	0.00	0.25	1.12
2-Phenylphenol	1.55	1.40	0.56	0.49	1.38
2-Phenyltoluene	1.33	0.88	0.00	0.26	1.47
2-Tolualdehyde	0.87	0.96	0.00	0.40	1.01
2-Toluamide	0.95	1.50	0.50	0.72	1.11
2-Toluidine	0.97	0.92	0.23	0.59	0.96
2-Tolunitrile	0.78	1.06	0.00	0.31	1.01
2,4-Dimethylphenol	0.84	0.80	0.53	0.39	1.06
2,5-Dimethylphenol	0.84	0.79	0.54	0.37	1.06
2,6-Dimethyl-4-nitrophenol	1.12	1.64	0.79	0.26	1.23
3-Aminophenol	1.13	1.15	0.65	0.78	0.88
3-Bromoaniline	1.13	1.19	0.31	0.34	0.99
3-Bromophenol	1.06	1.15	0.70	0.16	0.95
3-Bromotoluene	0.90	0.75	0.00	0.09	1.03
3-Chlorophenol	0.91	1.06	0.69	0.15	0.90
3-Chlorotoluene	0.74	0.67	0.00	0.07	0.98
3-Hydroxyacetophenone	0.98	1.35	0.72	0.55	1.07
3-Hydroxybenzaldehyde	0.99	1.37	0.74	0.40	0.93
3-Hydroxybenzonitrile	0.93	1.55	0.84	0.25	0.93
3-Methoxyphenol	0.88	1.17	0.59	0.39	0.98
3-Methylacetophenone	0.81	1.00	0.00	0.51	1.16
3-Methylanisole	0.71	0.78	0.00	0.30	1.06
3-Methylphenol	0.82	0.88	0.57	0.34	0.92
3-Nitroaniline	1.20	1.71	0.40	0.35	0.99
3-Nitrobenzyl alcohol	1.06	1.35	0.44	0.64	1.09
3-Nitrophenol	1.05	1.57	0.79	0.23	0.95
3-Nitrotoluene	0.87	1.10	0.00	0.25	1.03
3-Phenyl-1-propanol	0.82	0.90	0.30	0.67	1.20
3-Phenyl-1-propene	0.72	0.60	0.00	0.22	1.10
3-Phenyl-1-propionamide	0.94	1.65	0.52	0.80	1.26
3-Phenyl-1-propionitrile	0.77	1.35	0.00	0.51	1.15
3-Phenyl-1-propyl bromide	1.08	1.00	0.00	0.27	1.30
3-Phenyl-1-propyl chloride	0.79	0.90	0.00	0.24	1.26
3-Phenylphenol	1.56	1.41	0.59	0.45	1.38
3-Phenyltoluene	1.37	0.95	0.00	0.26	1.47
3-Tolualdehyde	0.84	0.97	0.00	0.42	1.01
3-Toluamide	0.99	1.50	0.49	0.63	1.11
3-Toluidine	0.95	0.95	0.23	0.55	0.96
3-Tolunitrile	0.76	1.08	0.00	0.34	1.01
4-Aminophenol	1.15	1.20	0.65	0.80	0.88
4-Bromophenol	1.08	1.17	0.67	0.20	0.95
4-Bromotoluene	0.88	0.74	0.00	0.09	1.03

Table 3 (*Contd.*)

Analyte	E	S	A	B	V
4-Chlorophenol	0.92	1.08	0.67	0.20	0.90
4-Chlorotoluene	0.71	0.74	0.00	0.05	0.98
4-Hydroxyacetophenone	1.01	1.51	0.76	0.54	1.07
4-Hydroxybenzaldehyde	1.01	1.54	0.85	0.37	0.93
4-Hydroxybenzonitrile	0.94	1.63	0.80	0.29	0.93
4-Methoxyphenol	0.90	1.17	0.57	0.48	0.98
4-Methylacetophenone	0.84	1.00	0.00	0.52	1.16
4-Methylphenol	0.82	0.87	0.57	0.31	0.92
4-Nitrobenzyl alcohol	1.06	1.39	0.44	0.62	1.09
4-Nitrophenol	1.07	1.72	0.82	0.26	0.95
4-Nitrotoluene	0.87	1.11	0.00	0.28	1.03
4-Phenyl-1-butanol	0.81	0.90	0.33	0.70	1.34
4-Phenyl-1-butyronitrile	0.76	1.38	0.00	0.51	1.29
4-Phenyl-2-butanone	0.75	1.14	0.00	0.65	1.30
4-Phenylphenol	1.55	1.40	0.56	0.49	1.38
4-Phenyltoluene	1.36	0.98	0.00	0.26	1.47
4-*t*-Butylphenol	0.81	0.89	0.56	0.41	1.34
4-Tolualdehyde	0.86	0.87	0.00	0.47	1.01
4-Toluamide	0.99	1.50	0.49	0.65	1.11
4-Toluidine	0.92	0.95	0.23	0.52	0.96
4-Tolunitrile	0.74	1.10	0.00	0.34	1.01
5-Phenyl-1-pentanol	0.80	0.90	0.33	0.72	1.48
Acetophenone	0.82	1.01	0.00	0.48	1.01
α-4-Dibromoacetophenone	1.35	1.61	0.00	0.44	1.36
Aniline	0.96	0.96	0.26	0.50	0.82
Anisole	0.71	0.75	0.00	0.29	0.92
Benzaldehyde	0.82	1.00	0.00	0.39	0.87
Benzamide	0.99	1.50	0.49	0.67	0.97
Benzene	0.61	0.52	0.00	0.14	0.72
Benzonitrile	0.74	1.11	0.00	0.33	0.87
Benzyl acetate	0.80	1.06	0.00	0.65	1.21
Benzyl alcohol	0.80	0.87	0.39	0.56	0.92
Benzyl bromide	1.01	0.98	0.00	0.20	1.03
Benzyl chloride	0.82	0.82	0.00	0.33	0.98
Benzyl cyanide	0.75	1.15	0.00	0.45	1.01
Biphenyle	1.36	0.99	0.00	0.26	1.32
Bromobenzene	0.88	0.73	0.00	0.09	0.89
Butyrophenone	0.80	0.95	0.00	0.51	1.30
Chlorobenzene	0.72	0.65	0.00	0.07	0.84
Dimethyl phthalate	0.78	1.40	0.00	0.84	1.43
Ethyl-3-phenylpropionate	0.65	1.20	0.00	0.62	1.50
Ethyl benzoate	0.69	0.85	0.00	0.46	1.21
Ethyl phenylacetate	0.66	1.01	0.00	0.57	1.35
Ethylbenzene	0.61	0.51	0.00	0.15	1.00
Heptanophenone	0.72	0.95	0.00	0.50	1.72
Hexanophenone	0.72	0.95	0.00	0.50	1.58
Isobutylbenzene	0.58	0.47	0.00	0.15	1.28
Isopropylbenzene	0.60	0.49	0.00	0.16	1.14
Methyl-2-hydroxybenzoate	0.85	0.84	0.04	0.46	1.13
Methyl-2-methylbenzoate	0.77	0.87	0.00	0.43	1.21
Methyl-3-hydroxybenzoate	0.91	1.40	0.66	0.45	1.13
Methyl-3-methylbenzoate	0.75	0.88	0.00	0.47	1.21
Methyl-3-phenylpropionate	0.69	1.21	0.00	0.59	1.35
Methyl-4-hydroxybenzoate	0.90	1.37	0.69	0.45	1.13
Methyl-4-methylbenzoate	0.73	0.88	0.00	0.47	1.21
Methyl-4-phenylbutyrate	0.69	1.29	0.00	0.59	1.50
Methyl benzoate	0.73	0.85	0.00	0.46	1.07
Methyl phenylacetate	0.70	1.13	0.00	0.58	1.21
n-Butyl benzene	0.60	0.51	0.00	0.15	1.28
N-Ethylaniline	0.95	0.85	0.17	0.51	1.10
N-Methylbenzamide	0.95	1.49	0.40	0.71	1.11
n-Propyl-4-hydroxybenzoate	0.86	1.35	0.69	0.45	1.41
n-Propylbenzene	0.60	0.50	0.00	0.15	1.14
N,N-Dimethylbenzamide	0.95	1.40	0.00	0.98	1.26
Nitrobenzene	0.87	1.11	0.00	0.28	0.89
Phenacyl bromide	1.06	1.44	0.00	0.44	1.19
Phenol	0.81	0.89	0.60	0.30	0.78
Phenylacetaldehyde	0.76	0.70	0.00	0.64	1.01
Phenylacetamide	0.95	1.27	0.44	0.89	1.11
Propiophenone	0.80	0.95	0.00	0.51	1.16

Table 3 (*Contd.*)

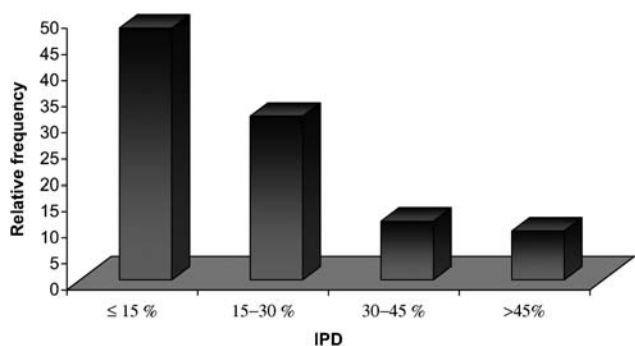| Analyte	E	S	A	B	V
s-Butylbenzene	0.60	0.48	0.00	0.16	1.28
t-Butylbenzene	0.62	0.49	0.00	0.18	0.13
Thymol	0.82	0.79	0.52	0.44	1.34
Toluene	0.60	0.52	0.00	0.14	0.86
Valerophenone	0.80	0.95	0.00	0.50	1.44

Fig. 1 The relative frequency of the individual percentage deviation (*IPD*), of the calculated retention factors (*NDP* = 1539), using eqn (7).

i.e. IPD ≤ 15, 15–30, 30–45 and >45%. This result revealed that in more than 48% of the cases, the retention factor was predicted with an error less than 15%.

The first line of eqn (7) pertains to the organic modifier (acetonitrile or methanol) effect on retention factor. We found that the size (v_1V) and hydrogen bond character (a_1A) of the organic modifier (basicity) and solute (acidity) receive the most importance. In fact these parameters determine the kind of modifier which we should select for special retention factor. The second line of the equation denotes the behavior of solute in pure aqueous mobile phase. All solvation parameters have a role in retention factor which is in agreement with previous models that were developed for a single organic modifier (eqn (10) or (11)). The main difference between this part of the model and similar models is the impotence of polarizability parameter (E) which is larger than the size parameter (V). This finding is chemically reasonable because of the polarizable nature of water. The polarizability of the mobile phase *versus* stationary phase is an important consideration that one uses in selecting the best mobile phase needed to achieve a desired chromatographic separation. The remaining terms in the model denote the effect of mobile phase (hydro–organic) in retention factor. Solute polarizability and molecular size have high importance here, as expected based on the above discussion. The hydrogen-bonding character of the organic modifier is also a determining factor.

Eqn (4) was developed using the retention factors of various analytes in aqueous mobile phases containing acetonitrile and methanol as organic modifiers, the model could be reduced to represent the retention factor of various analytes in a single organic modifier system. In such cases, the accuracy of the model will be improved; however, the derived equation could only be applied to the data of the same organic modifier employed in training processes. When a single organic modifier is considered,

the terms c_1, e_1, s_1, a_1, b_1, v_1, c_2, e_2, s_2, a_2, b_2, v_2, $(c_1-c_2)^2$, $(e_1-e_2)^2$, $(s_1-s_2)^2$, $(a_1-a_2)^2$, $(b_1-b_2)^2$ and $(v_1-v_2)^2$ are constants and can be incorporated into the α, β and W terms. The trained model after excluding non-significant model constants ($p > 0.05$) for acetonitrile system was:

$$\begin{aligned}\log k_m = f_1 &\{-0.345 - 0.575S + 1.411B - 0.413V\} \\ &+ f_2\{0.619E - 0.390S - 1.050A + 3.634B\} \\ &+ f_1f_2\{-15.145B + 6.175V\} \\ &+ f_1f_2(f_1 - f_2)\{1.876S - 1.173A + 11.961B - 7.039V\} \\ &+ f_1f_2(f_1 - f_2)^2\{-2.515 - 21.530B + 13.690V\}\end{aligned}$$

(8)

and the corresponding model for methanol was:

$$\begin{aligned}\log k_m = f_1 &\{-0.574 - 0.518S + 0.387V\} \\ &+ f_2\{0.635E - 0.897S - 1.056A - 3.449B + 3.866V\} \\ &+ f_1f_2(f_1 - f_2)\{2.803 - 2.079A - 3.048V\} \\ &+ f_1f_2(f_1 - f_2)^2\{-4.419 + 3.336E + 3.010V\}\end{aligned}$$

(9)

The overall *MPD* ($\pm$ *SD*) for the back-calculated k_m values using eqn (8) and (9) were 13.1 ($\pm$ 8.0) % (*NDS* = 139) and 16.1 ($\pm$ 13.5) % (*NDS* = 133), respectively (for details of *MPDs* see column 7 of Table 1). The obtained models proved the previous findings about the importance of polarizability parameter in aqueous mobile phases. As it can be seen from eqn (8) and (9) the polarizability parameter is significant in the second line which is the retention factor in pure aqueous mobile phase. In other parts which the water solvation parameters were not entered the size parameter received the highest importance.

Similar models were reported in the literature[13] to predict the retention factors of various analytes at different compositions of the mobile phase as for acetonitrile:

$$\begin{aligned}log\ k_m = {}&1.679 + 0.198E - 0.455S - 0.485A - 1.214B \\ &+ 1.291V - 4.328f_1 + 1.672f_1^2\end{aligned}$$

(10)

and for methanol:

$$\begin{aligned}log\ k_m = {}&1.877 + 0.286E - 0.643S - 0.495A - 1.374B \\ &+ 1.680V - 306f_1 + 1.096f_1^2\end{aligned}$$

(11)

The overall *MPD* ($\pm$ *SD*) for the back-calculated k_m values using eqn (10) and (11) were 25.3 ($\pm$ 17.5) % (*NDS* = 139) and 26.4 ($\pm$ 20.5) % (*NDS* = 133), respectively (for further details see column 8 of Table 1). There was significant reduction in *MPD* values when the pair similar equations (for acetonitrile and methanol) from this work and the previous work[13] were compared ($p < 0.0005$). Fig. (2) and (3) show the linear plots of the calculated retention factors using the proposed and previous
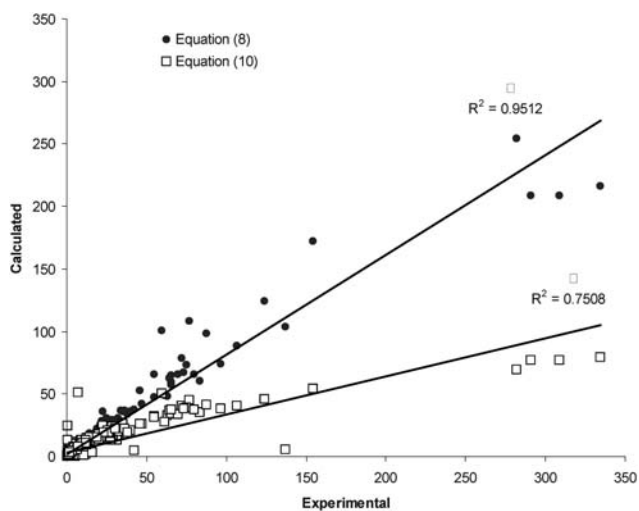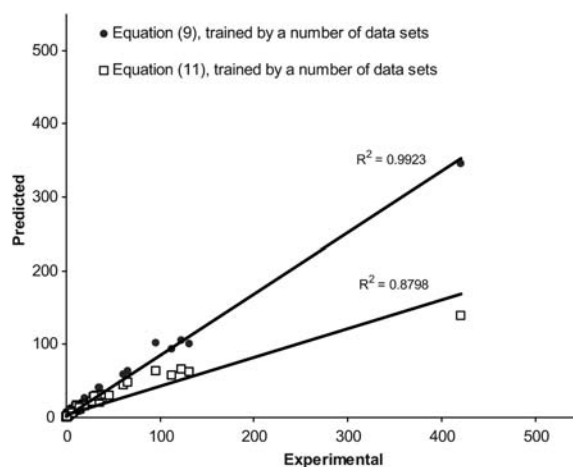
Fig. 2 The plot of the back-calculated retention factors of analytes in water–acetonitrile mixed mobile phases against the experimental values.
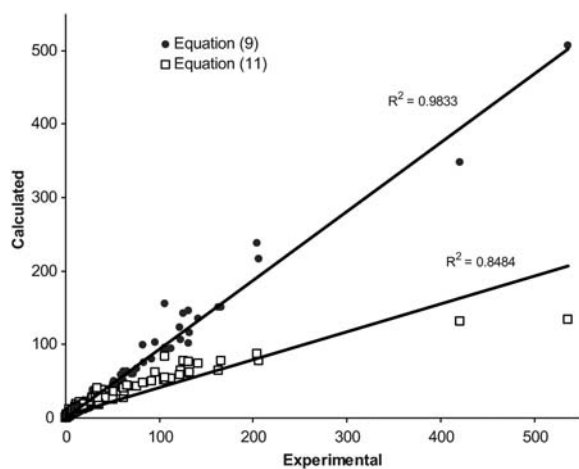
Fig. 3 The plot of the back-calculated retention factors of analytes in water–methanol mixed mobile phases against the experimental values.
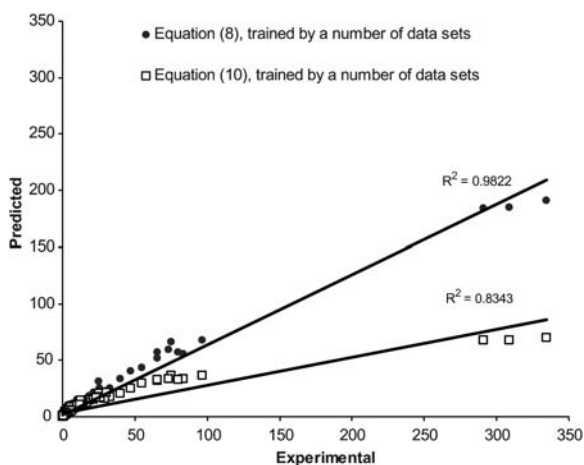
Fig. 4 The plot of the predicted retention factors of analytes in water–acetonitrile mixed mobile phases against the experimental values.

Fig. 5 The plot of the predicted retention factors of analytes in water–methanol mixed mobile phases against the experimental values.

models against the corresponding experimental values. To show the prediction capabilities of the compared equations, they were trained using a number of data points (2/3 data sets) and then the rest of data (1/3 data sets) was predicted by using trained models. The results were shown in Fig. (4) and (5). Better scattering of the data around the regression line and also higher coefficients of determinations of the proposed models revealed that eqn (8) and (9) provide better predictions when compared with eqn (10) and (11). The same pattern has been observed when these models were trained using a number of data sets and the retention factor of prediction sets were considered (see Fig. (2)–(5)).The main advantage of eqn (8) and (9) over eqn (10) and (11) is that they provide more accurate calculations; whereas the major limitation is the larger number of curve-fit constants. Eqn (8) and (9) require more experimental retention data in the training process.

To validate the proposed method for predicting the retention factor of analytes, the experimental data of analytes reported in each reference was removed from the training process of the eqn (7). Then the k_m of the excluded data sets was predicted using the trained model, the *MPD* values were computed and listed in Table 1. The overall *MPD* ($\pm$ *SD*) for this analysis was 19.1 ($\pm$ 13.4) % (*NDS* = 272) and there was no significant difference between *MPDs* of this analysis and that of the back-calculated k_m values using eqn (7), *i.e.* 19.3 ($\pm$ 11.9) % (paired t-test, $p >$ 0.05). This finding confirmed that the proposed model is robust and could be used for predicting the retention factor of other analytes with C_{18} column and acetonitrile and/or methanol as organic modifier. Due to the variations of different C_{18} columns purchased from different manufacturers and/or batches, it is better to train the model using a column and then to use the trained model to predict the retention data on the same column. Developing the training model for the specific column being used should improve the model's predictive capability.

4. Conclusions

A generally trained model was proposed for predicting the retention factor of analytes in *RPLC* using different organic modifiers by combining the Jouyban-Acree and Abraham

models. The constants of the proposed model could represent various interactions in the chromatographic system, and when their numerical values are computed for a given stationary phase, the model could be used to predict undetermined retention data, and therefore reduce the cost of the development process and also speed up the method development. The model has the advantage of modeling three variables, *i.e.* the analyte structure, the organic modifier type and the concentration of organic modifier in the mobile phase using a single model. To our knowledge, there is no such model reported in the literature to compare with the proposed one. It is obvious that the model is able to predict the effects of three mentioned variables on the retention of analytes and the other affecting variables usch as flow rate, pH of the buffer *etc.* should be fine tuned for achieving the best analytical conditions. The proposed model can be reduced to a simpler version to represent the effects of analyte structure and concentration of a given organic modifier. The accuracy of these versions was compared with two similar models taken from the literature and the results showed that the proposed models produce more accurate results.

Acknowledgements

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