Journal of Chromatography B, 912 (2013) 50–55

Contents lists available at SciVerse ScienceDirect

Journal of Chromatography B

journal homepage: www.elsevier.com/locate/chromb

Biopartitioning micellar chromatography with sodium dodecyl sulfate as a pseudo α_1-acid glycoprotein to the prediction of protein–drug binding

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A R T I C L E I N F O

Article history:
Received 26 July 2012
Accepted 5 November 2012
Available online 29 November 2012

Keywords:
Protein–drug binding
α_1-Acid glycoprotein (AGP)
Biopartitioning micellar chromatography
Sodium dodecyl sulfate (SDS)

A B S T R A C T

A simple and fast method is of urgent need to measure protein–drug binding affinity in order to meet the rapid development of new drugs. Biopartitioning micellar chromatography (BMC), a mode of micellar liquid chromatography (MLC) using micellar mobile phases in adequate experimental conditions, can be useful as an in vitro system in mimicking the drug–protein interactions. In this study, sodium dodecyl sulfate–micellar liquid chromatography (SDS–MLC) was used for the prediction of protein–drug binding based on the similar property of SDS micelles to α_1-acid glycoprotein (AGP). The relationships between the BMC retention data of a heterogeneous set of 14 basic and neutral drugs and their plasma protein binding parameter were studied and the predictive ability of models was evaluated. Modeling of $\log k_{BMC}$ of these compounds was established by multiple linear regression (MLR) and second-order polynomial models obtained in two different concentrations (0.07 and 0.09 M) of SDS. The developed MLR models were characterized by both the descriptive and predictive ability ($R^2 = 0.882$, $R^2_{CV} = 0.832$ and $R^2 = 0.840$, $R^2_{CV} = 0.765$ for 0.07 and 0.09 M SDS, respectively). The p values <0.01 also indicated that the relationships between the protein–drug binding and the $\log k_{BMC}$ values were statistically significant at the 99% confidence level. The standard error of estimation showed the standard deviation of the regression to be 11.89 and 13.87 for 0.07 and 0.09 M, respectively. The application of the developed model to a prediction set demonstrated that the model was also reliable with good predictive accuracy. The external and internal validation results showed that the predicted values were in good agreement with the experimental value.

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1. Introduction

The degree of protein binding is an important parameter in the evaluation of the pharmacological and pharmacokinetic properties of potential drugs, which greatly influences absorption, distribution, metabolism and the excretion (ADME) properties of typical drugs. It is widely accepted that the effect of a drug is related to the exposure of a patient to the unbound concentration of drug in plasma rather than its total concentration [1,2]. The binding of drugs to plasma proteins enables the transport of drugs via the blood to sites of action throughout the body. However, strong binding (above 95%) inhibits the ability of drugs to reach therapeutic level and can cause several adverse effects (low clearance, low brain penetration [3], drug–drug interactions [4], loss of efficacy, etc.). Therefore, the extent of protein–drug binding can have a significant impact on pharmacokinetic parameters such as clearance rates and volume of distribution. Among serum proteins, human serum albumin (HSA) and α_1-acid glycoprotein (AGP) play important roles in protein binding for many drugs, which is of key importance to drug distribution in the body. HSA is the most abundant plasma protein having a pronounced affinity for acidic and neutral compounds [5,6], while AGP has been reported to have a pronounced affinity to basic and neutral drugs [7]. This implies the formation of ionic bonds, although non-specific hydrophobic interactions are considered to be essential in binding [8]. The solute hydrophobicity as measured by its partition behavior between octanol and water ($\log P_{ow}$) has been widely used as a predictor to model protein binding [9,10]. However, the octanol/water partition coefficient is unfortunately an unreliable predictor for plasma protein binding, because recognition forces like ionic bonds are not encoded in this biphasic system [8].

Chromatography is a powerful technique for measuring the physicochemical parameters of drugs. A variety of chromatographic approaches have been used to evaluate protein–drug binding such as size-exclusion chromatography [11], high performance frontal analysis [12], and affinity chromatography using HSA or bovine serum albumin (BSA) columns [13–15]. However, protein columns due to their labor intensive and time consuming preparation, and also restriction by the protein activity and limited life are not

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http://dx.doi.org/10.1016/j.jchromb.2012.11.020

adapted to high throughput screening and cannot be accepted as viable, "quick" screening methods, especially in the drug discovery phase [16].

Recently, biopartitioning micellar chromatography (BMC) has been proposed as a high-throughput screening platform and attracted considerable attention as an in vitro model to predict the pharmacological and pharmacokinetic properties of drugs [17–20]. The BMC methodology has important advantages over other in vitro techniques used to protein binding assay (e.g. equilibrium dialysis [21], ultrafiltration [21], biosensors and 96-well fluorescence plate readers [22,23]) including accuracy, low cost, experimental simplicity, speed and reproducibility. In this chromatographic system, polioxyethylene 23 lauryl ether (Brij-35) micellar mobile phases and C_{18} reversed stationary phase in adequate experimental conditions are used. The use of retention data obtained in BMC has been demonstrated to be helpful in describing the biological behavior of the different kinds of drugs. There are a number of researches using BMC to predict protein–drug binding [16,19,24]. To the best of our knowledge, the protein–drug binding prediction using sodium dodecyl sulfate (SDS) in BMC system has not been found in the literature. However, some researchers ever used the mixed micellar system of Brij-35/SDS (85:15) as mobile phase in BMC to estimate bioactivities of drugs [25–27].

In this study, the usefulness of SDS was evaluated as a mobile phase in BMC to predict protein–drug binding for a heterogeneous set of 14 drugs including basic and neutral (training set). The use of SDS as an anionic surfactant leads to the formation of bio-mimetic protein similar to AGP and can be used to emulate both the ionic and hydrophobic interactions of protein and drugs. In addition, SDS micellar mobile phases prepared at physiological conditions could also mimic the environment of protein–drug binding. The retention of compounds in this chromatographic system depends on its interactions with the modified reversed stationary phase and micelles present in the mobile phase. These interactions are governed by hydrophobic, electronic and steric properties of compounds. Regression models for the prediction of protein–drug binding is derived from the training set using the backward-multiple linear regression (MLR) analysis and compared at two SDS concentrations, 0.07 and 0.09 M. Then, the predictive ability of models was evaluated by external and internal (leave-one-out method) [28–30] validations.

2. Experimental

2.1. Instruments

The chromatographic analysis was performed with an HPLC system equipped with model 1525 binary solvent pump and a model 2487 dual λ absorbance detector, all from Waters (Waters Assoc. Milford, MA, USA). The injector was a Reodyne, model 7725i (Cotati, CA, USA) fitted with a 20 μl loop. The analytical column used was REPROSIL 100 C18 (5 μm, 250 mm × 4.6 mm i.d.) from Dr. Maisch GmbH (Beim Brueckle, Germany). The mobile phase flow rate and temperature were maintained at 1.0 ml min^{-1} and 36.5 °C during chromatography. The detection wavelength was set at 240 nm.

2.2. Reagents and standards

Mobile phases were prepared by aqueous solutions of 0.07 and 0.09 M SDS (Fluka, Buchs, Switzerland). The pH of the micellar eluent was adjusted to 7.4 with 0.05 M phosphate buffer, prepared with disodium hydrogenphosphate and sodium dihydrogenphosphate (analytical grade, Fluka, Buchs, Switzerland). However, for mobile phases containing SDS, potassium salts are not recommended for adjusting SDS buffer pH, since potassium dodecyl sulfate has high Kraft point which can precipitate the aqueous mobile phase. To reproduce the osmotic pressure of biological fluids, NaCl (9.2 g l^{-1}, Merck, Darmstadt, Germany) was added to the micellar mobile phase. The training set of drugs used for building the quantitative retention–activity relationship (QRAR) models were obtained from the internal pharmaceutical laboratories in Iran (Sobhan, Pars-Daru and Abidi). The structures of the compounds studied are shown in Fig. 1. Stock standard solutions of 1 mg ml^{-1} of the model drugs were prepared separately in methanol and then diluted in proper concentrations when they were needed. The solutions were stored at 4 °C. The micellar solutions were prepared in double-distilled, deionized water and vaccum-filtered through a 0.45 μm Millipore solvent filter.

2.3. Data sources, software and data processing

Plasma protein binding data values of 19 therapeutic drugs were taken from the handbooks of Goodman and Gilman's [31] and of Martindale [32]. Of the 19 compounds, 14 compounds were chosen as the training set (Table 1) and the remaining ones were used for the prediction set. The logarithm of octanol–water partition coefficients ($\log P_{ow}$) and acidity constants (pK_a) in Table 1 was taken from Refs. [18,33–35]. The retention data in BMC were calculated as a retention factor, $k_{BMC} = (t_R - t_0)/t_0$ where t_R is the retention time of the test compound and t_0 corresponds to column dead time. The dead time value was determined for each injection as the first perturbation in the chromatogram and the average of these values (average t_0 = 1.975 min) was used for all 14 drugs. The logarithm of the retention factor values ($\log k_{BMC}$) calculated for modeling, was the average of at least triplicate measurements. The retention data were highly reproducible, the relative standard deviation (RSD) values were <1.0% for intra-day and <5.0% for inter-day assays. Fig. 2 shows the representative chromatogram of clonazepam eluted using 0.09 M SDS mobile phase at pH 7.4.

Excel 7.0 from Microsoft Office and SPSS 20.0 software were used to perform the statistical analysis of backward-MLR.

2.4. Evaluation of the QRAR model predictive ability

To evaluate the predictive ability of the model, the fit error (i.e. root-mean-square error of calibration, RMSEC), the prediction error based on cross-validation (i.e. root-mean-square error of cross-validation, RMSECV), a parameter which included both interpolation and extrapolation information, and the RMSECVi parameter for measuring only interpolation information, were compared. From a qualitative point of view, small differences between these three parameters would mean a major QRAR model robustness.

3. Results and discussion

3.1. Structure similarity of α_1-acid glycoprotein with SDS in BMC system

α_1-Acid glycoprotein or orosomucoid (ORM), a human plasma protein, is a 41–43-kDa glycoprotein with a low isoelectric point of 2.8–3.8. The peptide moiety is a single chain of 183 amino acids with two disulfide bridges in humans. The carbohydrate content represents 45% of the molecular weight attached in the form of five to six highly sialylated complex-type-N-linked glycans [36]. The high content of sialic acid results in high negative net charge in AGP. The biological function of AGP remains unknown but it has the ability to bind and carry numerous basic and neutral lipophilic drugs and decrease their bioavailability [36,37].

SDS is an organic compound with the formula $CH_3(CH_2)_{11}OSO_3Na$. It is an anionic surfactant consisting of a 12-carbon

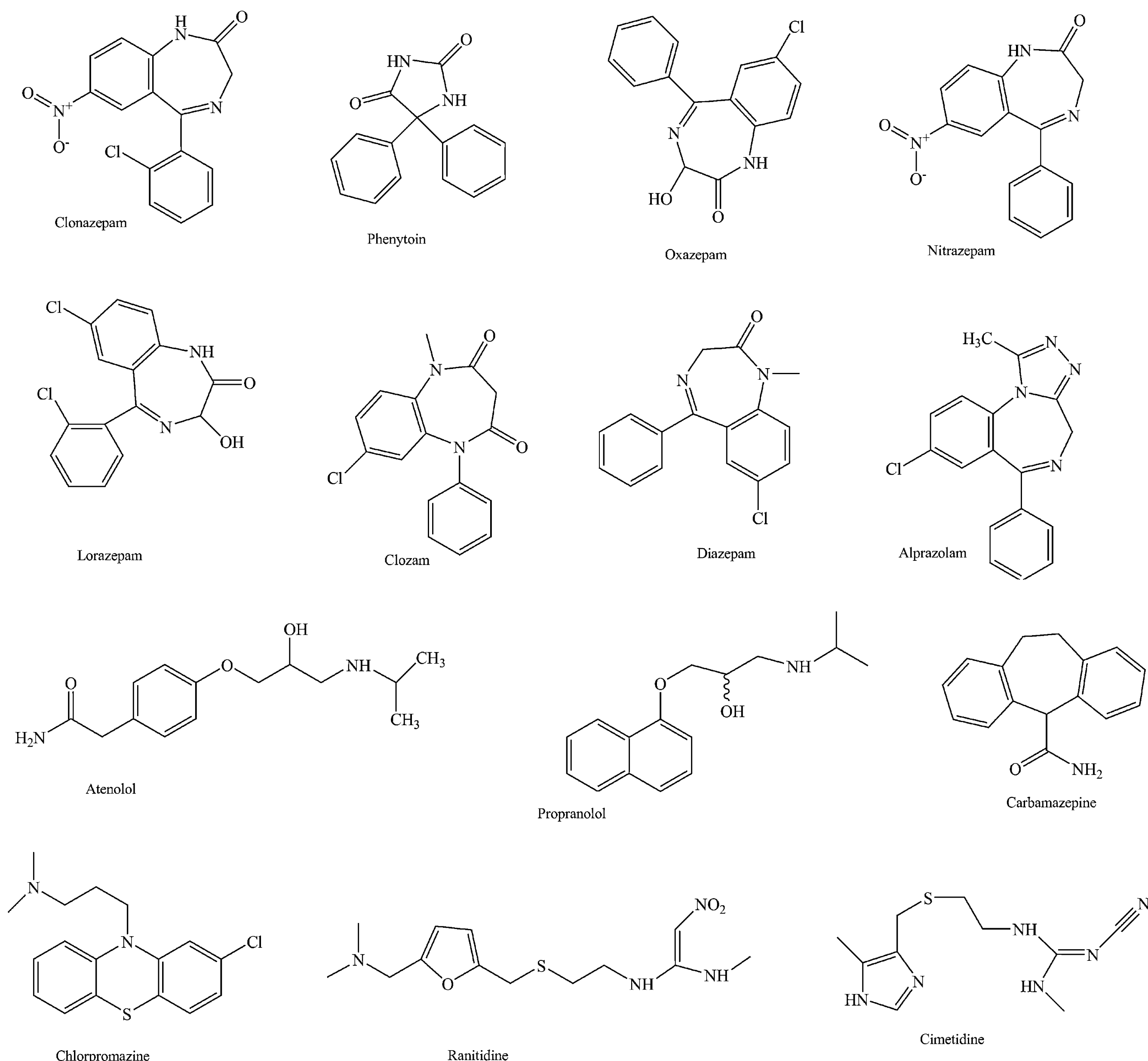

Fig. 1. Chemical structure of the model drugs studied.

tail (lipophilic) attached to a sulfate group (hydrophilic), giving the material the amphiphilic properties. The property of the micelles, which are formed by SDS anionic surfactant including sulfate group, is similar to AGP and can be used to emulate the interaction of protein and drugs. When SDS forms micelles in aqueous solution, the long hydrophobic tails clump into the center and the hydrophilic head groups such as negative sulfate group lie in the outside. This similarity to AGP in structure and especially negative charge results in the similar interactions with basic and neutral drugs. The usefulness of this surfactant in constructing models can be attributed to the fact that the stationary phase modified by the hydrophobic adsorption of SDS anionic surfactant monomers resembles sialic acid carbohydrate in AGP which has high negative charge.

3.2. Retention behavior of the model drugs

In order to study the retention–activity relationship, the retention data for a heterogeneous set of compounds (anxiolytics, H_2 antihistamines, β-blockers, antiepileptics and antipsychotics) was measured using 0.07 and 0.09 M SDS mobile phases at physiological pH 7.4. Table 1 shows the log P_{ow} values for the non-ionic forms and their corresponding retention data obtained using 0.07 and 0.09 M SDS as mobile phases for the studied compounds. As it can be observed, for the highly hydrophobic compounds, large changes in the retention were obtained upon increasing the surfactant concentration in the mobile phase, while for the slightly hydrophobic compounds (atenolol, cimetidine, ranitidine), the retention was scarcely modified. This behavior indicates, as expected, that the eluent strength of the surfactant increases as the hydrophobicity of the compounds increases. This fact indicates the modification of the surface of the stationary phase with monomers of SDS is continued even above the critical micelle concentration (CMC), i.e. the number of adsorbed monomers on the surface unit of stationary phase rises [38]. Therefore, the stationary phase becomes more hydrophilic and retention of highly hydrophobic compounds decreases sharply with an increase of concentration of SDS in the mobile phase.

Table 1
Logarithm of the retention factor in BMC (log k_{BMC}) and protein–drug binding values of model drugs.

Model drugs (training set)	log P_{ow} [a]	pK_a	log k_{BMC}/SDS (M)		Protein–drug binding[d] (%)
			0.07	0.09	
Clozam	2.12	N[c]	1.12	1.00	85
Alprazolam	2.12	6.2 (B)[b]	1.22	1.10	86
Carbamazepine	2.45	N	1.11	0.98	74
Diazepam	2.96	3.3 (B)	1.36	1.23	98.7
Chlorpromazine	5.20	9.3 (B)	1.96	1.27	97
Oxazepam	2.24	1.7 (B); 11.6 (A)[b]	1.34	1.30	97
Cimetidine	0.21	6.8 (B)	0.98	0.96	20
Ranitidine	0.27	2.3 (B); 8.2 (B)	0.97	0.89	15
Atenolol	0.16	9.6 (B)	0.96	0.84	11
Propranolol	3.56	9.45 (B)	1.48	1.31	90
Phenytoin	2.47	8.3 (A)	1.29	1.17	90
Nitrazepam	2.84	3.2 (B); 10.8 (A)	1.23	1.10	87
Lorazepam	2.48	1.3 (B); 11.5 (A)	1.25	1.16	85
Clonazepam	3.02	1.5 (B); 10.5 (A)	1.23	1.09	85

[a] Logarithm of the partition coefficient in the *n*-octanol/water system of the neutral form of compounds studied.
[b] pK_a value for an acidic (A) and for a basic group (B).
[c] Neutral compound or at least non-ionized at pH 7.4.
[d] Values from Refs. [31,32].

Indeed, the chromatographic behavior in a reversed-phase liquid chromatography (RP-LC) system of a solute eluted with a mobile phase containing a surfactant above the CMC can be explained by considering three phases: stationary phase, bulk aqueous solvent and micellar pseudophase. Solutes are separated on the basis of their differential partitioning between bulk aqueous solvent and micelles in the mobile phase or surfactant-coated stationary phase. The partitioning equilibria in MLC can be described by three

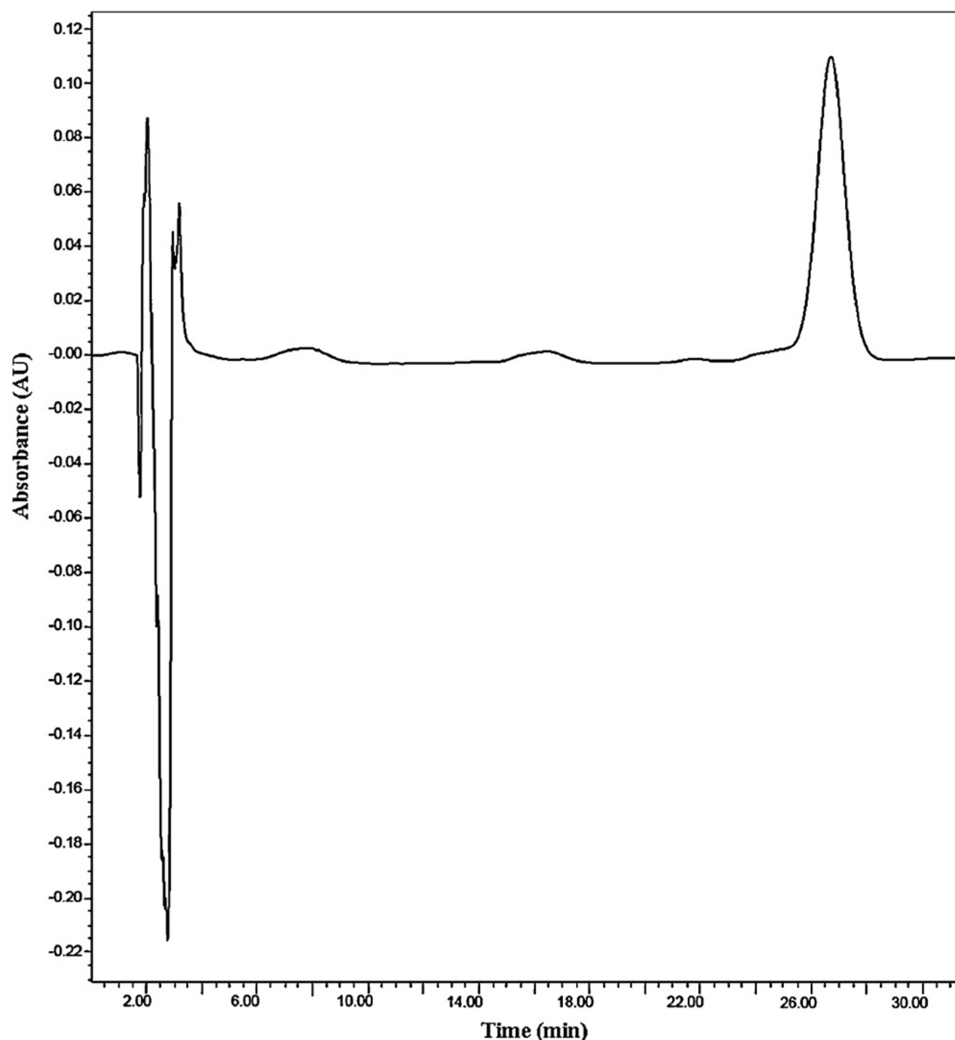

Fig. 2. The representative chromatogram of clonazepam eluted using 0.09 M SDS mobile phase at pH 7.4.

coefficients: P_{WS} (partition between aqueous solvent and stationary phase), P_{WM} (between aqueous solvent and micelles), and P_{MS} (between micelles and stationary phase). The coefficients P_{WS} and P_{WM} account for the solute affinity to the stationary phase and micelles, respectively, and have opposite effects on solute retention: as P_{WS} increases the retention increases, whereas as P_{WM} increases the retention is reduced due to the stronger association to micelles [39].

Also, it is necessary to remark that the CMC value of SDS in water (8.1×10^{-3} M) is depressed by the presence of added salts [40]. The depression of the CMC by added salts is the result of a decrease in the repulsive forces between the ionic headgroups of the surfactant molecules. The micellization becomes easier, since the hydrophobic effect on the non-polar chains is little modified or slightly enhanced (salting out effect) by the added electrolytes [41]. It is often crucial to buffer the micellar phases using electrolytes. Consequently, the effect of salts on the CMC of a surfactant should be kept in mind when using MLC. However, the concentrations of SDS in the studied mobile phases (0.07 and 0.09 M SDS) are considerably above the CMC value of SDS in the presence of salts. So, the micelles are definitely formed.

3.3. Retention–property relationships

The extent of protein–drug binding has a significant impact on pharmacokinetic parameters such as clearance rates and volume of distribution. The molecular features of drugs (mainly hydrophobicity, ionization and steric properties) determine their protein affinity and the drug–protein interaction, and consequently their biological activities [42]. Since these molecular features also determine the retention of compounds in BMC, retention–activity relationships can be expected. The possibility of establishing a relationship between model drugs retention data, $\log k_{BMC}$, and their corresponding protein binding values was studied. Plasma protein binding values of model drugs are also reported in Table 1.

3.3.1. Retention-protein–drug binding relationships

The amount of drug bound to protein determines how effective the drug is in the body. Only a fraction of drug unbound from plasma proteins is available to diffuse from the vascular system and accumulate in tissues thereby enabling interaction with therapeutic targets and accessibility to xenobiotic clearance pathways [43]. Thus, determining the fraction of drug bound to plasma proteins is a standard parameter evaluated in the process of drug discovery. In this study, the usefulness of SDS mobile phase for predicting protein–drug binding was evaluated; for this purpose, the retention factors (k_{BMC}) of 14 chemically different (basic and neutral) drugs (training set) were obtained using 0.07 and 0.09 M SDS micellar solutions buffered at pH 7.4 containing 9.2 g l^{-1} NaCl. The model drugs were chosen to cover a wide range of plasma protein binding data (10–100%).

Fig. 3 shows the relationships between the protein–drug binding of model drugs and their retention data when different concentrations of SDS mobile phase (0.07 and 0.09 M) were used. In both cases, there is practically an adequacy of the polynomial model to the data. Table 2 shows the statistical analysis and the predictive and interpretative features of the QRAR models obtained using 0.07 and 0.09 M SDS mobile phases. For both concentrations, the p values were less than 0.01 indicating that the relationships between the protein–drug binding and the $\log k_{BMC}$ values were statistically significant at the 99% confidence level. In addition, all coefficients were also significant ($p < 0.01$) at the same confidence level. The standard error of estimation showed the standard deviation of the regression to be 11.89 and 13.87 for 0.07 and 0.09 M, respectively. Therefore, from a statistical point of view, better criteria values (R^2, F and SE) were obtained in 0.07 M SDS than 0.09 M (Table 2).

Table 2
Statistical analysis and predictive features of the QRAR models [protein–drug binding (%) = $a + b(\log k_{BMC}) + c(\log k_{BMC})^2$] corresponding to the retention data obtained using 0.07 and 0.09 M SDS mobile phases.

[SDS] (M)	a (p value)	b (p value)	c (p value)	R^2 R^2_{adj} [a]	SE[b]	F[c] (p value)	RMSEC[d]	RMSECV[e] R^2_{CV} [g]	RMSECVi[f]
0.07 M	−458.273(0.000)	705.000 (0.000)	−216.255(0.000)	0.882(0.861)	11.89	41.138(0.000)	76.31	99.59 (0.832)	73.62
0.09 M	−840.237(0.003)	1511.403(0.004)	−609.688(0.008)	0.840(0.810)	13.87	28.794(0.000)	74.45	97.97 (0.765)	71.61

[a] R-Squared adjusted for degrees of freedom.
[b] Standard error of the estimate.
[c] Fisher-ratio.
[d] Root-mean-square error of calibration.
[e] Root-mean-square error of cross-validation (leave-one-out).
[f] Root-mean-square error of cross-validation (leave-one-out) for interpolated data.
[g] Cross-validated correlation coefficient.

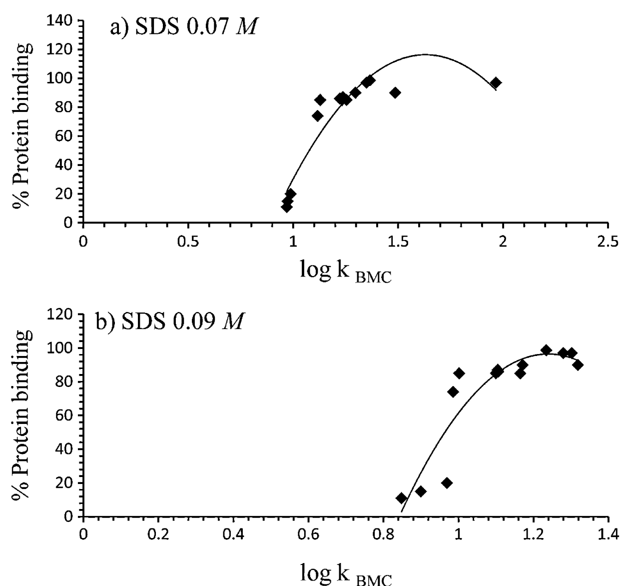

Fig. 3. Retention-protein–drug binding relationships of model drugs at (a) 0.07 M; (b) 0.09 M SDS mobile phase.

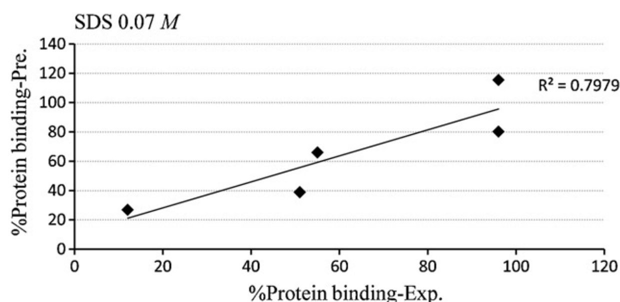

Fig. 4. Plot of predicted protein–drug binding (according to the regression model reported in Table 2) versus experimental protein–drug binding values for the prediction set.

Also, it will be possible to estimate the corresponding protein–drug binding values of other drugs (in these families) with non-reported data.

3.3.2. *Predictive ability of QRAR-protein–drug binding model*

Table 2 contains the statistical parameters of RMSEC, RMSECV and RMSECVi for the QRAR-plasma protein binding model obtained. As it can be observed, the RMSEC and RMSECVi values are similar, but lower than RMSECV values, suggest that interpolation parameters based on these QRAR models should be reasonably adequate. However, caution should be exercised with regard to extrapolation values. The predictive ability of the QRAR model in 0.07 M SDS can also be evaluated from external validation method. Fig. 4 shows the plot of predicted versus actual activity for a prediction set of 5 compounds. The fair R^2 indicates good stability and predictive ability of the developed model for the drugs not included in modeling.

4. Conclusions

Biopartitioning micellar chromatography (BMC) is a mode of RP-LC, which can be used as an in vitro system to model the protein–drug interactions. The present study shows that useful retention data for prediction of protein–basic drug binding can be obtained by MLC using SDS. In fact, the use of SDS in BMC, which encompasses negative charge, can reproduce pseudo protein similar to AGP on stationary phase and guarantee a progressive protein–drug binding model into the drug discovery scheme. Satisfactory results were obtained with the proposed method for the basic and neutral set of drugs.

These models must be used carefully with consideration of the similarity between the tested compound and the compounds that were used in the model building. It should be clear that it is impossible for such models to provide the meaningful estimates for the compounds whose structural features and consequently mechanism of action at biological level are not represented in the original compound databases from which the models were developed.

References

[1] E. Krueger-Thiemer, P. Buenger, Chemotherapia 10 (61–73) (1965) 129.
[2] L.Z. Benet, D.L. Kroetz, L.B. Sheiner, in: G.A. Goodman, Gilman (Eds.), The Pharmacological Basis of Therapeutics, McGraw-Hill, New York, 1996, p. 3.
[3] M. Rowley, J.J. Kulagowski, A.P. Watt, D. Rathbone, G.I. Stevenson, R.W. Carling, R. Baker, G.R. Marshall, J.A. Kemp, A.C. Foster, S. Grimwood, R. Hargreaves, C. Hurley, K.L. Saywell, M.D. Tricklebank, P.D. Leeson, J. Med. Chem. 40 (1997) 4053.
[4] P.E. Rolan, Br. J. Clin. Pharmacol. 37 (1994) 125.
[5] K. Williams, E. Lee, Drugs 30 (1985) 333.
[6] F. Jamali, R. Mehvar, F.M. Pasutto, J. Pharm. Sci. 78 (1989) 695.
[7] K. Schmid, in: F.W. Putnam (Ed.), Plasma Proteins, vol. 1, Academic Press, New York, 1975, p. 184.
[8] M. Chrysanthakopoulos, C. Giaginis, A. Tsantili-Kakoulidou, J. Chromatogr. A 1217 (2010) 5761.
[9] J.J. Morris, P.P. Bruneau, in: H.-J. Boehm, H. Schneider (Eds.), Virtual Screening for Bioactive Compounds, Wiley-VCH Verlag GmbH, Weinheim, 2000, p. 33.
[10] F.D.-M. Perhourc, A. Radouane, L. Labat, B. Bannwarth, Pharm. Res. 12 (1995) 1535.
[11] T.C. Pinkerton, K.A. Koeplinger, Anal. Chem. 62 (1990) 2114.
[12] F.M. Li, X.J. Guo, M.X. Qiao, Z.L. Xiong, D.W. Zhou, Chin. J. Chromatogr. 22 (2004) 349.
[13] E. Domenici, C. Bertucci, P. Salvadori, S. Motellier, I.W. Wainer, Chirality 2 (1990) 263.
[14] F. Beaudry, M. Coutu, N.K. Brown, Biomed. Chromatogr. 13 (1999) 401.
[15] S. Allenmark, B. Bomgren, H. Boren, J. Chromatogr. 264 (1983) 63.
[16] H. Jia, G. Yang, Z. Li, P. Xin, Y. Zhao, Y. Chen, J. Chromatogr. A 1143 (2007) 88.
[17] S. Wang, G. Yang, H. Zhang, H. Liu, Z. Li, J. Chromatogr. B 846 (2007) 329.
[18] L. Escuder-Gilabert, M. Molero-Monfort, R.M. Villanueva-Camañas, S. Sagrado, M.J. Medina-Hernández, J. Chromatogr. B 807 (2004) 193.
[19] J.J. Martínez-Pla, S. Sagrado, R.M. Villanueva-Camañas, M.J. Medina-Hernández, J. Chromatogr. B 757 (2001) 89.
[20] C. Quiñones-Torrelo, S. Sagrado, R.M. Villanueva-Camañas, M.J. Medina-Hernández, J. Chromatogr. B 761 (2001) 13.
[21] M.A.L. Eriksson, J. Gabrielsson, L.B. Nilsson, J. Pharm. Biomed. Anal. 38 (2005) 381.
[22] L.A.A. de Jong, D.R.A. Uges, J.P. Franke, R. Bischoff, J. Chromatogr. B 829 (2005) 1.
[23] H.H. Parikh, K. McElwain, V. Balasubramanian, W. Leung, D. Wong, M.E. Morris, M. Ramanathan, Pharm. Res. 17 (2000) 632.
[24] L.P. Wu, Y. Chen, S.R. Wang, C. Chen, L.M. Ye, Biomed. Chromatogr. 22 (2008) 106.
[25] L.P. Wu, C. Chen, C.J. Sun, L.M. Ye, J. Bioequiv. Availab. 3 (2011) 169.
[26] L.P. Wu, Y. Cui, M.J. Xiong, S.R. Wang, C. Chen, L.M. Ye, Biomed. Chromatogr. 22 (2008) 1243.
[27] Y. Chen, L.P. Wu, C. Chen, L.M. Ye, Biomed. Chromatogr. 24 (2010) 195.
[28] S. Wold, Technometrics 20 (1978) 397.
[29] R.D. Cramer, D.E. Patterson, J.D. Bunce, J. Am. Chem. Soc. 110 (1988) 5959.
[30] D.W. Osten, J. Chemometr. 2 (1988) 39.
[31] A. Goodman Gilman, J.G. Hardman, L.E. Limbird (Eds.), The Pharmacological Basis of Therapeutics, 10th ed., McGraw-Hill, New York, 2001.
[32] S.C. Sweetman (Ed.), Martindale: The Complete Drug Reference, 36th ed., Pharmaceutical Press, London, 2009.
[33] J. Ghasemi, S. Saaidpour, Anal. Chim. Acta 604 (2007) 99.
[34] A. Yazdanipour, J. Iran. Chem. Res. 2 (2009) 293.
[35] A.T. Florence, D. Attwood (Eds.), Physicochemical Principles of Pharmacy, 4th ed., Pharmaceutical Press, London, 2006.
[36] T. Fournier, N. Medjoubi-N, D. Porquet, Biochim. Biophys. Acta 1482 (2000) 157.
[37] K. Schmid, J.P. Binette, Nature 190 (1961) 630.
[38] M.F. Borgerding, W.L. Hinze, L.D. Stafford, G.W. Fulp Jr., W.C. Hamlin Jr., Anal. Chem. 61 (1989) 1353.
[39] M.J. Ruiz-Ángel, S. Carda-Broch, J.R. Torres-Lapasió, M.C. García-Álvarez-Coque, J. Chromatogr. A 1216 (2009) 1798.
[40] K. Shinoda, in: K. Shinoda, B. Tamamushi, T. Isemura (Eds.), Colloidal Surfactants, Academic Press, New York, 1963.
[41] P. Becher, J. Colloid Sci. 17 (1962) 325.
[42] J.J. MacKichan, in: W.E. Evans, J.J. Schentag, W.J. Jusko, M.V. Relling (Eds.), Applied Pharmacokinetics. Principles of Therapeutic Drug Monitoring, Applied Therapeutics, Vancouver, 1992.
[43] M.J. Banker, T.H. Clark, Curr. Drug Metab. 9 (2008) 854.