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Application of Biopartioning Micellar Chromatography in Screening Active Ingredients of Traditional Chinese Medicine

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This research was aim to investigate the potential of biopartitioning micellar chromatography for screening bioactive ingredients of tradition Chinese medicine. Twenty-seven kinds of Chinese herbs with clear drug properties were selected and decocted with water, then retention factor of each Chinese herb in biopartitioning micellar chromatography was measured. In conjunction with molecular descriptors and retention factor (kBMC), support vector machine algorithm, one of the classification techniques of data mining, was used to classify and predict the drug properties of tradition Chinese medicine. The result obtained higher accuracy rate (accuracy = 74 %), which indicate that support vector machine can accurately classify drug properties of tradition Chinese medicine.

Keywords: Active ingredients, Traditional Chinese medicines, Biopartioning micellar chromatography, Support vector machine.

INTRODUCTION

Traditional Chinese medicines (TCM) makes great contributions for the prosperity and proliferation of people as their successful treatment and prevent for various diseases. They are usually very complex mixtures containing up to hundreds or even thousands of different ingredients and thus differ greatly from synthetic drugs in some aspects. However, only a limited number of compounds in TCM are responsible for their pharmaceutical and/or toxic effect. For this reason, screening and analysis of bioactive ingredients of TCM are very important not only for quality control of the crude drugs but also for elucidating the principles of therapeutic action of TCM[1].

To circumvent several problems associated with screening new drugs in animal, such as the costs and ethics, many *in vitro* models for the prediction of pharmacokinetic and pharmacodynamic parameters have been set up including the use of physicochemical parameters of drugs, the permeability data from cell culture lines and chromatography models[2-5]. Development of a new tool for biological parameter of new compounds for clinical applications supports the postulation of predictive models as an alternative to conventional classical assays, so that, in the future, the use of experimentation in animals will be reduced[6]. Chromatographic models are universally used to study passive absorption and screen bioactive compounds due to experimental simplicity, low cost, accuracy and high throughput, among which the immobilized artificial membrane (IAM), immobilized-liposome chromatography (ILC) and biopartitioning micellar chromatography (BMC) system are well recognized models[7,8]. biopartitioning micellar chromatography is a chromatographic modality optimized in order to describe the biological behaviour of drugs which usually is comprised of a C_{18} reversed stationary phase and polyoxyethylene (23) lauryl ether (Brij 35) micellar mobile phases in adequate experimental conditions provides a partitioning environment that can be used as a system that mimics drug biopartitioning[9]. Biopartitioning micellar chromatography is a new type of high-throughput screening technology is simple, rapid and well reproducible. It has been studied comprehensively in the chemical drugs, protein-drug binding and has great significance in guiding the drug design and the development of new drugs[10]. It also has been testified to be useful to study HOA prediction, chemical toxicity, skin permeability and penetration of drugs across the blood-brain barrier (BBB)[11-13]. Moreover, biological activity of different oral drugs were researched by our research group[14-16].

In biopartitioning micellar chromatography, the unique amphiphilic of micellar in RP-HPLC provides hydrophioc, hydrophilic, hydrogen bond, space and electrostatic force between the molecules like biofilm. Drug's retention behaviour in the stationary phase to some extent reflected the transfer process in the biofilm[17], so that active screening and separation

integrated into biopartitioning micellar chromatography could also be used in screening active ingredients and prediction pharmacodynamic effect /drug property of TCM[18]. Quantitative structure-activity relationship (QSAR) studies play an important role in the research. The application of chromatographic parameters in QSAR gives rise to a new field, quantitative retention-activity relationship (QRAR)[19,20]. Structure-activity relationships have been proposed by modern medicinal chemistry as an alternative to *in vivo* measurements. The usual physicochemical parameter employed in traditional quantitative structure-activity relationship (QSAR) studies is the octanol-water partition coefficient (log p). But it sometimes fails to encode some important recognition forces, such as ionic bonds, which are notably important because charged forms of some molecules are able to partition into phospholipids bilayer. In this investigation, we adopt retention factor (k) and molecular structure descriptors to construct quantitative retention-activity relationship.

The drug properties of TCM can be divided into cold, hot, warm and cool and it plays an important role in the therapeutic effect of TCM. This property depends on the chemical compositions in the TCM, especially the biologically active substances and it is also the collection of attribute of TCM. The therapeutic effect depends on drug property, while the former reflects the latter. For instance, the property of Ephedra herb is warm, thus it is inferred that Ephedra herb could be applied to cold. Usually, cold and cool traditional Chinese medicines contain alkaloid, anthraquinone, halogen and their salts, while warm and hot ones contain volatile oil, hormone-like substance, glycoside, amino acids and other nutrients[21,22]. In this paper, we screened active ingredients of traditional Chinese medicine by biopartioning micellar chromatography in conjunction with support vector machine.

EXPERIMENTAL

The mobile phase consisted of 0.04 mol/L polyoxyethylene (23) laurylether (Brij35, Acros, NJ, USA) with 0.01 mol/L sodium dihydrogenphosphate (analytical-reagent grade, Kelong, Chengdu, China) and was adjusted to pH 7.4 which is the plasmatic pH value by sodium hydroxide. In order to reproduce the osmotic pressure of biological fluids, sodium chloride (9.20 g/L, analytical-reagent grade, Kelong, Chengdu, China) was added to the micellar mobile phase. Sodium chloride concentration was close to physiological concentration of biological fluids. Water was procured from a Millipore (Billerica, MA, USA) synergy™ 185 system and was degassed before HPLC. The mobile phases injected into the chromatograph were filtered through 0.45μm micro porous membrane.

Among the 35 chemical drugs piroxicam, isoniazid, verapamil, hydrochlorothiazide and furosemide were provided by analysis test center of West China School of Pharmacy and the others were crude drug or formulations which would not affect their retention behaviour in this study because of the dilution of the mobile phase, donated by the pharmaceutical and pharmaceutical chemistry laboratories of West China School of Pharmacy, Sichuan University (Chengdu, China). Three herbs were used to investigate the changes of chemical composition in Chinese herbal compound. Twenty-seven herbs were used to classify the property of traditional Chinese medicines. All traditional Chinese medicines were purchased from Frierson Pharmacy(Chengdu, China).

Water-soluble drugs were dissolved in mobile phase solution. Lipophilic drugs were first dissolved in methanol (analytical-reagent grade, Kelong, Chengdu, China) and then were diluted with water to get appropriate concentration. Crude herbal drug was immersed in water for 0.5 h. The mixture was then boiled under reflux for 1 h and the decoction was repeated two times. The extract was filtered and merged together, then was concentrated. 1 mL concentrated solution was piped to 10 mL volumetric flask and methanol was filled into volumetric flask till reach the scale, then the solution was centrifuged at 1000 × 10 r/min for 5 min. The working solutions injected into the chromatograph were filtered through 0.22 μm microporous membranes (Xinya, Shanghai, China), respectively. All the solutions were stored under refrigeration at 4 °C before analysis.

The retention of drugs was measured using a chromatograph with an LC-20AB pump, an SPD-M20A DAD detector and a CTO-20A column thermostat (Shimadzu, Japan). Data were collected and processed on a Compaq computer installed with LC-SOLUTION software. The solutions were injected into the chromatograph through a Rheodyne valve (Cotati, CA, USA), with a 20 μL loop. The HPLC column was a Kromasil C_{18} column (5 μm, 150 × 4.6 mm i.d.) with a phenomenex security Guard ™C_{18} guard cartridge. The mobile phase flow rate was 1 mL/min. The UV detection of chemical drugs was monitored at 220, 254, 270 and 300 nm and active ingredients of TCM were set at 254 nm.

All the assays were carried out at 37 °C for simulating human body temperature. The retention data in biopartitioning micellar chromatography were calculated as capacity factors, $k = (t_r-t_0)/t_0$, where t_r is the retention time of test compound and t_0 is the column dead time, which is the first fluctuation of baseline, determined by injecting water. The 'k' values used in this study were the average value of triplicate. The retention data were highly reproducible.

Statistical analysis: For many attractive features and promising empirical performance, support vector machine (SVM) is gaining popularity[19]. This method has proven to be very effective for addressing general purpose classification and regression problems[23]. SVM is used to chemical problems due to its remarkable generalization performance in modeling non-liner problems. Waikato Environment for Knowledge Analysis (Weka) is a machine learning software developed by Waikato university of New Zealand. As a public workbench of data mining, Weka assembles a lot of machine learning algorithms which can undertake data mining tasks, including the pretreatment, classification, regression, clustering and association rules of data. In this paper, Weka and SVM were adopted to profile the bioactive ingredients of TCM.

The data set was analyzed using Microsoft® Excel 2003 (Microsoft Corporation). MLR was used to carry out on the date set using SPSS 16.0 software (Math Works, SPSS Inc. Chicago, USA).

RESULTS AND DISCUSSION

Construction of quantitative retention-activity relationship: Drugs should penetrate the cell membrane, so that they can play a therapeutic role. It relies on the ability of the molecule

to partition into and move across gastrointestinal epithelium membranes. The most important features of a drug that influence this partitioning are solubility, permeability and molecular size, polarity and lipophilicity. In this section, 35 chemical drugs with different structure were selected, for which were dominated by passive transport. The various structural parameters, including calculated log P (Clog P), rotation bond (Rot B), molecular weight (MW), Rings, number of bonds of oxygen hydrogen and nitrogen hydrogen (OHNH), number of oxygen and nitrogen atoms (ON), hydrogen bond acceptor (HBA), polar surface area (PSA) and total surface area (TSA), were obtained from literatures.

The regression equation was obtained by observing each molecular descriptor using direct regression analysis. The relationship was calculated by MLR equation (1) as followed, while the specific drugs and molecular descriptors were shown in Table-1.

$$\log k_{BMC} = 0.307\text{-}1.43ROB\text{-}0.305Rings + 0.565HBD\text{-}0.014HBA + 0.001\ MW\text{-}7.27OHNH + 0.105ON + 0.001PSA + 0.002TSA + 0.3\ Clog\ P \quad (1)$$

$N = 35$; $R^2 = 0.631$; S.E = 0.519; F = 12.128; $P < 0.001$

From eqn 1, we can see the molecular descriptors are related to k_{BMC}. The regression coefficient of each molecular descriptor proves its significant degree with k_{BMC}, among those, HBD is positive correlated with k_{BMC}, while OHNH is negative. By adopting stepwise regression, the structure data of 35 different drugs were analyzed and the final regression equation was shown as followed:

$$\log k_{BMC} = 0.789\ (\pm\ 0.244) + 0.181\ (\pm)\ Clog\ P\text{-}0.168\ (\pm\ 0.76)\ OHNH \quad (2)$$

$N = 35$; $R^2 = 0.756$; S.E = 0.497; F = 12.128; $P = 0.000$ ($P < 0.001$)

The Clog P is the indicator of drugs' lipophilic and Clog P is bigger, lipophilic is stronger. Generally, drugs with little lipophilic are difficult to permeate the cell membrane, while those too strong ones are difficult to dissociate from lipid membrane and dissolve into water-soluble body fluid. OHNH reflects the number of hydrogen bond and bigger OHNH is, more difficultly drugs permeate the membrane, thus poorer absorption is. Lipinski's five principles are that when the number of hydrogen bone donator is bigger than 5, Clog P bigger than 5 and the number of hydrogen bone acceptor is bigger than 10, membrane permeability and absorption maybe poor. The experimental result was consistent with the Lipinski's five principles. It proved that molecular descriptors were well correlated with k_{BMC}, thus k_{BMC} could demonstrate the molecular structure and consequently, retention factor in biopartioning micellar chromatography k_{BMC} could be used to screen the bioactive ingredients of TCM.

TABLE-1
MOLECULAR DESCRIPTORS AND BMC RETENTION OF DIFFERENT DRUGS

Drug	log k	Rot B	Ring	HBD	HBA	MW	ON	OHNH	PSA	TSA	Clog P
Carbamazepine	1.12	1	3	1	1	180.2	4	0	65.006	216.801	1.023
Ibuprofen	1.09	4	1	0	2	206.3	2	0	42.077	290.96	3.679
Phenylbutazone	1.02	5	3	0	2	308.4	4	0	42.688	389.623	3.385
Prazosin	1.69	5	4	1	5	383.4	9	1	105.531	421.875	1.21
Procaine	0.59	7	1	2	2	236.3	4	2	58.753	327.411	2.538
Sulpiride	0.17	7	2	3	4	341.4	7	3	107.974	402.435	1.11
Amitriptyline	1.84	3	3	1	0	277.4	1	1	7.105	372.26	4.851
Amlodipine	1.32	10	2	2	4	408.9	7	2	98.152	477.878	3.646
Amobarbital	1.48	4	1	2	3	226.3	5	2	88.732	286.126	2.112
Atenolol	-0.29	8	1	3	2	266.3	5	3	95.277	359.887	-0.109
Atropine	0.63	5	3	2	2	289.4	4	2	48.969	361.815	1.229
Cimetidine	0.48	7	1	4	4	252.3	6	4	92.541	333.965	0.351
Digoxin	0.20	7	8	6	7	780.9	14	6	200.47	825.203	1.623
Fluphenazine	-0.25	7	4	2	2	437.5	4	2	38.437	474.774	4.618
Furosemide	0.86	5	2	2	6	330.7	7	2	125.21	326.157	1.9
Haloperidol	1.63	6	3	2	2	375.9	3	2	40.178	435.473	3.849
Hydrochlorothiazide	1.00	1	2	3	7	297.7	7	3	131.62	263.77	-0.365
Imipramine	1.80	4	3	1	0	280.4	2	1	8.33	372.007	5.307
Isoniazid	-0.24	2	1	2	3	137.1	4	2	74.888	172.788	-0.668
Metformin	-0.44	3	0	3	2	129.2	5	4	83.622	180.243	-0.236
Midazolam	1.70	1	4	0	2	325.8	3	0	30.677	354.181	3.222
Minoxidil	0.037	1	2	2	4	209.2	6	2	94.558	255.682	0.541
Naproxen	0.85	3	2	0	2	230.3	3	0	54.902	283.1819	2.816
Omeprazole	1.30	5	3	1	3	345.4	6	1	84.956	399.375	2.565
Pentobarbital	1.47	4	1	2	3	226.3	5	2	84.529	276.47	2.112
Phenobarbital	1.08	2	2	2	3	232.2	5	2	90.549	263.313	1.365
Phenytoin	1.31	2	3	2	2	252.3	4	2	64.252	284.009	2.085
Piroxicam	0.94	3	3	2	6	331.3	7	2	98.31	342.738	1.888
Prilocaine	0.92	6	1	2	1	220.3	3	2	37.065	318.67	1.807
Propranolol	0.64	6	2	2	1	259.3	3	2	45.177	350.702	2.753
Theophylline	0.33	0	2	1	3	180.2	6	1	74.365	207.742	-0.034
Timolol	0.48	7	2	2	5	316.4	7	2	84.723	385.896	1.578
Tramadol	0.84	4	2	2	1	263.4	3	2	33.151	339.398	3.1
Verapamil	1.66	13	2	1	1	454.6	6	1	81.702	558.816	4.466
Warfarin	0.97	4	3	1	2	308.3	4	1	59.092	351.264	2.901

Changes of chemical component of traditional Chinese medicine compound recipe: Shengmaisan is a famous TCM compound recipe whose history is as long as 810 years, which is composed by red ginseng, ophiopogonis tuber and fructus schizandrae. This recipe contains various kinds of chemical compositions, such as panaxsaponin, volatile components, organic acid and ester, sterols, alkaloid, amino acid, flavonoids, carbohydrate, lignin and inorganic elements. It was reported that the therapeutic effect of shenmaisan was better than each herb which composed the recipe, including the decoction of any other two herbs of the recipe. In this experiment, biopartitioning micellar chromatography was used to observe the change of chemical component in compound recipe and construct the relationship between the retention factor of new chemical component in biopartitioning micellar chromatography and the therapeutic effect of traditional Chinese medicine compound recipe.

As shown in Tables 2 and 3, the RSD of dead time t_0 and biopartitioning micellar chromatography retention are both smaller than 2 %, which shows that biopartitioning micellar chromatography possess good reproducibility and robustness. The error range of k_{BMC} of each component is k ± 0.09, thus two k_{BMC} will be considered as represent of different components respectively once the distinction of which beyond this range. Figs. 1 and 2 are biopartioning micellar chromatography spectrum of each herb decoction of shengmaisan and the mix decoction of three herbs. The retention of new chemical composition was listed in Table-4. As shown in Figs. 1 & 2 and Table-4, after mixed decoction of compound recipe, some former chemical compositions disappeared and some new chemical compositions emerged. During decocting, many chemical compositions had reacted. The compositions included active and inactive substance and lots of them were contained in the single herb, but a few were produced during processing of the compound recipe. Inactive compositions also play an important role in therapeutic effect, because traditional Chinese medicine compound recipe mostly contain amphipathic substance, such as phospholipids, saponin, higher fatty alcohol and sterol, they may emerge micelle during mixed decocting and then increase the solubility of active composition.

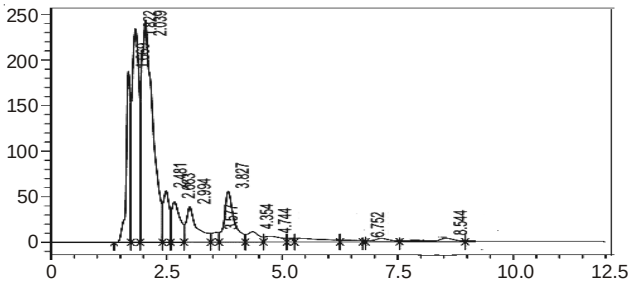

Fig. 1(a). Fructus schizandrae decoction of biopartitioning micellar chromatography (BMC) chromatogram

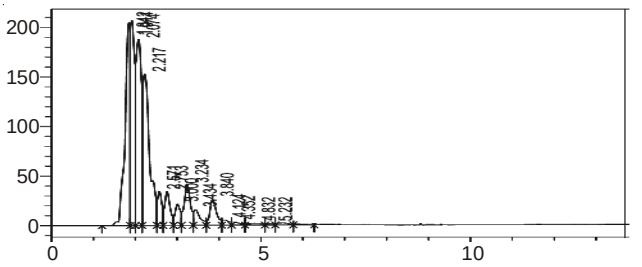

Fig. 1(b). Red ginseng decoction of biopartitioning micellar chromatography (BMC) chromatogram

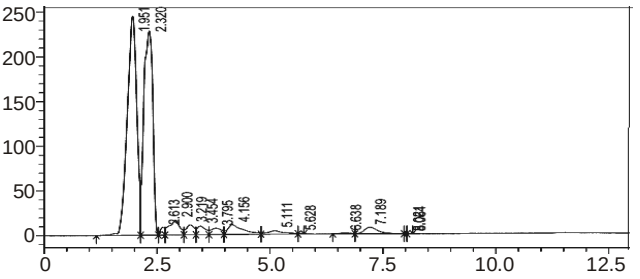

Fig. 1(c). Ophiopogonis decoction of biopartitioning micellar chromatography (BMC) chromatogram

TABLE-4
NEW CHEMICAL COMPOSITIONS' RETENTION t_0 = 1.554 $k_{BMC} = (tr-t_0)/t_0$

t_r (min)	2.85	3.727	7.48	13.62	15.96
k_{BMC}	0.835	1.398	3.81	7.76	9.27

Classification of drug properties of traditional Chinese medicine

Evaluation of classifier performance: For classifiers under the environment of Weka, the evaluation indexes are true positive rate (TPR), false positive rate (FPR), precision, recall, F-measure and area under the ROC (AUC). The prediction may produce four results, including true positive (TP), true negative (TN), false positive (FP) and false negative (FN). For instance, something belongs to X, thus TP is that classifier predicts it belongs to X correctly, while FN is that classifier predicts it does not belong to X incorrectly. Likewise, if something does not belong to X, TN is that classifier predicts it does not belong to X correctly, while FP is that classifier predicts it belongs to X incorrectly. The formulas of true positive rate and false positive rate are shown as followed:

TABLE-2
PRECISION OF DEAD TIME t_0

	Intra-day precision							Inter-day precision					
Time	0h	2h	4h	6h	8h	Average	RSD	1d	2d	3d	4d	Average	RSD
t_0	1.549	1.540	1.558	1.547	1.552	1.549	0.4 %	1.549	1.552	1.568	1.549	1.554	0.5 %

TABLE-3
INTRADAY/INTERDAY PRECISION OF BMC RETENTION

t_r Range (min)	Chemical drug	RSD (Intra-day precision) (%)	RSD (Inter-day precision) (%)
0-10	Gatifloxacin	0.41	1.5
10-20	Captopril	0.16	0.7
20-30	Propranolol	0.79	1.2

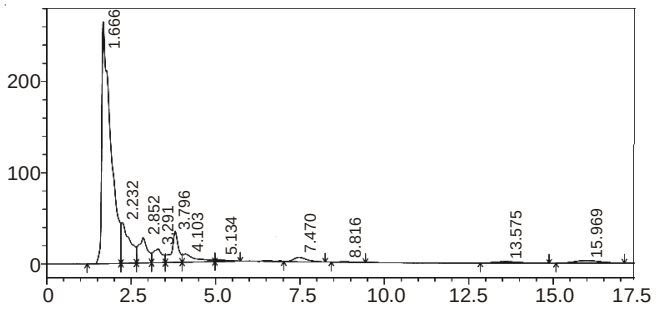

Fig. 2. Shengmaisan mixed decoction of biopartitioning micellar chromatography (BMC) chromatogram

$$TPR = \frac{TP}{TP + FN} \quad (3)$$

$$FPR = \frac{FP}{FP + TN} \quad (4)$$

Recall (R) and precise (P) are measure indexes used extensively in the field of information retrieval and statistical classification. Precise is the proportion that those exactly belong to A in the all classifier judges belong to A, while recall is the proportion that those classifier judges correctly belong to A in the all originally belong to A. The formulae of precise and recall are shown as followed:

$$p = \frac{TP}{TP + FP} \quad (5)$$

$$R = \frac{TP}{TP + FN} \quad (6)$$

F-measure is the comprehensive consideration of precise and recall, because sometimes precise and recall are not the bigger the better. In a large sample data, they are mutually constraints, so it is necessary to find a balance between precise and recall. The formula of F-measure is shown as followed:

$$F = \frac{2P \times R}{P + R} \quad (7)$$

Receiver operating characteristic curve (ROC) could be completed by describing TPR and FPR. True positive rate (TPR) decided the performance of a classifier to judge positive samples correctly in all positive samples, while FPR decided the performance of a classifier to judge how many false positive in all negative samples. For comparing the performance of different classifiers to divert the classifier's nature which ROC describes into numerical value, area under the ROC (AUC) was introduced. The value of AUC is between 0.0 and 1.0, however, the AUC value of actual classifier should bigger than 0.5.

Forecast results: Twenty-seven traditional Chinese medicines were selected for modeling, including 14 cold medicines and 13 warm medicines, but no training set and test set were divided and ten-fold cross-validation was used to establish classification model. Data obtained from 27 medicines was normed before modeling, making each medicine represented by the same number of attributes, so that SVM could be carried out. Attributes of different TCM after data processing are shown in Table-5. As shown in Table-6, the value of TP rate, precise, recall, F-measure and AUC are all bigger than 0.5, thus it illustrates the model has good performance. This model is suitable to process data which has little characteristic attributes, such as the relationship between the attribute that retention value in biopartioning micellar chromatography and pharmacodynamic action depended on multivariate factors. The confusion matrix of prediction result was as followed:

TABLE-5
ATTRIBUTES OF DIFFERENT PROPERTY TRADITIONAL CHINESE MEDICINE (TCM) AFTER DATA PROCESSING

TCM	Attribute	Attr-1	Attr-2	Attr-3	Attr-4	Attr-5	Attr-6	Attr-7	Attr-157
Cold	Phellodendri	4	0	8	0	7	0	2	0
	Scutellaria	0	1	8	0	6	1	7	0
	Ophiopogonis	8	1	7	0	1	7	1	0
	Isatis Root	0	0	8	0	1	8	0	0
	Forsythiae	0	0	5	3	5	2	7	0
	Hogfennel root	7	1	8	0	1	3	7	0
	Golden Thread	0	0	7	1	8	2	0	0
	Paeoniae radix	6	0	8	1	6	2	7	0
	Alisma rhizoma	0	0	8	0	4	1	7	0
	Anemarrhenae	0	0	8	0	3	0	8	0
	Danshen root	0	0	8	0	2	1	4	0
	Starwort root	0	0	7	0	1	1	7	0
	Cyrtomii rhizoma	1	5	7	0	1	0	5	0
	Artemisiae capillaris	0	0	0	8	2	4	6	0
	Periplocae	0	1	6	0	2	0	4	0
Warm	Houttuyniae	0	7	1	0	2	0	5	0
	Angelica	2	0	8	0	8	0	7	0
	Prepared rehmannia	0	9	0	0	0	0	0	0
	Notoginseng	8	0	8	0	8	0	4	0
	Atractylodes macrocephala	2	0	8	0	6	0	7	0
	Medicinal cornel	14	2	4	0	7	0	8	0
	Magnolia bark	0	0	8	0	6	0	6	0
	Agastache rugosa	0	7	1	0	6	0	6	0
	Fructus schizandrae	0	0	8	0	0	0	0	0
	Atractylodes rhizome	0	2	8	0	1	0	8	0
	Radix ginseng	9	4	5	2	3	3	6	0
	Ligustici	0	0	8	0	8	7	0	0

TABLE-6
RESULT OF CLASSIFICATION OF 27 DIFFERENT TRADITIONAL CHINESE MEDICINES

Item	TP Rate	FP Rate	Precision	Recall	F-Measure	ROC Area
Warm properties TCM	0.846	0.357	0.688	0.846	0.759	0.745
Cold properties TCM	0.643	0.154	0.818	0.643	0.72	0.745
Weighted Average	0.741	0.252	0.755	0.741	0.739	0.745

TABLE-7
VARIANCE ANALYSIS OF CLASSIFICATION OF 27 DIFFERENT TRADITIONAL CHINESE MEDICINES

Total number of instances	Correctly classified instances	Incorrectly classified instances	Kappa statistic	Mean absolute error	Root mean squared error	Relative absolute error	Root relative squared error
27	20 (74.0741 %)	7 (25.9259 %)	0.485	0.2593	0.5092	51.41245 %	100.8628 %

Confusion matrix (8)

a	b	---classified as
11	2	a = warm
5	9	b = cold

As is shown in the confusion matrix, two warm medicines were classified as cold medicines incorrectly, while five cold medicines were classified as warm medicines. Eleven plus nine and then divide by twenty-seven equals 0.74 and this is just right the proportion of accurate prediction (Table-7). The better the numerus in diagonal of the matrix were, the better prediction was and the more precise the algorithm adopted was. The main components responsible for the pharmacological activity of warm medicine are volatile oils and the primary components of cold medicines are alkaloids, however, cross components may result in error prediction. Some categories of component exist both in warm medicines and cold medicines, including anthraquinone glycoside, cardiac glycoside and flavonoid glycoside. For example, in cold medicines, paeoniae radix contains peoniflorin and anemarrhenae contains steroid saponin, while in warm medicine, ginseng contains panaxsaponin and notoginseng contains notoginsenoside. These compounds posses similar precursor structure, only diversity in substituent group, which may posses the same retention factor in biopartitioning micellar chromatography, resulting in the prediction result out of accuracy.

Conclusion

After the construction of QRAR, biopartitioning micellar chromatography behaviour of TCM as well as compound recipe could reflect the change of chemical components of TCM, on this basis, the prediction of drug property of TCM was completed. Further more, the material base of drug property is chemical components which TCM contain, thus, retention factor (log k_{BMC}) of which can be adopted as an estimate or, at lease, useful qualitative information about bioactivity ingredient of TCM. The results show that biopartitioning micellar chromatography is a potentially powerful technique for screening active ingredient of TCM. In addition, combination with other chromatography models, for example CMC, biochromatography and other complementary techniques, such as MS and NMR and mathematical statistics method such as SVM, biopartioning micellar chromatography will further improve the accuracy and structural identification of screening bioactive ingredients of TCM.

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