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Determination of venlafaxine in human plasma by high-performance liquid chromatography using cloud-point extraction and spectrofluorimetric detection

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ABSTRACT

A new straightforward method based on cloud-point extraction (CPE) has been developed, optimized and validated for the determination of venlafaxine in human plasma by reversed-phase high-performance liquid chromatography with fluorescence detection. The non-ionic surfactant Triton X-114 (polyethylene glycol *tert*-octylphenyl ether) was chosen as the extract solvent. Separation was obtained using a reversed-phase Diamonsil column (C_{18}, 250 mm × 4.6 mm I.D., 5 μm) and a mobile phase composed of acetonitrile–phosphate buffer solution (pH 3.0)–triethylamine (33.5:66.5:0.4). Fluorescence detection was used (λ_{ex} 276 nm, λ_{em} 598 nm). Maprotiline was used as the internal standard. Under the optimum conditions, the linear range of venlafaxine in human plasma was 10–800 ng mL^{-1} (r^2 = 0.9995). The limit of detection (LOD) was less than 2 ng mL^{-1} (S/N = 3) and the limit of quantification (LOQ) was less than 10 ng mL^{-1} (S/N = 10). The method was successfully applied for the evaluation of pharmacokinetic profiles of venlafaxine capsules in nine healthy volunteers.

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1. Introduction

Venlafaxine (1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl] cyclohexanol hydrochloride, Fig. 1), a second generation antidepressant drug [1], has a neuropharmacologic profile distinct from that of existing antidepressants including tricyclic compounds, selective serotonin reuptake inhibitors and monoamine oxidase inhibitors [2,3]. It is suitable for treating various depressions conditions, and acts by inhibiting the neuronal uptake mechanisms of norepinephrine, serotonin, and to lesser extent, dopamine [4–6]. Besides, it has less adverse side effects than tricyclic compounds when administrated [7]. Since the clinical use of venlafaxine has become increasingly common, it is essential to use a specific and rapid method for the determination of venlafaxine in human plasma or serum.

The reported methods for venlafaxine analyses in human plasma or serum included GC [8,9], HPLC [10–17] and capillary electrophoresis [18]. All of these analytical techniques require a large sample volume and are quite labor intensive, time-consuming and high-cost because a sample pretreatment step prior to chromatographic analysis is essential, such as liquid–liquid extraction (LLE) and solid-phase extraction (SPE). In particular, the traditional liquid–liquid extraction method is dangerous to analysts and the environment as it involves relatively high volumes of toxic and hazardous organic solvents.

Recently, the cloud-point extraction (CPE) method has aroused much attention as a convenient alternative to the conventional extraction systems. Compared with the traditional organic liquid–liquid extraction, this CPE methodology requires a very small amount of relatively non-flammable and non-volatile surfactants. Also, compared with classical organic solvents, it offers the advantages of safety, low cost, high concentration efficiency, easy disposal of surfactants, low toxicity, less environmental pollution and simple procedure [19–25].

With the advantages of the CPE method, originally introduced by Watanabe and Tanaka [26], it has been increasingly applied for the selective extraction of various analytes, including estrogens, vitamins, proteins and metal ions from biological and environmental samples [27–32]. All of these indicate that CPE can be used as an effective enrichment method due to great analytical potential, but

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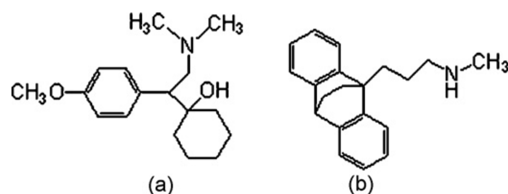

Fig. 1. Chemical structures of venlafaxine (a) and maprotiline (internal standard) (b).

only a few reports involve the extraction of drugs from plasma for the purpose of clinical and biomedical studies [20,29,31]. In the present work, CPE was used for the preconcentration of venlafaxine in human plasma as a step prior to its determination by HPLC-FD using Triton X-114 as non-ionic surfactant.

2. Experimental

2.1. Chemicals and solutions

Venlafaxine (99.9% purity) was provided by Sichuan HYGIEN Pharmaceutical Co., Ltd. (Chengdu, Sichuan, China). Maprotiline (*N*-methyl-9,10-ethanoanthracene-9(10H)-propanamine, MAP, Fig. 1), used as the internal standard (IS), was purchased from National Institute for the Control of Pharmaceutical and Biological Products (Beijing, China). The non-ionic surfactant Triton X-114 was purchased from Sigma (USA) and used without further purification. Acetonitrile and methanol (HPLC grade) were purchased from Fisher (USA). Monobasic potassium phosphate and dibasic potassium phosphate (AR), sodium hydroxide and sodium chloride (AR), and *o*-phosphoric acid and triethylamine (AR) were purchased from the Beijing Chemical Factory (Beijing, China). Ultrapure water (18.2 MΩ cm) was obtained by means of a MilliQ apparatus by Millipore (Milford, USA).

Stock solutions of venlafaxine (10 μg mL^{-1}) and maprotiline (10 μg mL^{-1}) were prepared by dissolving suitable amounts of each pure substance in methanol–water (50:50, v/v) and kept stable for 2 months when stored at 4 °C in the refrigerator (assessed by HPLC). Blank plasma and drug plasma were obtained from Department of Pharmacy, Xijing Hospital, Fourth Military Medical University (Xi'an, China).

2.2. Instrumentation and chromatographic conditions

The chromatographic system was composed of a Dionex P680 HPLC pump, a thermostatted column compartment TCC-100, a Dionex Chromatography Management System, a Rheodyne 7225i injector and an RF-2000 spectrofluorimetric detector (California, USA) set at λ_{ex} = 276 nm, λ_{em} = 596 nm. Separations were obtained on a Diamonsil C_{18} reversed-phase column (250 mm × 4.6 mm I.D., 5 μm, Beijing, China) kept at 25 °C. The mobile phase was acetonitrile–phosphate buffer solution (pH 3.0)–triethylamine (33.5:66.5:0.4) and was filtered through a 0.2-μm filter and degassed prior to use. The flow rate was maintained at 1.0 mL min^{-1}. The injections were carried out through a 20-μL loop. A thermostatic bath (HH-2, Guohua Medical Instrument Company, Guangzhou, China), set at 40 °C, was used to implement cloud-point extraction. To accelerate the phase separation process, high-speed centrifuge was employed to centrifuge the sample solutions (Anke TCL-16G, Shanghai, China) in calibrated centrifugal tubes. Vortex Genie Mixture was used for the mixed sample (CAY-1, Beijing Chang'an Instrumental Factory, China).

2.3. CPE procedure

The plasma was prepared by a cloud-point extraction method. In a 5-mL capped centrifugal tube, 1.0 mL of human plasma was spiked with 40 μL of maprotiline solution (internal standard, 10 μg mL^{-1}) and 200 μL of mixed solution containing 0.1 M sodium hydroxide, 0.3 M sodium chloride. The contents were mixed well with a Vortex Genie Mixture for 2 min, and then followed by the addition of 1 mL of 5% Triton X-114 (v/v) aqueous solution. After that, the obtained contents were well mixed again for 5 min, and then incubated in the thermostatic bath at 40 °C for 20 min. After the phase separation was formed by centrifugation at 5000 rpm for 5 min, the surfactant-rich phase was obtained in the bottom of the tube by removal of the water phase. 200 μL of mobile phase was spiked to the surfactant-rich phase. Then the contents were mixed and centrifuged at 16,000 rpm for 5 min respectively. Most of the surfactants and co-extractants such as hydrophobic proteins were precipitated in the bottom of the tube, and twenty microliters of supernatant fluid was injected into the HPLC system for analysis.

2.4. Method validation

2.4.1. Calibration curves

By spiking the appropriate stock solution containing the IS at a constant concentration to 1.0 mL of blank plasma, six effective concentrations were obtained separately 10.00, 50.00, 100.00, 200.00, 400.00, 800.00 ng mL^{-1} for venlafaxine. The quality control (QC) samples were separately prepared in blank plasma at the concentrations of 30.00, 150.00, 600.00 ng mL^{-1} containing the IS at a constant concentration, respectively. The spiked plasma samples (standards and quality controls) were then treated following the previously described CPE procedure and injected into the HPLC. The procedure was carried out in triplicate for each concentration. The obtained analyte/IS peak area ratios were plotted against the corresponding concentrations of venlafaxine and the calibration curves were set up by the least-squares method. The values of limit of quantification (LOQ) and limit of detection (LOD) were calculated, according to Chinese Pharmacopoeia [33] guidelines, as the analyte concentrations gave rise to peaks whose heights were 10 and 3 times the baseline noise, respectively.

2.4.2. Extraction yield (absolute recovery)

By assaying the samples at three QC levels, absolute recoveries of venlafaxine were determined. The analyte/IS peak area ratios were compared to those obtained from the direct injection of the compounds dissolved in the supernatant of the processed blank plasma at the same theoretical concentrations. The extraction yield values were calculated as follows:

$$\left[\frac{(\text{analyte/IS peak area ratio})_{\text{spiked blank}}}{(\text{analyte/IS peak area ratio})_{\text{corresponding standard}}}\right] \times 100\%$$

2.4.3. Precision and accuracy

The precision, including intraday and interday precision expressed as %R.S.D. values, was assessed by assaying the samples at three QC levels five times within the same day and over five different days, respectively. The accuracy was evaluated by mean recovery and expressed as (mean measured concentration)/(spiked concentration) × 100% and %R.S.D. values.

2.4.4. Selectivity

Blank plasma and drug plasma samples from volunteers were subjected to the CPE procedure and injected into the HPLC. The

resulting chromatograms were checked for possible interference from endogenous substances and metabolites of venlafaxine. The acceptance criterion was no interfering peak in the place of an analyte peak.

2.5. Application to pharmacokinetic study

The above validated method was applied to analyze the plasma samples from nine healthy Chinese male volunteers (between 18 and 40 years old) receiving an oral dosage capsule (containing 150 mg venlafaxine). This pharmacokinetic study was approved by the Ethics Committee of Xijing Hospital, Fourth Medical University, China. According to the principles of the Declaration of Helsinki, all volunteers participating in the study offered written informed consent. Blood samples (5 mL) from the antecubital vein were collected into sodium heparin-containing tubes before (0 h) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 8, 10, 12, 24, 36 h after dosing and then immediately centrifuged at 5000 rpm for 10 min. The plasma obtained was stored frozen at −20 °C until analysis.

3. Results and discussion

3.1. Choice of the chromatographic conditions

As the molecular structure of Triton X-114 contains a phenyl-ring, it produces the high background absorbance in the UV region [24], and both venlafaxine and maprotiline are natively fluorescent molecules. The excitation (276 nm) and emission (598 nm) wavelengths were chosen for the subsequent assays [34].

The mobile phase was initially composed of acetonitrile and pH 5.5 phosphate buffer (30/70, v/v). However, this assay condition caused extensive long retention time for the analyte and internal standard. As venlafaxine and maprotiline are ionic compounds, the retention time of venlafaxine and internal standard was markedly influenced by the pH value of the mobile phase. Thus, the range of pH values from 2 to 7 was tested. Good results were obtained with all pH values lower than 3.5. In order to obtain the least retention time, pH 3.0 was chosen. Since the analyte peaks were sometimes asymmetric, 0.4% triethylamine was added to the mobile phase enough for obtaining good peak shapes. Under these optimum chromatographic conditions, the peaks were neat, symmetric and well separated (Fig. 2).

3.2. Optimization of the extraction process

Triton X-114 was chosen as the CPE surfactant because its low cloud-point temperature and high density facilitate phase separation by centrifugation and without FS absorbance [30]. Four different parameters that can influence the extraction efficiency were investigated in our experiments through the fluorescence emission peak area from the spiked samples of venlafaxine at concentration of 400 ng mL^{-1} in plasma. Three repeated tests were performed to obtain a mean value.

3.2.1. Effect of the concentration of surfactant

The theoretical preconcentration factor depends on the concentration of surfactant. From Fig. 3a, it can be seen that the highest extraction efficiency was at 5.0% when the concentration of surfactant in solution varied in the range 0.50–10.0%. When the concentration of surfactant was below 1.0%, it was always suspended in the aqueous phase and was very difficult to separate into two phases. Additionally, when more than 5.0% of surfactants were used, accuracy and precision decreased because the surfactant-rich phase was too large a volume. Also, this phase was more difficult for subsequent analysis. With these experiment results, 5.0% Triton

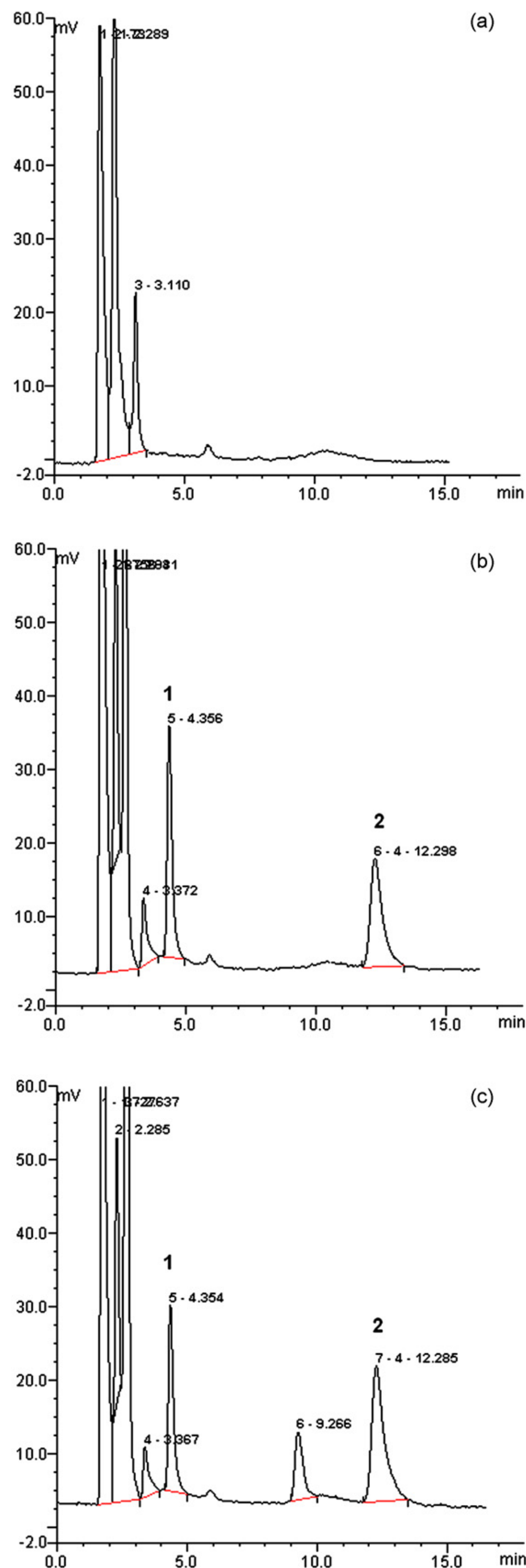

Fig. 2. Typical HPLC chromatograms of a cloud-point extract of plasma samples: (a) a blank plasma sample; (b) a blank plasma sample spiked with venlafaxine and maprotiline; (c) plasma sample 2.0 h after oral administration. Peak identification: 1, venlafaxine; 2, maprotiline.

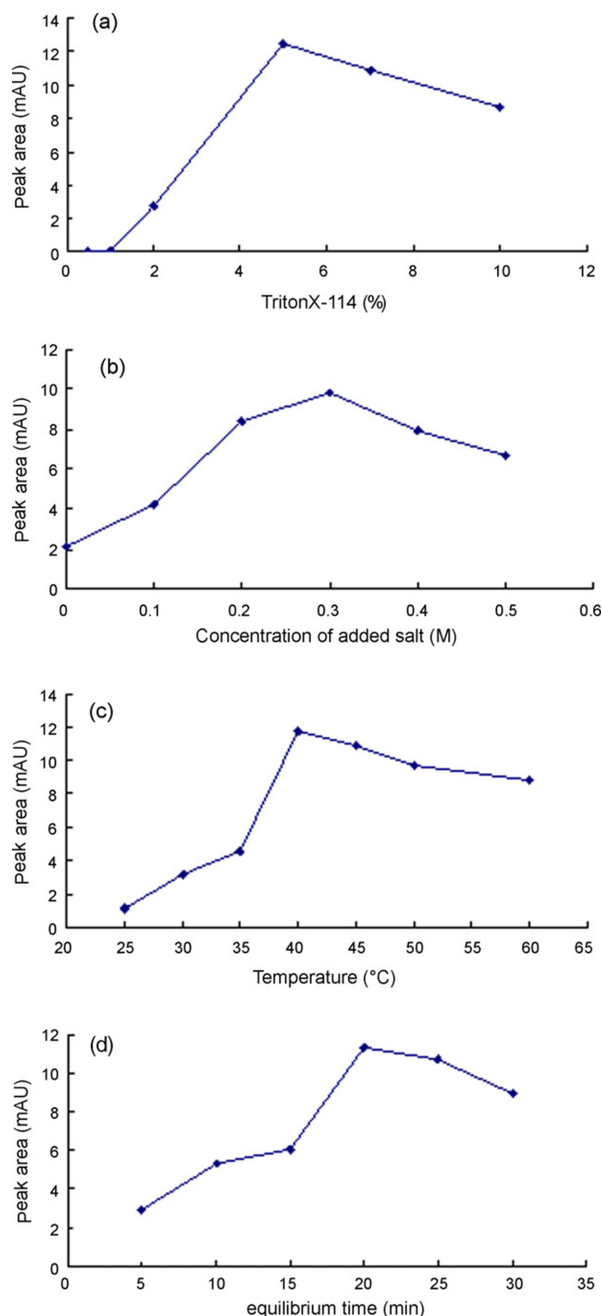

Fig. 3. (a), (b), (c) and (d), respectively, represent the effect of Triton X-114 concentration (%), ionic strength, equilibrium temperature and time on the extraction efficiency of venlafaxine. Other extraction conditions: (a) equilibrium temperature, 40 °C; equilibrium time, 20 min; concentration of sodium chloride, 0.3 M; (b) equilibrium temperature, 40 °C; equilibrium time, 20 min; (c) equilibrium time, 20 min; concentration of sodium chloride, 0.3M; (d) equilibrium temperature, 40 °C; concentration of sodium chloride, 0.3 M.

X-114 was chosen for obtaining best response signals and highest extraction efficiency.

3.2.2. Effect of concentration of sodium chloride

The addition of salts to the solution can facilitate phase separation since they increase the density of the aqueous phase for most non-ionic surfactants. Electrolytes can also change the cloud-point temperatures of the non-ionic surfactant, presumably by a salting-in or salting-out mechanism. The relevant electrolytes are usually used in high concentrations (exceeding 0.1 M). To free venlafaxine from venlafaxine hydrochloride, 0.1 M sodium hydroxide solution is essentially offered. As shown in Fig. 3b, when the concentration of salt reached 0.3 M, the extraction rate was optimal. When the concentration was higher than 0.3 M, the surfactant-rich phase was on the surface of the solution due to the increasing density of the aqueous phase, which made it more difficult for subsequent analysis—the accuracy and precision suffered accordingly [20,30,35,36].

3.2.3. Effect of the equilibrium temperature

It is known that two phases are formed when aqueous solutions of a non-ionic surfactant are heated above the cloud-point temperature. As the equilibration temperature increases, the volumes of the surfactant-rich phase decrease because hydrogen bonds are disrupted and dehydration occurs. The amount of water in a surfactant-rich phase also decreases. Theoretically, the optimal extraction efficiency can be observed on condition that the equilibration temperature is 15–20 °C greater than the cloud-point temperature of the surfactant [35]. As can be seen from Fig.3c, the highest extraction efficiency occurred when the equilibrium temperature reached 40 °C. Higher temperatures only led to the more difficult separation of phases due to the increasing rate of molecular thermodynamic movement.

3.2.4. Effect of the equilibrium time

The analytes must interact with the micelles and get into their core [36]. In order to optimize the extraction process, the equilibration time needs to be considered for a given temperature above the cloud temperature. It has been reported that an equilibration time of 20 min is sufficient to obtain a good extraction and that a longer equilibration time (more than 30 min) does not have any significant effect on the extraction efficiency [37]. As can be seen from Fig. 3d, the extraction rate increased within the range of the equilibrium time from 5 to 20 min, but then decreased slightly in the following 10 min. So the equilibrium time of 20 min was adopted to obtain the highest signal response. This phenomenon was in accordance with a previous report [21]. The procedure was then accelerated by centrifugation at 5000 rpm for 5 min to get a complete phase separation.

3.3. Analysis of standard solutions

The calibration curve was $Y = 0.0038X + 0.0293$ (Y = analyte/IS peak area ratio; X = analyte concentration (ng mL^{-1})). Good linearity ($r^2 = 0.9995$) can be obtained in the concentration range of 10–800 ng mL^{-1}, with the values of LOD (2.0 ng mL^{-1}) and LOQ (10 ng mL^{-1}). Precision was evaluated by assaying the QC samples. The lowest R.S.D. values for intraday precision arrived at 1.3% for venlafaxine while the lowest for interday precision reached 0.6%. The results were listed in Table 1.

3.4. Extraction yield, selectivity and stability

Extraction yield (absolute recovery) of venlafaxine was evaluated by assaying the QC samples. The results of these assays are reported in Table 1. Mean extraction yields were always higher than 90% for venlafaxine.

Selectivity was evaluated by comparing the chromatograms of blank plasma and drug plasma samples from volunteers, which were subjected to the CPE procedure and injected into the HPLC. Fig. 2 shows the typical chromatograms of a blank plasma sample, of a spiked plasma sample with venlafaxine (400 ng mL^{-1}) and IS, and of a plasma sample from a healthy volunteer 2 h after an oral administration. It also shows no significant interference from

Table 1
Precision and extraction yield results

Compound	Concentration ($ng\,mL^{-1}$)	Intraday (R.S.D.%)[a]	Interday (R.S.D.%)[a]	Extraction yield (%)[a]
Venlafaxine	30	9.6	7.2	93
	150	2.9	8.7	95
	600	1.3	0.6	96
IS	400	3.5	2.1	89

[a] $n = 5$.

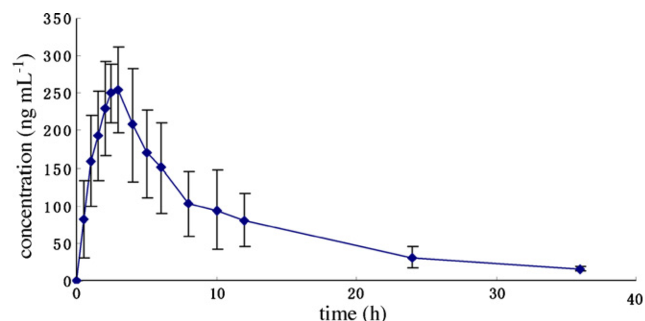

Fig. 4. Mean venlafaxine concentration–time curves after a single oral dose of 150 mg venlafaxine capsule in nine healthy volunteers.

Table 2
Pharmacokinetic data of venlafaxine in humans ($n = 9$)

Parameters	Estimate (mean ± S.D.)
C_{max} ($ng\,mL^{-1}$)	296.5 ± 40.6
T_{max} (h)	2.9 ± 0.7
$AUC_{0\to12}$ ($ng\,h\,mL^{-1}$)	2263.6 ± 922.5
$AUC_{0\to\infty}$ ($ng\,h\,mL^{-1}$)	2455.0 ± 937.7
$t_{1/2}$ (h)	6.6 ± 2.8
V/F ($L\,kg^{-1}$)	326.0 ± 70.0
CL/F ($L\,h\,kg^{-1}$)	47.6 ± 21.4

endogenous substances and metabolites of venlafaxine observed in the place of the analytes.

The results of stability experiments showed that no significant degradation occurred at −20 °C for 30 days and at room temperature for 24 h for venlafaxine plasma samples. The accuracy values of low (30.0 $ng\,mL^{-1}$), medium (150.0 $ng\,mL^{-1}$) and high (600.0 $ng\,mL^{-1}$) concentrations of venlafaxine in human plasma were 30.2 ± 7.23%, 150.80 ± 6.89% and 559.29 ± 3.91%, respectively, at −20 °C for 30 days.

3.5. Pharmacokinetic study of venlafaxine in human plasma samples

The plasma concentrations of venlafaxine at different points were expressed as mean ± S.D., and the mean plasma concentration–time curves were plotted (Fig. 4). The main pharmacokinetic data listed in Table 2 was obtained using the DAS 2.0 (Drug And Statistics, version 2.0) statistical software (Pharmacology Institute of China). Fig. 4 shows venlafaxine reached its C_{max} at about 3.0 h after oral dosing.

4. Conclusion

The cloud-point extraction technique has been successfully applied for the first time as an effective method for the extraction and preconcentration of venlafaxine from human plasma samples. The proposed CPE procedure is less polluting and time-consuming than the liquid–liquid and solid-phase extraction procedures. It was shown that this method is suitable for the analysis of venlafaxine in human plasma samples collected for pharmacokinetic study or therapeutic drug monitoring in humans.

References

[1] M. Tzanakaki, M. Guazzelli, I. Nimatoudis, N.P. Zissis, E. Smeraldi, F. Rizzo, Int. Clin. Psychopharm. 15 (2000) 29.
[2] E.A. Muth, J.T. Haskins, J.A. Moyer, G.E.M. Husbands, S.T. Nielson, E.B. Sigg, Biochem. Pharmacol. 35 (1986) 4493.
[3] E.A. Muth, J.A. Moyer, J.T. Haskin, T.H. Andree, G.E.M. Husbands, Drug Dev. Res. 23 (1991) 191.
[4] J.T. Haskins, J.A. Moyer, E.A. Muth, E.B. Sigg, Soc. Neurosci. 10 (1984) 262.
[5] J.T. Haskins, J.A. Moyer, E.A. Muth, E.B. Sigg, Eur. J. Pharmacol. 115 (1985) 139.
[6] M.W. Rudorfer, W.Z. Potter, Drugs 37 (1989) 713.
[7] E.A. Muth, J.T. Haskins, J.A. Moyer, G.E. Husbands, S.T. Nielsen, E.B. Sigg, Biochem. Pharmacol. 35 (1986) 4493.
[8] C. Salgado-Petinal, J.P. Lamas, C. Garcia-Jares, M.L. Iompart, R. Cela, Anal. Bioanal. Chem. 382 (2005) 1351.
[9] S.M. Wille, P. Van Hee, H.M. Neels, C.H. Van Peteghem, W.E. Lambert, J. Chromatogr. A 1176 (2007) 236.
[10] R. Mandrioli, L. Mercolini, R. Cesta, S. Fanali, M. Amore, M.A. Raggi, J. Chromatogr. B 856 (2007) 88.
[11] R. Waschgler, W. Moll, P. Kónig, A. Conca, Int. J. Clin. Pharmacol. Ther. 42 (2004) 724.
[12] R. Nageswara Rao, A. Narasa Raju, J. Sep. Sci. 29 (2006) 2733.
[13] C. Duverneuil, G.L. de la Grandmaison, P. de Mazancourt, J.C. Alvarez, Ther. Drug Monit. 25 (2003) 565.
[14] J.L. Lima, D.V. Loo, C. Delerue-Matos, A.S. da Silva, Farmaco 54 (1999) 145.
[15] E.M. Clement, J. Odontiadis, M. Franklin, J. Chromatogr. B 705 (1998) 303.
[16] Z. Wei, X. Bing-Ren, W. Cai-Yun, Biomed. Chromatogr. 21 (2007) 266.
[17] J. Bhatt, A. Jangid, G. Venkatesh, G. Subbaiah, S. Singh, J. Chromatogr. B 829 (2005) 75.
[18] S. Rudaz, C. Stella, A.E. Balant-Gorgia, S. Fanali, J.L. Veuthey, J. Pharm. Biomed. Anal. 23 (2000) 107.
[19] F. Merino, S. Rubio, D. Pérez-Bendito, J. Chromatogr. A 998 (2003) 143.
[20] A. Ohashi, M. Ogiwara, R. Ikeda, H. Okada, K. Ohashi, Anal. Sci. 20 (2004) 1353.
[21] B. Delgado, V. Pino, J.H. Ayala, V. González, A.M. Afonso, Anal. Chim. Acta 518 (2004) 165.
[22] J.C. Shen, X.G. Shao, Anal. Chim. Acta 561 (2006) 83.
[23] K.-C. Hung, B.-H. Chen, L.E. Yu, Sep. Purif. 57 (2007) 1.
[24] C. García-Pinto, J.L.P. Pavón, B.M. Cordero, Anal. Chem. 66 (1994) 874.
[25] Z.S. Ferrera, C.P. Sanz, C.M. Santana, J.J.S. Rodriguez, Trends Anal. Chem. 23 (2004) 469.
[26] H. Watanabe, H. Tanaka, Talanta 25 (1978) 585.
[27] L. Wang, Y.Q. Cai, B. He, C.G. Yuan, D.Zh. Shen, J. Shao, G.B. Jiang, Talanta 70 (2006) 47.
[28] M. Du, W. Wu, N. Ercal, Y. Ma, J. Chromatogr. B 803 (2004) 321.
[29] M.D. Rukhadze, S.K. Tsagareli, N.S. Sidamonidze, V.R. Meyer, Anal. Chem. 287 (2000) 279.
[30] R. Carabias-Martínez, E. Rodríguez-Gonzalo, B. Moreno-Cordero, J.L. Pérez-Pavón, C. García-Pinto, E. Fernández Laespada, J. Chromatogr. A 902 (2000) 251.
[31] J. Zhou, S.W. Wang, X.L. Sun, Anal. Chim. Acta 608 (2008) 158.
[32] I. Casero, D. Sicilia, S. Rubio, D. Pérez-Bendito, Anal. Chem. 71 (1999) 4519.
[33] The Pharmacopoeia Committee of China, The Chinese Pharmacopoeia: Part I, The Chemical Industry Publishing House, Beijing, China, 2005, Appendix p. 115.
[34] R.L. Vu, D. Helmeste, L. Albers, C. Reist, J. Chromatogr. B 703 (1997) 195.
[35] R.P. Frankewlch, W.L. Hlnze, Anal. Chem. 66 (1994) 944.
[36] C.M. Santana, Z.S. Ferrera, J.J.S. Rodríguez, Analyst 127 (2002) 1031.
[37] P.M. Holland, D.N. Rubingh (Eds.), Mixed Surfactant Systems, American Chemical Society, Washington, DC, 1992.