Available online at www.sciencedirect.com
SCIENCE DIRECT
Talanta 68 (2006) 928–931
Talanta
www.elsevier.com/locate/talanta

Screening of domperidone in wastewater by high performance liquid chromatography and solid phase extraction methods

Imran Ali [a,*], V.K. Gupta [b], Prashant Singh [c], H.V. Pant [c]

[a] *Environmental Hydrology, National Institute of Hydrology, Roorkee 247667, India*
[b] *Department of Chemistry, Indian Institute of Technology, Roorkee 247667, India*
[c] *Department of Chemistry, D.A.V. (P.G.) College, Dehradun 248001, India*

Received 15 March 2005; received in revised form 14 June 2005; accepted 14 June 2005
Available online 22 July 2005

Abstract

Domperidone is a dopamine D_2 receptor antogonist, which has been used as antiemetic agent in human beings. It has been found in wastewater released by some pharmaceutical industries leading to the contamination of surface and ground water. Therefore, a sensitive, inexpensive and reproducible HPLC-SPE method was developed for the analysis of domperidone in the wastewater. The column used was Waters symmetry C_{18} (15 cm × 0.46 mm, 5 μm). The mobile phase used was phosphate buffer (50 mM, pH 3.5) acetonitrile (80:20, v/v) at the flow rate 2.0 mL/min. The detection was achieved by using UV mode at 230 nm. The retention, separation and resolution factors were 2.63, 3.00 and 3.20, respectively. The percentage recovery of domperidone from wastewater was 95.0%. Celiprolol was used as the internal standard to access the percentage extraction of domperidone from wastewater.

Keywords: Domperidone; Wastewater; High performance liquid chromatography; Solid phase extraction

1. Introduction

Drugs are life saving catalysts but their unnecessary administration into human body is not desirable. Many drug residues have been found in water and the analysis of drug residues is the recent area and increasing its importance day by day [1]. The undesired administration of many drugs into human body possesses certain side effects and also alter the body biological activities leading into notorious effect on the health [2]. Domperidone is a dopamine D_2 receptor antagonist used as antiemetic agent into human beings for preventing nausea and vomiting [3–5]. It is being used widely all over the world for its unique pharmaceutical activity. Some pharmaceutical industries and hospitals are discharging domperidone in their effluents resulting into the contamination of our natural water resources. The presence of any undesirable biodegradable and non-biodegradable constituent into water and other foodstuffs is not desirable [6] and called as pollutant. Therefore, the analysis of domperiodone into wastewater is required and urgent needed. Some HPLC methods are available on the determination of domperidone in biological samples [7–13] but no report is available on its analysis in surface/wastewater. Therefore, attempts are made to develop fast, sensitive, selective and reproducible methods for its analysis into wastewater. The present research describes the analysis of domperidone, which is in the wastewater by using solid phase extraction and high performance liquid chromatography methodologies.

2. Experimental

2.1. Materials and equipments

Domperidone and celiprolol (Fig. 1) were obtained from Kyowa Hakko, Japan and Sigma Chem. Co., USA. Purified water was prepared by Millipore Milli-Q (Bedford, MA,

* Corresponding author. Tel.: +91 1332264471; fax: +91 1332272123.
E-mail address: drimran_ali@yahoo.com (I. Ali).

0039-9140/$ – see front matter © 2005 Published by Elsevier B.V.
doi:10.1016/j.talanta.2005.06.027

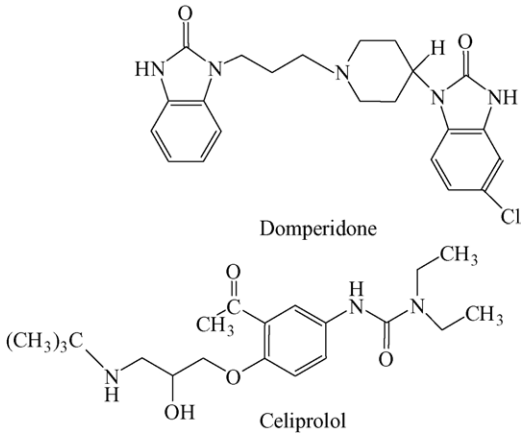

Fig. 1. Chemical structures of domperidone and celliprolol.

USA). Acetonitrile, methanol, acetone, acetic acid reagents were purchased from Merck, Bombay, India. pH was adjusted with a pH meter (Hach, Loveland Co., USA). SPE was carried out using C_{18} Sep-Pak Vac (1.0 mL) cartridge, which was obtained from Waters, Milford Massachusetts, USA. HPLC system (Shimadzu, Japan) consisting of solvent delivery pump (model LC-10AD), injector (model SC), UV–vis absorbance detector (model SPD-10A) and hp laser jet printer was used for this work. The software used in this HPLC system was Agilent LC ChemStation.

2.2. Methodology

2.2.1. Solid phase extraction

To determine the percentage recovery of domperidone in the wastewater, celiporolol was used as the internal standard. 1.0 mL solutions of celiprolol (0.01 mg/mL in ethanol) was mixed in 1.0 L of tap water. This mixture was shaked for about 5 min manually and kept at room temperature for over night. C_{18} cartridge (1.0 mL capacity) was pre-conditioned using methanol (1.0 mL) followed by water (1.0 mL) for 5 min. 1.0 L of the spiked water sample was passed through this cartridge at 50.0 mL/min flow rate. Cartridge was washed with 2.0 mL of deionized water and celiprolol was eluted with methanol (1.0 mL) thrice at 0.50 mL/min flow rate. Three fractions of eluted methanol (1.0 mL each extracted three times) were combined together. Besides, the elution was also tried with other solvents such as dichloromethane, acetonitrile, acetone and ethyl acetate. This methodology was applied to the natural condition by replacing tap water with wastewater. Wastewater sample was collected from municipal discharge and filtered through Whatman filter papers No. 24. The filtered wastewater sample (1 L) was spiked with 0.1 mg/L celiprolol and treated as in case of tap water. After determining the repeatability and percentage recovery of celiprolol, the same SPE extraction procedure was used for domperidone extraction from wastewater.

2.2.2. Analysis by HPLC

An aliquot of 5.0 μL of a standard mixture of domperidone and celiprolol (0.10 mg/mL of each in ethanol) was injected on to a HPLC system described above. The column used was symmetry C_{18} (15 cm × 0.46 mm, 5 μm) and obtained from Waters, USA. The mobile phase used was phosphate buffer (50 mM, pH 3.5) – acetonitrile (80:20, v/v). The mobile phase was filtered and degassed before the use. The flow rate of the mobile phase was 2.0 mL/min under isocratic conditions. All the experiments were carried out at 27 ± 1 °C with column operated at room temperature. The detection was carried out at 230 nm. The peaks of domperidone and celiprolol were identified by their retention times. Domperidon and celiprolol in wastewater sample were identified by comparing their retention times with those of standards. The peaks of these molecules were also confirmed by internal addition method. The percentage recovery of domperidone into wastewater was calculated by using celiprolol (internal addition method). The chromatographic parameters such as retention factor (k), separation factor (α) and resolution factor (R_s) were calculated [14,15]. The quantitative determination of domperidone was calculated as given below:

$$\text{concentration of domperidone} = \frac{C_{\text{std}} \times A_{\text{samp}}}{A_{\text{std}}}$$

in wastewater sample, where C_{std} is the concentration into standard, A_{samp} the peak area of sample and A_{std} is the peak area of standard.

3. Results and discussion

3.1. Solid phase extraction

The recoveries of domperidone from tap and wastewater samples were 96.0 and 95.0% indicating a good efficiency of solid phase extraction methods. The slightly lower values of recoveries in the wastewater may be due the presence of other impurities in the wastewater. No other peaks were observed into HPLC chromatogram showing the selectivity of SPE. SPE was optimized by using different eluting solvents (ethanol, ethyl acetate, acetone, diethylether, chloroform, hexane and dichloromethan), pH of wastewater, flow of eluting solvents and other factors. As a result of extensive experiments the optimized SPE conditions were developed and reported herein.

3.2. Chromatography

Retention factor (k), separation factor (α) and resolution factor (R_s) for the separated domperidone and celiprolol in tap and wastewater samples are given in Table 1. The chromatograms for the separated domperidone and celiprolol, in tap and wastewater samples are given in Figs. 2 and 3, respectively. It is clear from Table 1 that the values of separation and resolution factors for domperidone and celiprolol are 3.0 and

Table 1
Retention (k), separation (α), resolution (R_s) factors and percentage recoveries of domperidone and celiprolol in tap and wastewater samples

Compounds	t_R	Δt	k	α	R_s	Recovery (%)
Domperidone						
Tap water sample	8.29	–	7.63	–	–	96.0
Wastewater sample	8.26	–	7.61	–	–	95.0
Celiprolol						
Tap water sample	3.52	4.78	2.63	3.00	3.20	99.0
Wastewater sample	3.50	4.76	2.60	2.96	3.15	98.5

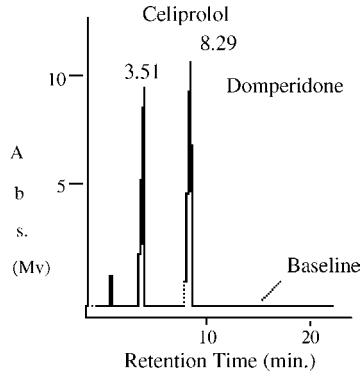

Fig. 2. Chromatograms of domperidone and celiprolol in standard solution (0.10 mg/L of each in ethanol). Column: Waters symmetry C_{18} (15 cm × 0.46 mm, 5 μm). Mobile phase: phosphate buffer (50 mM, pH 3.5) – acetonitrile (80:20, v/v).

3.2 in tap water samples while these values were reported as 2.96 and 3.15 in the wastewater samples. These values and a look of Figs. 2 and 3 clearly indicate a good separation of domperidone and celiprolol in tap and wastewater, respectively. A variation in these values may be because of the interference due to the impurities in the wastewater. A variation in the chromatographic parameters was carried out to obtain the best resolution by using various mixtures of buffer and acetonitrile. As a result of extensive experiments the optimized chromatographic conditions were developed and reported herein.

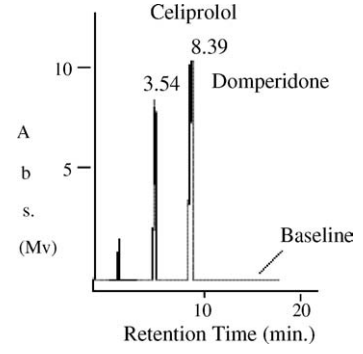

Fig. 3. Chromatograms of domperidone and celiprolol in wastewater. Column: Waters symmetry C_{18} (15 cm × 0.46 mm, 5 μm). Mobile phase: phosphate buffer (50 mM, pH 3.5) – acetonitrile (80:20, v/v).

4. Validation of the methods

The validation of SPE and HPLC methodologies was confirmed by carrying out these experiments three times ($n = 3$) under the identical experimental conditions. The regression analysis was carried out using Microsoft Excel program. The values of standard deviations obtained were ±0.15 to ±0.18 and ±0.21 to ±0.25 for HPLC (retention times) and SPE (percentage recoveries) methods, respectively. The values of the correlation coefficients (R^2) were 0.9999 and 0.9998 for HPLC and SPE methods, respectively. The confidence levels were 98.0–99.0% and 97.0–98.0% for SPE and HPLC methods, respectively. The limit of detection (LOD) and the limit of quantitation (LOQ) were determined as three and five times the baseline noise, respectively, following the United States Pharmacopoeia [16]. The values of limit of detection and limit of quantification were 10 and 50 μg/mL, respectively. These values of validation parameters indicate good reproducibilities of SPE and HPLC methodologies.

5. Conclusion

The reported SPE and HPLC methods are rapid, selective, reproducible and inexpensive in the nature. The percentage extraction of domperidone from wastewater is quite good (95.0%). Therefore, these methods can be used for the analysis of domperidone in waste, surface, ground and mineral water samples satisfactorily.

References

[1] K. Kümmerer, A. Al-Ahmad, B. Bertram, M. Wießler, Chemosphere 40 (2000) 767.
[2] K. Kümmerer, Chemosphere 45 (2001) 957.
[3] J. Heykants, A. Kueaps, W. Meuldermans, M. Michiels, Eur. J. Drug Metab. Pharmacokin. 6 (1981) 27.
[4] J. Heykants, R. Hendriks, W. Meuldermans, M. Michiels, H. Scheygrond, H. Reynjens, Eur. J. Drug Metab. Pharmacokin. 6 (1981) 61.
[5] Y.C. Huang, J.L. Colaizi, R.H. Bierman, R. Woestenborghs, J. Heykants, J. Clin. Pharmacol. 26 (1986) 628.
[6] I. Ali, H.Y. Aboul-Enein, Chiral Pollutants: Distribution, Toxicity and Analysis by Chromatography and Capillary Electrophoresis, John Wily & Sons, Chichester, UK, 2004.
[7] G.B. Biship-Preunding, H. Vergin, J. Chromatogr. 273 (1983) 453.

[8] H. Takahashi, H. Ogata, H. Echizen, T. Ishizaki, J. Chromatogr. 419 (1987) 243.
[9] K. Yamamoto, M. Hagino, H. Kotaki, T. Iga, J. Chromatogr. B 720 (1998) 251.
[10] A.P. Argekar, S.J. Shah, J. Pharm. Biomed. Anal. 19 (1999) 813.
[11] A.P. Zavitsanson, C. MacDonald, E. Bassoo, D. Gopaul, J. Chromatogr. B 730 (1999) 9.
[12] M. Kobylinska, K. Kobylinska, J. Chromatogr. A 744 (2000) 207.
[13] M.J. Smit, F.C. Sutherland, H.K. Hundt, K.J. Swart, A.F. Hundt, J. Els, J. Chromatogr. A 949 (2002) 65.
[14] M.C. McMaster, HPLC: A Practical User's Guide, Wiley & Sons, 1994.
[15] G. Lunn, N.R. Schmuff, HPLC Methods for Pharmaceutical Analysis, Wiley & Sons, 1997.
[16] The United State Pharmacopeia, 24th ed., United States Pharmacopeial Convention Rockville, MD, 2000, p. 2150.