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Simultaneous determination of cinnarizine and domepiridone maleate from tablet dosage form by reverse phase ion pair high performance liquid chromatography

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Abstract

A new simple, precise, rapid and selective reverse phase ion pair high performance liquid chromatography (HPLC-RP) method has been developed for the simultaneous determination of cinnarizine (CINN) and domepiridone maleate (DOME) from tablets using acetonitrile–methanol–water–0.1 N sulfuric acid (37:10:48:5 v/v/v/v) containing sodium lauryl sulfate (0.01 M), as a mobile phase and a Machery Nagel nitrile column (10 μ, 25 cm × 4.0 mm i.d.) as the stationary phase. The flow of mobile phase through the column was kept at 1.0 ml min^{-1} through out the analysis. Detection was carried out using a UV detector at 225 nm. The retention times for CINN and DOME were 4.73 and 9.41 min, respectively. The linearity range and percentage recoveries for CINN and DOME were 4–1000 and 60–750 μg ml^{-1} and 99.90 and 99.60%, respectively.

Keywords: Ion pair HPLC; Cinnarazine; Domepiridone maleate; Simultaneous determination

1. Introduction

Cinnarizine (CINN), chemically (*E*)-1-(diphenylmethyl)-4-3-phenyl(prop-2-enyl) piperazine, is a piperazine derivative with a histamine H_1-receptor and calcium channel blocking activity. It is used for the symptomatic treatment of a nausea and vertigo caused by Meniers disease and other vestibular disorders. It is also used for the prevention and treatment of motion sickness and in the management of various peripheral and vascular disorders [1]. It is officially in the B.P. [2].

Domepiridone, chemically 5-chloro-1-(1-(3-(2,3-dihydro-2-oxo-1*H*-benzimidazol-1-yl)propyl)-4-piperdinyl)-1,3-dihydro-2*H*-benzimidazol-2-one, is a dopamine antagonist. In the form of its maleate salt, Domepiridone maleate (DOME), it is used as an antiemitic for the short term treatment of nausea and vomiting in various aetiologies, including that associated with cancer therapy including nausea and vomiting associated with levodopa or bromocriptine therapy for parkinsonism [3]. It is officially in the B.P. [4].

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There are few combination dosages of CINN and DOME on the market these days. CINN and DOME are determined from the active substance by a titrimetric method [2,4]. CINN is determined by spectrophotometry [5–7], titrimetry [8], HPLC [9] and an ion selective electrode method [10] and DOME is determined by spectrophotometry [11,12] and HPTLC [13] from formulations. However there is no method available for the simultaneous determination of these two drugs. An attempt was, therefore, made to develop a new, rapid and sensitive method for the simultaneous determination of CINN and DOME. The results are presented and discussed in this paper.

2. Experimental

2.1. Instrumentation

A liquid chromatographic system from Waters comprising of an autoinjector, a quaternary gradient low-pressure pump and a UV–vis variable wavelength detector connected to Millenium software for controlling the instrumentation as well as processing the data generated, was used.

2.2. Reagents and chemicals

Sodium lauryl sulfate, sulfuric acid and methanol for sample preparation were of AR grade whereas acetonitrile and methanol were HPLC grade supplied by S.D. Fine Chemicals, Tarapur, Thane, Maharashtra, India.

2.2.1. Reference standards

CINN and DOME were obtained from FDC, Mumbai, and their purity was 99.51 and 99.41%, respectively.

2.3. Chromatographic condition

The mobile phase consisted of acetonitrile–methanol–water–0.1 N sulfuric acid (37:10:48:5 v/v/v/v) containing sodium lauryl sulfate (0.01 M), flowing through the column at a constant flow rate of 1.0 ml min^{-1}. A Machery Nagel nitrile column (10 μ, 25 cm × 4.0 mm i.d.) was used as the stationary phase. Detection was carried out using a UV detector at 225 nm.

2.4. Standard preparation

2.4.1. Standard stock solution

Standard stock solutions of 1.0 mg ml^{-1} CINN and 0.95 mg ml^{-1} DOME were prepared by dissolving 100 mg standard CINN and 95 mg standard DOME in 100 ml methanol.

2.4.2. Working standard solution

Each standard stock solution (10 ml) was diluted to 50 ml with the mobile phase. This gave a concentration of 200 μg ml^{-1} CINN and 190 μg ml^{-1} DOME. This solution was used as the working standard for analysis of all the samples.

2.5. Sample preparation

Twenty tablets were weighed and crushed to fine powder. Powder equivalent to 20 mg CINN and 19 mg DOME was weighed in a 100 ml volumetric flask. Methanol (50 ml) was added and, after sonnication for 10 mins, the solution was cooled and made up to the mark with methanol. The solution was centrifuged and the supernatant was used for the analysis.

2.6. Calibration

From above stock solutions various dilutions were made to get solutions of 1–1000 μg ml^{-1} CINN and 0.95–950 μg ml^{-1} DOME.Microsoft Excel software was used to plot the peak areas versus concentrations in μg ml^{-1}.

2.7. Evaluation

The peak areas for all the peaks were recorded. From the peak areas the respective amounts were computed as follows:

$$\text{Amount} = \frac{R_{\text{spl}} \times C \times D \times \text{Av. wt.}}{R_{\text{std}} \times W}$$

Where R_{spl} is the area of the CINN/DOME peak in the sample solution, R_{std} is the area of the CINN/DOME peak in the standard solution, C is

the concentration of the standard CINN/DOME in mg ml^{-1}, D is the dilution factor for the sample and W is the weight of the tablet powder in mg.

3. Results and discussions

3.1. Chromatography

Reverse phase LC using a buffer in the pH range 3–4 CINN and DOME gave a tailing peak which was not deemed fit for analytical purposes considering the system suitability criterion and the resolution required for the mixture of these two drugs. The ion pair approach was therefore thought of as an alternative in order to reduce the tailing and improve the resolution. Sodium lauryl sulfate at a 0.01 M concentration level was selected to serve this purpose. The tailing for both the peaks was reduced considerably and brought close to 1 which is an ideal requirement for chromatographic analysis. Sodium lauryl sulphate was used as the ion pairing agent as it is well known that compared to the salts of lower chain acids such as octane sulfonic acid sodium lauryl sulphate helps to remove the tailing to a greater extent. CINN and DOME were well resolved in a reasonable time of 12 min. The initial separation was developed using methanol and water only. Subsequently it was felt that the same separation could carried out by adding acetonitrile which can help in reducing the viscosity of the mobile phase and hence reduce the back pressure and increase the column life. A representative graph of this is shown in Fig. 1.

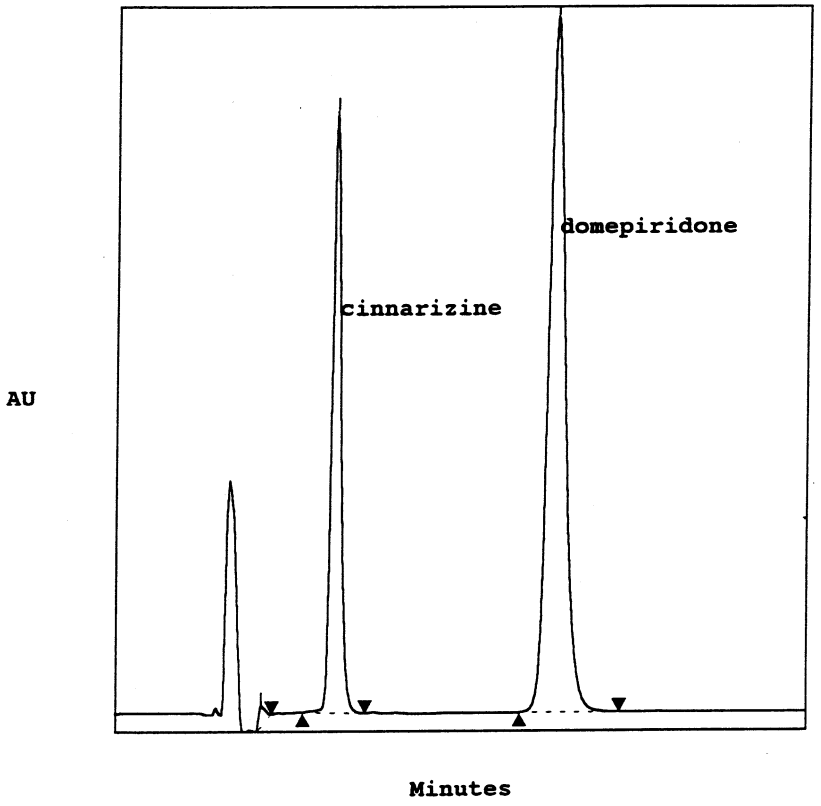

Fig. 1. A chromatogram showing the separation between CINN and DOME.

Table 1
Parameters of system suitability

No.	Parameters	CINN	DOME
1	Theoretical plates	2926	3378
2	Resolution factor	—	9.33
3	Tailing factor	1.11	1.10
4	R.S.D. of seven injections	0.45	0.37

3.2. System suitability

The system suitability test was applied to a representative chromatogram to check the various parameters such as column efficiency, resolution, precision and peak tailing. The results obtained are shown in Table 1. The resolution between CINN and DOME was 9.33. The number of theoretical plates for CINN and DOME were 2944 and 3416, respectively. All these parameters were evaluated with the background of general regulatory requirements which also suggests good chromatographic conditions.

3.3. Linearity

CINN showed a linearity of response between 4 and 1000 μg ml^{-1}. DOME showed a linearity of response between 60 and 750 μg ml^{-1}. These linearities were represented by a linear regression equation as follows:

Table 2
Results of the HPLC analysis of the tablets

	Sr. No.	CINN (%)	DOME (%)
Johnson and Johnson	1	97.35	95.30
	2	97.60	95.75
	3	98.02	96.24
	4	97.58	95.98
	5	98.54	96.12
Mean		97.81	95.87
R.S.D.		0.48	0.38

$$Y_{CINN} = 11.051x + 63.79 \quad (r = 0.9998)$$

$$Y_{DOME} = 32.84x - 11.75 \quad (r = 0.9999)$$

3.4. Assay

The content of CINN and DOME found in the tablets by the proposed method are shown in Table 2. The low values of R.S.D. indicates that the method is precise and accurate.

3.5. Accuracy and precision

The recovery experiments were carried out by spiking the already analysed samples of the tablets with three different known concentrations of standard CINN and DOME. These results are summarised in Table 3. The percent recoveries for

Table 3
Results of the recovery analysis

	Amount present (mg 100 ml^{-1})	Amount found (mg 100ml^{-1})	Recovery (%)
CINN			
1	18.95	18.91	99.77
2	20.26	20.29	100.13
3	22.42	22.40	99.98
Average			99.96
S.D.			0.18
DOME			
1	19.45	19.40	99.77
2	21.57	21.54	99.90
3	23.47	23.40	99.74
Average			99.80
S.D.			0.08

CINN ranges from 99.77 to 100.13% and for DOME the is range is from 99.30 to 99.90%.

3.6. Stability of sample solution

The sample solution injected after 12 h did not show any appreciable change.

4. Conclusions

The proposed method is fast, accurate and precise for the determination of CINN and DOME from tablets. Hence it can be employed for routine quality control of tablets containing these two drugs.

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