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A QUICK, PRECISE AND ACCURATE METHOD FOR THE DETERMINATION OF NITRAZIPAM BY THE RING – OVEN TECHNIQUE

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A convenient, simple, sensitive, accurate, reproducable and less time consuming method for the determination of nitrazipam using sodium hydroxide as colour producing reagent has been devised by ring-oven technique and is recommended for routine analysis.

INTRODUCTION

Nitrazipam (1,3-dihydro-7 nitro-5 phenyl 1-2 H-1,4 benzodiazepin-2 one) is widely used as tranqualizer in medicine. The British Pharmacopoeia method for its determination is lengthy, laborious, complicated and associated with may chances of added error. Due to the importance of the compound in pharmacy, standardisation of a convenient, precise and accurate method was considered desirable.

The Weisz ring-oven technique has established its importance in the analysis of a variety of substances in nanograme amounts. Simplicity and convenience are the other salient features for which its use is popular in analytical chemistry.

Nitrazipam gives bright yellow colour with sodium hydroxide[1], which reaction has been made the basis of the present studies for the standardisation of a convenient, sensitive, accurate and reproducable method for the determination of nitrazipam using ring-oven technique and some of the results of these studies have been reported in this communication.

EXPERIMENTAL

Reagents

Nitrazipam standard Solution. Nitrazipam-10 tablets (ROCHE) were well ground and extracted 10 times using 30 ml of alcohol for each extraction and after filteration the solution so obtained was standardised potentiometrically[2]. The standard solution so preparaed contained 1.465 μg/μl.

Sodium Hydroxide Solution. Sodium hydroxide solution was prepared by dissolving 4.0 g of the A.R. Grade substance (Merck) in 100 ml double distilled water and used as such.

Apparatus

A ring-oven with 110° working temperature, Whatman filter paper No.41 and automatic filling micropipettes of 1,2, and 5 μl capacity (Karl-Kolb Scientific and Technical Supplies, Buchschlag, Frankfort-BRD) were used for these experiments.

All other reagents used were also of analytical grade or equivalent purity and glass-ware was also A-grade officially calibrated.

Procedure

Nitrazipam unknown solution was applied at the center of the filter paper with micropipette. A volume of 2μl of sdium hydroxide (4.0 %) was also applied to the same point. The filter paper was placed in the ring-oven and the product was washed from the centre to the ring zone with distilled water. A sharp yellow colour ring was obtained immediately. About 3-4 washings were enough to wash the product to the ring zone. The rings prepared so were evaluated by comparison with a standard scale according to the known method[3]. Shelf-life of the standard scale was also studied.

Since the colour of the standard scale was stable for two days only hence Segment technique was also employed. According to this method 1 μl of each of the unknown and two different standard solutions were separately spotted at the three points marked around the centre of the filter paper so as to make an equilateral triangle, 2 μl of sodium hydroxide solution was applied at the centre, placing this

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Table. Determination of nitrazipam using

	Segment technique			Universal scale method		
	Amount given ng	Amount found ng	Error %	Amount given ng	Amount found ng	Error %
1.	150.00	160.00	+6.66	530.00	560.00	+5.65
2.	300.00	310.00	+3.33	630.00	620.00	−1.57
3.	450.00	450.00	±0.00	750.00	719.00	−4.13
4.	600.00	600.00	±0.00	810.00	810.00	±0.00
5.	750.00	700.00	−6.66	1060.00	990.00	−6.60
6.	1050.00	1000.00	−4.76	1280.00	1200.00	−6.25
7.	1200.00	1200.00	±0.00	1610.00	1530.00	−4.96
8.	1800.00	1800.00	±0.00	2180.00	2300.00	+5.51
9.	2400.00	2400.00	±0.00	2800.00	2800.00	±0.00
10.	3000.00	3000.00	±0.00	3650.00	3650.00	±0.00

paper on the rign-oven washing with distilled water was done. About 2-3 washings were sufficient to wash the product to the ring-zone. Immediately three sharp segments were obtained which were evaluated according to the already described method (4-5).

RESULTS AND DISCUSSION

The reaction between nitrazipam and sodium hydroxide is very sensitive. Colour was produced immediately when the reactants were applied on the paper. The accuracy and reliability of the method can be seen from the results given in the table and the method described here can be used for routine analysis of nitrazipam in pharmaceuticals.

The standard scale method could not be recommended because after two days of the preparation of the scale its colour started deteriorating in a way that results loaded with error and hence not acceptable analytically were obtained.

As the standard scale was stable only for two days, hence alternately Segment techniques was preferred as the stability of the colour of the end product is not desired here for a longer period. Nitrazipam can be determined within the range from 530 ng to 3.65 μg with a maximum error of −6.6 % by making use of universal scale while by Segment Technique, the error of determination within the range from 150 ng to 3.00 μg/μl is of the the order of ± 6.66 %.

The method reported here is convenient, simple, sensitive, accurate, reproduceable and less time consuming. Hence it is recommended for the routine analysis of nitrazipam.

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