DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 17(16), 2239-2244 (1991)

ANALYSIS OF NIFEDIPINE AND RELATED COMPOUNDS IN SOFT GELETIN CAPSULES BY LIQUID CHROMATOGRAPHY

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ABSTRACT

A simple, sensitive, highly specific, stability-indicating, reversed-phase HPLC method for the quantitation of nifedipine and its related compounds such as nitrophenyl pyridine, nitrosophenyl pyridine analogs with average recoveries greater than 100% were obtained using a mobile phase methanol-water (55:45, v/v) at 265 nm.

INTRODUCTION

Nifedipine (3,5-pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-,dimethyl ester, is available in tablet and capsule formulations (1). There are several chromatographic methods (2-10) for the analysis of nifedipine and its related compounds from dosage forms. However, USP method is insufficient to

establish the separation of related compound nitrophenyl pyridyne analog from capsule excipients. This paper proposes an HPLC method which overcomes the deficiencies in the USP method due to its capability of separating interfering component propyl paraben.

MATERIALS, METHODS AND APPARATUS

Nifedipine and its related analogs were obtained from the USP commission. All excipients used were I.P. grade while acetonitrile or methanol were of HPLC grade. Water used was double distilled. The liquid chromatograph consisted of a model 510 pump, model 712 WISP, model 484 tunable detector and a data module 745B from Water's, fitted with a 7125, 20 µl Rheodyne valve injector. An ODS column, TSK-GEL, 250 mm X 3.9 mm, 5 µm, TOSOH, Tokyo, Japan was used.

The standard solutions of USP nifedipine, 0.1 mg/ml, nifedipine nitrophenyl analog, 0.0015 mg/ml, nifedipine nitrosophenyl analog, 0.0075 mg/ml were prepared in the mobile phase. The sample preparation was same as reported earlier (10). For comparison, mobile phase as per USP XXII was also prepared and used.

RESULTS AND DISCUSSION

The proposed HPLC method is quite specific as evident from the separation of nifedipine, nitrophenyl pyridine, nitrosophenyl pyridine analogs and propyl

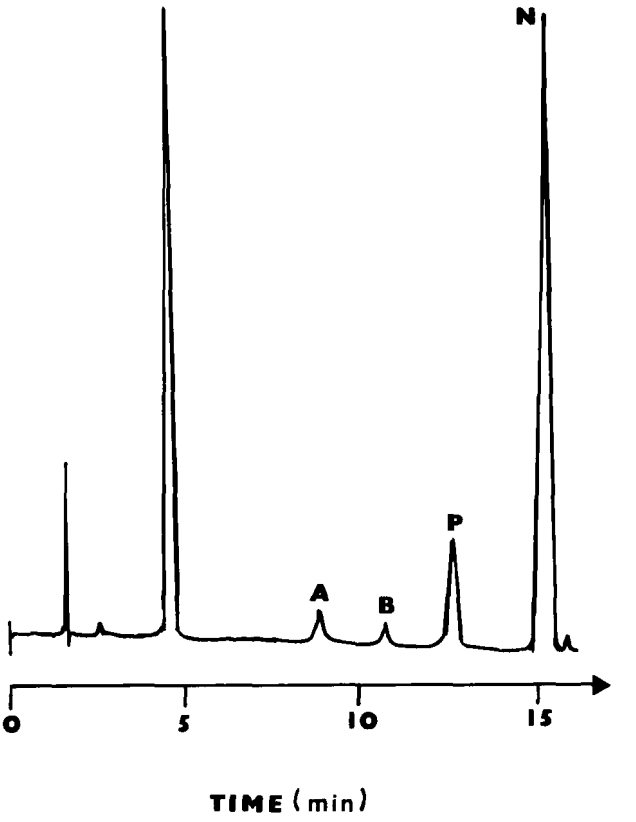

FIGURE 1

A chromatogram of sample as obtained with the proposed method. Peak labels : A : nitrophenyl pyridine analog of nifedipine, B : nitrosophenyl pyridine analog of of nifedipine, P : propyl paraben and N : nifedipine.

paraben (Figure 1). As per the official USP method, propyl paraben was found to co-elute along with nitrophenyl pyridine analog. The linearity of the method was established by analysing nifedipine in the concentration range 0.05 to 0.25 mg/ml, regression equation being $y = 1.0298 x + 4.8599$.

TABLE 1

Compound	% Recoveries		Detection Limits (µg/ml)	
	Proposed	USP XXII	Proposed	USP XXII
Nifedipine	102.6 ± 1.6	103.1 ± 1.35	0.5	0.5
Nitrophenyl analog	103.8 ± 1.8	102.1 ± 1.15	0.25	-
Nitrosophenyl analog	101.9 ± 2.05	102.8 ± 1.6	0.05	-
Nifedipine (5 mg/capsule)	96.2 ± 1.5	97.4 ± 1.78	-	-
Nifedipine (10 mg/capsule)	100.4 ± 1.9	98.3 ± 1.95	-	-

The accuracy and sensitivity of the method is assessed by determining the recovery of related impurity analogs and nifedipine by both the methods as summarised in Table 1. Six replicate assays of commercially available nifedipine soft geletin capsules (5 mg or 10 mg) were performed by present method and also by the USP XXII method. Relative retention time for nifedipine and its related analogs as well as excipients were comparable by both the methods. Theoretical plates achieved were in the order of 16,980 and 22,890 by the USP XXII and that with the proposed method respectively.

This procedure is recommended for regular in-check Quality Control release and evaluating shelf-life stability of capsules and bulk drug equivalently.

ACKNOWLEDGEMENTS

The authors are grateful to Dr.V. Srinivasan of USP Commission for supplying reference standards and for continued cooperation in establishment of public standards for drugs. Thanks are also due to Dr.P.D. Sethi for its useful comments, discussions and suggesstions made from time to time during the course of this work.

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