International Journal of Pharmaceutics, 6 (1980) 87–88

Letter to the Editor

HPLC-separation of codergocrine-mesylate (dihydroergotoxine-methanesulfonate)

Dear Sir,

In 1978 the separation of dihydroergotoxine-methanesulfonate into its 4 components dihydroergocornine-, dihydroergocristine-, dihydro-α-ergocryptine- and dihydro-β-ergocryptine-mesylate was reported (Hartmann et al., 1978). This separation was achieved by means of reversed-phase high performance liquid chromatography (HPLC). The objective was to determine the quantitative ratio of these components in the drug substance as well as in various types of pharmaceutical dosage forms, because all relevant clinical studies, particularly with respect to safety and efficacy, were carried out with a product containing a well defined ratio of the 4 components (Hartmann et al., 1978). Ali and Strittmatter (1979) claim in this journal that the separation of the isomers dihydro-α-ergocryptine and dihydro-β-ergocryptine should be avoided because of analytical problems and pharmacodynamic thoughts.

Based on the following facts which have been published, I do not agree with the arguments used:

(1) Wehrli et al. (1978) demonstrated in a general article the advantages of using organic amines in order to achieve optimum chromatographic separation under alkaline conditions.

(2) Animal data published by (Berde and Schild, 1978; Müller-Schweinitzer and Weidmann, 1978) indicate important differences in the pharmacodynamic properties of the two isomers, in particular in tests involving the central nervous system. According to Loew et al. (1978) significant differences in the activities of the alpha- and beta-isomer were discovered in the Ungerstedt rat.

The analytical procedure described by Hartmann et al. (1978) is being widely used in many routine laboratories in the world, including test laboratories of pharmacopoeia commissions without revealing any particular difficulty. With the special mobile phase used, as many injections can be made on the same HPLC-column as with other solvent systems used in reversed-phase HPLC. A progress report on the method and its extended applicability is being prepared and will be published in this journal.

(Received June 2nd, 1980)
(Accepted June 2nd, 1980)

H. BETHKE
Analytical Research and Development,
Pharmaceutical Department,
Sandoz Ltd.,
CH 4002 Basel,
Switzerland.

Hartmann, V., Rödiger, M., Ableidinger, W. and Bethke, H., Dihydroergotoxine: separation and determination of four components by high-performance liquid chromatography. J. Pharm. Sci., 67 (1978) 98–103.

Ali, S.L. and Strittmatter, Th., Separation and determination of four ergot alkaloids, dihydro-

ergotamine-, dihydroergocornine-, dihydroergocryptine- and dihydroergocristine methanesulfonates by high performance liquid chromatography. Int. J. Pharm., 4 (1979) 111–118.

Wehrli, A., Hildebrand, J.C., Keller, H.P., Stampli, R. and Frei, R.W., Influence of organic bases on the stability and separation properties of reversed-phase chemically bonded silica gels. J. Chromatogr., 149 (1978) 199–210.

Berde, B. and Schild, H.O., Ergot alkaloids and related compounds. Handb. Exp. Pharmacol., 49 (1978).

Müller-Schweinitzer, E. and Weidmann, H., Basic pharmacol. properties. Handb. Exp. Pharmacol., 49 (1978) 87–319.

Loew, D.M., van Deusen, E.B. and Meier-Ruge, W., Essentials of central nervous system. Handb. Exp. Pharmacol., 49 (1978) 421–531.