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Letter to the Editor

Separation and determination of four ergot alkaloids

Dear Sir,

Bethke et al. have been able to separate dihydro-alpha-ergocryptine-, and dihydro-beta-ergocryptine methanesulfonates along with dihydroergocornine and dihydroergocristine methanesulfonates using a mobile phase with a strong alkaline pH value of 12 in about 18 min (1978). In our work the 4 ergot alkaloids, dihydroergotamine-, dihydroergocryptine-, dihydroergocornine- and dihydroergocristine methanesulfonates were elegantly separated with a mobile phase having only a pH value of about 7 (1979). Nevertheless alpha- and beta-isomers of dihydroergocryptine methanesulfonate were eluted together with this mobile phase. We further reported that the separation of the two isomers could also be obtained with the mobile phase (in our work marked as mobile phase V: acetonitrile–water–diethylamine; 37.5 : 62.5 : 2.1) of more alkaline pH of about 12.

(1) In our experience, contrary to literature reports, prolonged exposure of an analytical reversed-phase column to strongly alkaline aqueous mobile phases does effect the column efficiency.

(2) We quoted the paper of Schlientz et al. (1968), who incidently belong also to Sandoz Corporation, Basel, as do Bethke et al. in which is mentioned: 'pharmacological investigations showed that alpha-ergocryptine and dihydro-alpha-ergocryptine differed only insignificantly in their pharmacodynamic properties from beta-ergocryptine and dihydro-beta-ergocryptine respectively'.

(3) Due to this fact we wrote in our communication that there should be no immediate need for the routine separation of these isomers with a strongly alkaline mobile phase (pH 12) which ultimately effects the column efficiency. It was further anticipated that if the need still arises for the separation of isomers, this could be then obtained with the mobile phase V (pH 12).

(4) Bethke et al. have not chosen proper words ('pharmacodynamic thoughts!') or cited us incorrectly (the word 'avoided' was not used by us) to make their point.

(5) Remark no. 2 by Bethke, 'Animal data published indicate important difference' is misleading. The literature cited (Müller-Schweinitzer et al. (1978), pp. 87–319) contains almost 230 pages of information on ergot alkaloids. Nothing could be found in this article which indicates important and significant differences in the pharmacodynamic properties of the two isomers. Pharmacological effect attributed to alpha- and beta-isomers of dihydrogen-ergocryptine is given on p. 142, but the literature quoted here (Schlientz et al., 1968) is the same, which has been correctly cited by us in our original paper. On p. 102 only a slight difference of the two isomers in respect to their antagonism of 5-HT is mentioned. It would have been better on part of Bethke et al. if they had quoted exact page number(s) of such a lengthy article to show where the important differences lie.

The second reference quoted by Bethke (Loew et al., 1978, pp. 421–531) is a lengthy article of 110 pages where again no specific page numbers are given. Although different activities of alpha- and beta-compounds are given (p. 460) there is no difference in two

isomers in respect to their inductions of the stereotyped behaviour in the rat (p. 464; see also p. 466).

We would like to stress that our paper was written from a purely chromatographic point of view and only marginal attention was paid to the pharmacological aspects of individual isomers.

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Ali, S.L. and Strittmatter, Th., Separation and determination of four ergot alkaloids, dihydroergotamine-, dihydroergocornine- and dihydroergocristine methanesulfonates by high performance liquid chromatography. Int. J. Pharm. 4 (1979) 111–118.

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.

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

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