AMINOPHYLLINE SUPPOSITORY DECOMPOSITION: GC MASS SPECTROMETRY AND GC-MASS SPECTROMETRY OF THE DECOMPOSITION PRODUCTS

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As yet there is no completely satisfactory method for accurately measuring the concentrations of the alkanylyl diamides of ethylene diamine that are known to be products of aminophylline suppository decomposition (Brower et al, 1980). Differential scanning calorimetry showed that the diamides appeared to interact with the triglycerides in the suppositories to give endotherms at temperatures which are shifted compared to those of the pure diamides.(Pryce-Jones, et al, 1987, 1989). This, and the difficulty of incorporating standard concentrations of pure diamides into the suppository bases, made quantitation imprecise. Thus, another method for detecting the presence of diamides in aminophylline suppositories was required.

Suppository bases do not contain any odd carbon chain alkoyl groups (Pryce-Jones, et al, 1987). Extraction of diamides into butan-2-ol and hydrolysis of the diamides with 10% H_2SO_4 in butan-2-ol at high temperature (120°C) allowed the fatty acid content to be assayed by GLC (Pye 304 2m 3% OV-17 on Gas Chrom Q 100/120 Temp. 120 to 200°C at 10°/min) confirming that the distribution of alkanylyl diamides recovered from decomposed aminophylline suppositories is very similar to that of the suppository bases. However, the method did not facilitate the determination of the different species of diamides and did not detect the presence of, or measure the concentrations of heterogeneous diamides.

High resolution electron impact mass spectrometry allowed the determination of molecular ions of all the expected homogeneous diamides and many of the heterogeneous diamides. However, similar experiments on pure homogeneous diamides showed that molecular ions of some heterogeneous and odd carbon number diamides were detected. This could only be explained as an artefact of the fragmentation process.

The alkanylyl diamides were separated by capillary gas/liquid chromatography (10m BP1 column on a Hewlett Packard 5980) temperature gradient of 200 to 327°C at 30°C/min and held at 327° for 20 min. Flame ionisation detection showed that all of the pure homogeneous diamides (odd and even alkoyl carbon numbers 12 to 18) were separated. This was transferred onto the Hewlett Packard Model 5988A GC mass spectrometer (70eV electron impact) allowing the detection of molecular ions corresponding to each of the homogeneous diamides (Table 1). Separate peaks could not be detected for heterogeneous diamides where their masses coincided with those of the homogeneous diamides implying co-elution of different diamides of identical masses. Peaks which corresponded to heterogeneous diamides whose masses are the same as those of homogeneous diamides containing two odd carbon chain alkoyl groups were detected (e.g. C14-C16 = C15-C15, Table 2).

It is concluded that the reaction of aminophylline with triglyceride suppository bases produces a range of homogeneous and heterogenous alkanylyl diamides whose content of fatty acids residues broadly reflects that of the acids in the suppository base.

Table 1: Pure diamides

C.No.	Mass	R_t(min)
26	424.40	4.45
28	452.44	4.85
30	480.46	5.29
32	508.50	5.83
34	536.52	6.55
36	564.56	7.49
38	592.59	8.93

Table 2: Extracted suppositories

R_t(min)	Corresp.C.No.	% Total
4.41	12-12	31.7
4.83	12-14(13-13)	30.6
5.27	14-14	19.3
5.82	14-16(15-15)	16.5
6.50	16-16	1.8

Brower, J.P. et al (1980), J.Pharm.Sci., 69(8), 942-945
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