THE DETERMINATION OF THIOMERSAL IN THE PRESENCE OF ITS BREAKDOWN PRODUCTS: AN EVALUATION OF THE NEURATH METHOD

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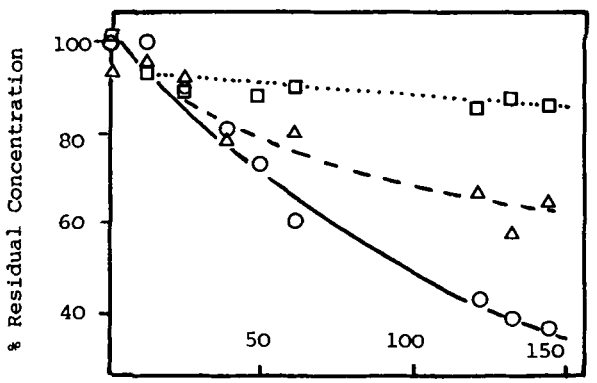
At a previous British Pharmaceutical Conference, during discussion of a paper concerned with the storage of thiomersal and chlorhexidine gluconate in glass and plastics containers (McTaggart et al 1979), it was claimed that the dithizone method of Neurath (1961) was stability indicating for thiomersal. The Neurath method involves extraction of the complex formed between thiomersal and dithizone in the cold into toluene and determination of the absorbance in the solvent at 610 nm. It thus differs from the commonly used hot oxidation method (Richardson et al 1977) which converts organic to inorganic mercury before complex formation with dithizone. Clearly the latter cannot be stability-indicating and since no evidence was offered to substantiate the claim made for the Neurath method, both dithizone techniques have been evaluated against an improved HPLC method for thiomersal in the presence of its breakdown products.

The current technique involves the injection of 20µl samples on to a 15cm Hypersil ODS (5µm) column, jacketed at 30°, using a mobile phase of 40% v/v acetonitrile in 0.013M Sørensen's phosphate buffer, pH 5.8, containing 1.2×10^{-3}M CTAB; 0.005% cinnamic acid is used as external standard with detection at 235nm, 0.04 AUFS and flow rate 2 ml min^{-1}. The technique is capable of detecting more breakdown products than that described previously (Meakin & Khammas 1978) whilst retaining the original's specificity in the presence of 0.1% EDTA. Thiomersal content of samples is calculated from peak area ratios. The figure shows that the Neurath method is a better stability indicator than the "hot" dithizone technique but still overestimates thiomersal in heavily degraded solutions. With degradation levels below 25% there is reasonable agreement between the Neurath and HPLC methods but the former is less reproducible. For instance relative standard deviations of calibration plots for the Neurath method are 2 - 3 times larger than for the HPLC system (∿ 2%). The slow loss of thiomersal demonstrated by the "hot" dithizone method is akin to that observed using atomic absorption which also assays total mercury and was discussed previously (Meakin & Khammas 1978).



Degradation of Thiomersal (0.004%) in 0.133M Sørensen's Phosphate Buffer, pH 5.8 on Exposure to High Intensity Simulated Daylight.

(O HPLC; Δ Neurath method

□ "hot" dithizone method)

McTaggart, C.M., Ganley, J., Eaves, T., Walker, S.E., Fell, M.J. (1979) J.Pharm. Pharmac. 31: 60P.
Meakin, B.J., Khammas, Z.M. (1978) J.Pharm. Pharmac. 30: 52P.
Neurath, A.R. (1961) Cesk Farm., 10: 75-78, (through Chem. Abs., (1964) 61: 11854g)
Richardson, N.E., Davies, D.J.G., Meakin, B.J., Norton, D.A. (1977) J.Pharm. Pharmac. 29: 717-722.

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