DIFFERENTIAL PULSE POLAROGRAPHIC ASSAY OF GLYCERYL TRINITRATE SUBLINGUAL TABLETS

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The B.P. 1980 method of analysis for glyceryl trinitrate (GTN) tablets is difficult and time consuming when many samples are to be analysed. Electrochemical techniques of analysis are more rapid than the B.P. chemical/spectrophotometric method. Flann (1969) in describing the use of D.C. Polarography for single tablet assays has pointed out the advantages of this technique in uniformity of content determinations. Pugh (1974) has described a modification of this method in which an internal standard was incorporated, and Woodson and Alber (1969) have developed a similar assay in non-aqueous media. We now report the development of a differential pulse polarographic (DPP) method for GTN single tablet assay using simple reagents and with particular emphasis on minimisation of sample preparation and the effects of tablet excipients on response. The standard used was 10% GTN in lactose which is more convenient for handling than the alcoholic solution and is now more frequently used in the preparation of GTN tablets. This standard in a solvent of 20% ethanol/0.1M NH_4OH, 0.1M NH_4Cl gave a DPP wave with three distinct peaks of which the largest, occurring at -200mV applied potential with respect to the Ag/AgCl reference, was used for the analysis and for construction of a calibration curve which was linear over the GTN concentration range of 0 - 20 µg/ml.

For the single tablet assays, one tablet was crushed and mixed vigorously with 10 ml of ethanol then diluted to 50 ml with the buffer. DPP was performed with a Princeton Applied Research 174A polarographic analyser with a Model 303 dropping mercury electrode, using a drop time of 0.5 s and a pulse height of 50mV. In the composite assays 20 tablets were weighed and crushed, and an amount of powder equivalent to about 500 µg of GTN was treated as above.

Single tablet assay results for 500µg GTN B.P. tablets gave a coefficient of variation of 5.4%, and a range of ±15% of the mean. For composite tablet assays the coefficient of variation was 2.8% and the range ±3.8% of the mean. Both methods gave results consistent with the B.P. limits. It is believed that the differences in coefficient of variation between the assays are probably due to inter-tablet variation rather than lack of precision in the assay which on standard measurements gave a coefficient of variation of 0.9% and a range of ±1.30% of the mean. Better precision was found with the DPP method than with the B.P. method.

The DPP wave was unaffected by concentrations around 1mg ml^{-1} of inorganic nitrate, an interferent in the B.P. assay, or nitrite, a product of alkaline hydrolysis. Similar concentrations of the excipients lactose and mannitol showed no interference either, but the GTN stabiliser polyvinylpyrrolidone (PVP) of molecular weight 700,000 shifts the main DPP peak by about +100mV and increases the peak height by 50%. As this PVP concentration is a thousand times greater than that expected from a tablet these effects were not seen during the assays, but possible explanations for them, including electrode surface phenomena, change in diffusion characteristics, or an excipient - GTN interaction are being investigated.

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