GLUCOSE DEGRADATION AND F_0 STUDIES ON PARENTERAL INJECTIONS IN A CONTROLLED AUTOCLAVE

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Glucose is one of a number of pharmaceuticals known to degrade when subjected to heat sterilisation, leading to loss of active drug and formation of potentially harmful degradation products. Glucose degradation products have been implicated in thrombophlebitis in patients receiving long-term intravenous therapy. The injection (5% w/v) has been used as a model system to study the relationship between extent of degradation and the parameter F_0 (as specified in BP 1980, Addendum 1983) in a microprocessor-controlled autoclave.

The principal degradation product of glucose, 5-hydroxymethylfurfural (5-HMF), was assayed by high-pressure liquid chromatography (HPLC), using a 100 x 4.6 mm column packed with 5-µm ODS-Hypersil. The modular HPLC system comprised: Gilson 302-802C pump; 20-µl Rheodyne injector; Gilson Holochrome UV-detector (283 nm, 0.02 AUFS). The mobile phase for optimum efficiency (ca. 35,000 plates/metre) was: methanol-KH_2PO_4 (15:85, v/v) at pH* 5.7 and 2 ml/min. The internal standard (IS) employed was 2-furaldehyde. Over the range 0-3 µg/ml the area ratio of 5-HMF: IS regressed linearly with concentration: $y = 1.90 x + 0.025$ ($r = 0.9977$; $n = 6$). The RSD of replicate injections at 2.5 µg/ml was 0.93% ($n = 6$). The microprocessor-controlled autoclave (14 cu.ft. Drayton Castle), equipped with an Apotec 2000 control system, yielded highly reproducible sterilisation cycles. The cycle could be controlled to yield F_0 values within a specified range: 8, 10, 12, 14 and 16 were the notional values used in the present work. The minimum F_0 recommended in the BP is 8. These studies were conducted at 115, 117, 119, 121 and 124°C, respectively. Glucose 5% was filled in 500-ml MRC bottles. The temperature probe was located in one sample bottle, other samples being disposed in identical positions nearby for each cycle. Glucose B.P. was obtained from Roquette Ltd. (Tunbridge Wells, UK).

The logarithm of 5-HMF concentration was related to the F_0 observed at each temperature (Fig. 1). For control to a specified F_0 value, it was found that low temperature cycles yielded more degradation than that observed at higher temperature. A number of heat-labile pharmaceuticals subjected to heat sterilisation would be expected to display similar behaviour, assuming that first-order kinetics were to apply. It is suggested that, for glucose injections, control to specified F = 8, is important and that degradation can be substantially reduced by employing high-temperature sterilisation cycles.

Fig. 1