SUSTAINED RELEASE POTASSIUM CHLORIDE PRODUCTS: IN VITRO - IN VIVO CORRELATIONS

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Pellets of about 0.8 mm diameter containing 80% KCl were designed so that they released the drug over an 8 hour period under aqueous conditions over the pH range 1 to 7.5 with the intention that their oral use in man would avoid local high concentrations of potassium chloride which have been shown to be highly corrosive to mucous membranes. The rate controlling step of drug release from the pellets involved diffusion through the membranes constituting the pellet coats. In vivo studies in rabbits showed that the pellets produced considerably less mucosal damage than occurred using enteric coated tablets or sustained release tablets of potassium chloride.

The release of drug from the pellets and from other products was investigated in vitro under different conditions of temperature, pH and agitation using rotating basket, rotating paddle and rotating bottle methods. The rate of release from these pellets was not affected significantly by pH change in the ranges 1.5 to 6.8 and thereafter progressively increased with higher pH values. The pellets released the drug over the designed time i.e. more slowly than did currently available slow release potassium tablets (i.e. 2 to 6 h.).

An in vivo method to demonstrate the rate of input into the circulation in man of potassium ions from products used orally and exhibiting different dissolution characteristics was therefore sought. The rate of urinary excretion of potassium under varying conditions of time of day, diet, pH etc. was investigated using five subjects until conditions could be specified which gave an acceptable base line of potassium excretion. The input of potassium from solution and from different sustained release pellets could then be observed by the profile of rate of urinary excretion of potassium plotted against time. The sustained release effect of the pellets relative to the solution of potassium chloride was demonstrated by the relative profiles; complete bioavailability of drug from the former was established over an 8 to 10 h period.

Potassium/sodium urinary excretion ratios under controlled conditions in man were used to show the input of potassium from different products taken orally by the elevated ratios obtained over the test period.

Batches of pellets designed with different in vitro dissolution profiles were investigated in vivo by the above methods; after ignoring the initial lag in the in vivo excretion, a straight line correlation was obtained between dissolution rate profiles and urinary excretion rate profiles from the same products.

A simple in vivo test was also sought which could be useful for batch to batch monitoring of sustained release potassium chloride pellets. The 'buccal absorption test' was adopted for this purpose and good correlations obtained between this test and the in vitro dissolution tests.

The above in vivo tests facilitated the investigation of the effect of storage on the in vivo release of potassium chloride from the sustained release pellets; storage under very adverse conditions, i.e. temp. 30-50°C, had little effect on potassium release through the membranes of the pellets.