# THE STABILITY OF SALBUTAMOL SOLUTION

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Only one study into the stability of salbutamol has been previously reported (Wall and Sunderland,1976). This work was of limited scope and utilised fluorimetric and colorimetric assay techniques, but neither of these was proven to be stability indicating. We have therefore initiated a more complete study into the stability profile of salbutamol and developed a reversed phase, ion paired HPLC assay method. The technique involves a preliminary separation of non-basic degradation products by passage through an SP-Sephadex C-25 cation exchange column. The drug and basic degradation products are then eluted with dilute ammonia and 10µl aliquots of the eluant injected onto a 10cm Spherisorb S5 ODS column, using a mobile phase consisting of 0.06% perchloric acid and 0.004% sodium dodecyl sulphate in 20% acetonitrile. 1-(4-hydroxy-3-methylphenyl) -2-(t-butylamino) ethanol is used as internal standard and detection is at 278nm; quantification involves peak area ratios obtained via a Pye-Unicam DP88 Minigrator. Thin layer chromatograms of degraded drug solutions exhibit up to 6 additional spots and it has been verified that none of these breakdown products appear under the salbutamol peak on the HPLC trace.

Kinetic studies have been carried out with salbutamol sulphate concentrations of 0.1-2.0%, using a pH stat to avoid the use of buffers, which are known to affect drug stability. Figure 1 shows that when oxygen is bubbled through the solution, first order plots are linear down to about 30% residual salbutamol; the data are reproducible with the derived first order rate constants having coefficients of variation of less than 3%. The degradation rate is dependent upon temperature, pH and drug concentration but not ionic strength. With the solutions merely open to the atmosphere through a condenser, the plots show a lag phase, and have poor reproducibility.

Applying the half-life method to the concentration dependence data obtained at pH 9.0 and 70°, gives the reaction order to be 1.3 which suggests the possibility of variation in the reaction mechanisms in dilute and concentrated solution. The activation energy for the degradation of a 0.5% solution at pH 9.0 is 101 kJ. mole $^{-1}$ over the temperature range 50-75°.

Figure 2 shows the salbutamol content of a degraded solution assayed by the HPLC technique and the BPC indoaniline colorimetric method for salbutamol inhalation. The latter clearly overestimates the salbutamol content in degraded systems and is therefore unsuitable for accelerated kinetic studies.

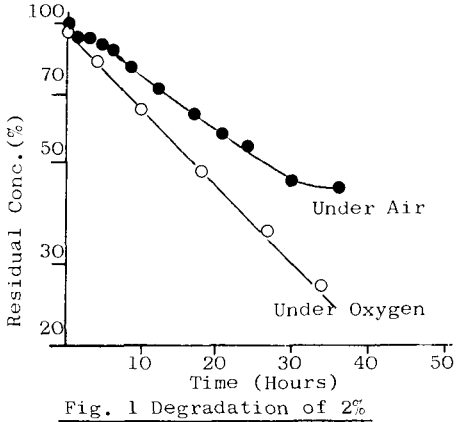


Fig. 1 Degradation of 2% Salbutamol Sulphate at pH 9.0 and 70°

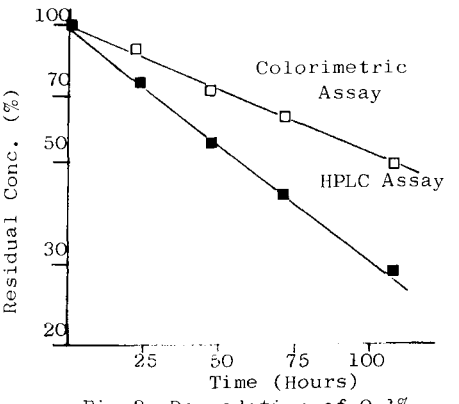


Fig.2. Degradation of 0.1% Salbutamol Sulphate at pH 9.0 and 70° under Oxygen.

Wall B.P. and Sunderland V.B. (1976) Aust.J.Hosp.Pharm. 6, 156-160