# IN VIVO EVALUATION OF THE EFFECT OF FIVE DISINTEGRANTS ON THE BIOAVAILABILITY OF FRUSEMIDE FROM 40MG TABLETS

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The effect on the bioavailability of frusemide from tablets prepared with each of 5 tablet disintegrants has been assessed. Urinary excretion data were used and the bioavailability of each formulation was determined with reference to an oral frusemide solution using the methods of Oser & others (1945) and Niebergall & others (1975).

Tablets of frusemide 40mg were prepared containing approximately 10% w/w of the disintegrants, Explotab, Polyplasdone XL, Amberlite IRP 88, Maize starch B.P. and Elcema P100. The tablets were compacted at 150 $MNm^{-2}$ and dissolution rates measured in the B.P. apparatus using a variety of pH buffers. Bioavailability studies were carried out in 5 healthy men aged 18-31 years on a double blind basis. Urine was collected over a period of 24 hours and analysed by a modified method of Bratton & Marshall (1939). The in vivo and in vitro results are summarised in Table 1.

Table 1. In vitro and in vivo data for frusemide formulations.

| | Disintegrant | | | | |
|---|---|---|---|---|---|
| | Explotab | Poly plasdone | Amberlite | Maize Starch | Elcema |
| Disintegration time(min) | 3.8 | 1.06 | 7.8 | 10.35 | 120.0 |
| Hardness scu | 4.36 | 4.04 | 4.54 | 3.62 | 4.04 |
| Dissolution rate $T_{50\%}$ min | | | | | |
| pH 6.5 | 1.91 | 3.17 | 36.58 | 18.69 | 430.13 |
| pH 5.0 | 2.56 | 6.34 | 8.42 | 15.33 | 122.21 |
| pH 3.5 | 16.43 | 118.96 | 356.78 | 26.58 | - |
| Biological half life | 1.8-4.5 | 1.9-4.3 | 2.0-3.7 | 2.0-3.9 | 2.1-4.4 |
| Mean bioavailability % | | | | | |
| Oser & others | 68.68 | 61.49 | 58.22 | 41.40 | 32.64 |
| Neibergall & others | 68.44 | 63.55 | 57.38 | 40.21 | 33.96 |

No quantative relation was found between disintegration time and dissolution rate or bioavailability. Maize starch and Elcema P100 rendered the drug significantly less bioavailable than the other three disintegrants; the tablets containing Explotab gave the highest bioavailability. The biological half life, varied from subject to subject over the range 1.8-4.4h and was independent of formulation. If the $T_{50\%}$ value for the formulation containing Elcema was excluded, a good correlation, $r = 0.998$ was found between dissolution half life at pH 5.0 and bioavailability. However, if the value for $T_{50\%}$ for the Elcema containing tablets was included the correlation coefficient r fell to 0.791. Even poorer results were obtained for attempted correlations at different pH values; at a dissolution pH of 6.5, $r = 0.753$ and at pH 3.5, $r = 0.071$.

The results indicate that the choice of a disintegrant can significantly affect the bioavailability of the final product and that the pH of the dissolution medium must be carefully selected to obtain a good in vivo - in vitro correlation.

Niebergall, P.J. & others (1975). J.Pharm. Sci.,64, 1721-1724.
Bratton, A.C. & Marshall, E.K. (1939). J. Biol. Chem., 128, 537-550
Oser, B.L. & others (1945). Ind. Eng. Chem., Anal. Ed., 17, 405-412.