# GLASS BEADS AS A MODEL MATRIX FOR SOLVENT-DEPOSITION OF DRUGS

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Solvent-deposition, i.e. the precipitation of solute onto a powdered excipient matrix, is a technique commonly used to produce mixtures containing relatively small amounts of drugs e.g. contraceptive steroids. Reports on process variables like drug-excipient ratios, substrate and solvent properties have largely been concerned with their effects on the particle size of deposited drug (Shah et al 1974; Johansen & Moller 1976, 1977) and little attention has been paid to the possibility of solvent-mediated polymorphic phase transformations, which may also affect dissolution rate. With a view to investigating polymorphism in solvent-deposited systems, a substrate which would accentuate solvent effects was sought: a non-porous glass bead matrix seemed an interesting possibility.

Spironolactone, a poorly soluble steroidal diuretic with a history of polymorphism and susceptibility to comminution (Mesley 1966; Florence & Salole 1976), was selected as a model drug. Crystalline polymorphs were prepared from saturated solutions in acetone and methanol; evaporating a solution in chloroform resulted in a viscous residue which could only be dried under vacuum, producing an amorphous phase. The same solvents were also used to deposit the drug onto glass beads (150μm mean diameter), in a modified tablet-coating pan with hot-air blower at 60°, in 1:10 weight ratio. Differential thermal analysis (DTA) indicated that acetone- and methanol- deposited spironolactone had forms corresponding to those obtained on crystallization, while chloroform seemed to produce a form similar to that from acetone. Scanning electron microscopy (SEM) of crystallized and deposited samples confirmed that chloroform-deposited drug was crystalline and not, as expected, an amorphous film. SEM also revealed that methanol-deposited crystals were acicular and apparently less firmly attached to glass.

These preliminary results support the notion that glass beads are useful as a model substrate for solvent-deposited solid-state studies. In addition to being relatively uniform, they are available in sizes comparable to those for excipients like lactose, starch and dicalcium phosphate which have been used as matrices (see refs.); their smooth surfaces obviate complications due to deposition in inaccessible fissures because of solvent surface tension (Amman, 1973); their insolubility also precludes matrix dissolution and recrystallization affecting solute precipitation and dissolution (Johansen & Moller 1976, 1977). Being thermally inert they are suited to thermoanalytical techniques, which are widely used to characterise drugs in the solid state. They may also be amenable to direct X-ray powder diffraction analysis.

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