LUCIDEON
insight creating advantage

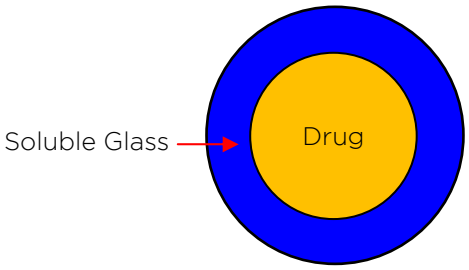
LUCIDEON'S INORGANIC CONTROLLED RELEASE TECHNOLOGY (iCRT)

Lucideon has developed a platform technology for delivering APIs based on ceramics/glasses (GRAS materials), using a selection of synthesis methods and internal expertise in modifying material properties. This allows control and versatility over the formulation to meet specific requirements of chosen drug, including:

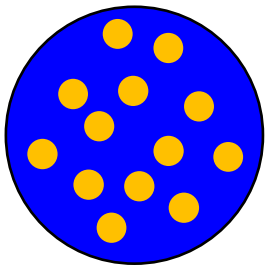
- Chemical durability, solubility
- Design and control over release rate
- Micro/nanostructure with controlled porosity (size, number)
- Carrier can be inert or a functional agent
- Levels of drug loading
- Tamper resistance
- "Easy to swallow"

iCRT allows drug to be introduced into an inorganic glass-like matrix and subsequently released by either:

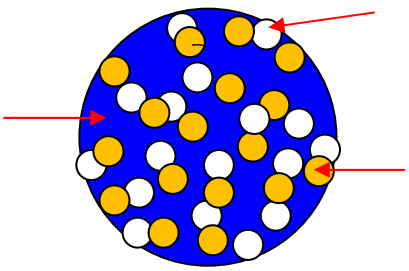
- Embedding into solid soluble glass matrix
  - Release via dissolution of carrier
  - As a thin glass coating around drug (delayed release)
  - As a homogenously dispersed drug in a glass (sustained release)



Or .....



- Embedding within a solid, porous matrix by sol-gel processing
  - Release via pore mediated diffusion (sustained release)
  - Can be synthesised to produce a range of micro and macro structures



BENEFITS OF iCRT

Tamper Resistance	Drug Loading	Variable Release Rate
Chemically and physically stable structure when required e.g. no increase in dissolution rates in alcohol	Potential for high loading levels (30 wt% tested to date, higher expected) and ability to control pore number	Wide range of variables allows for significant tailoring of release rate (mins, hours, days)
Active is intrinsically included into the material and stored within the stable structure – inherent tamper resistance	Multiple loading methods allows for sensitive drugs to be effectively loaded	Chemical alteration allows pH, temperature and biologically triggered release
Synthesised as a monolith and milled to a fine powder to run dissolution tests, thereby alleviating risk of abuse through crushing of tablet	Varied synthesis methods allow for highly and poorly water soluble drugs to be loaded with relative ease	Level of burst release ranging from 0 - 60% - allows rapid establishment and sustained maintenance of therapeutic levels
	Homogenous dispersion (nano, possibly molecular) and no phase separation of API throughout the porous structure	

BENEFITS AND APPLICATIONS OF iCRT FOR DRUG DELIVERY

Poor Compliance	Substance Abuse	Manufacture
High loading of active with sustained release profile extends activity, reducing dosing frequency	Glass structure resists further milling or dissolution in alcohol thereby providing an inherent tamper resistance	Synthesis is comparable to industrially produced materials currently on the market – scale up cheaper and easier than alternatives
High loading of active reduces tablet size, making it easier to swallow	Removal of burst release significantly lowers the risk of overdose thereby reduces opportunities for abuse	Manufacture of sol-gels is 'green' e.g. minimal waste, solvent is water, process occurs at room temperature, etc.
Carrier is synthesised in powder form providing alternative to tablets for e.g. geriatrics/paediatrics i.e. powder can be suspended in water/melt on the tongue	Due to controlled/sustained release, lower, more effective dosing can be supplied, lowering overdose risk, as well as reducing cost	Better loading/dispersion means potentially less drug is wasted/required to achieve therapeutic levels and reduction in uncontrollable burst (highly soluble drugs)
Loading methods allow for multiple drugs to be loaded simultaneously, reducing dosing frequency		Loss of drug crystallinity in carrier improves solubility/bioavailability (poorly soluble)

SOME ASSOCIATED DATA

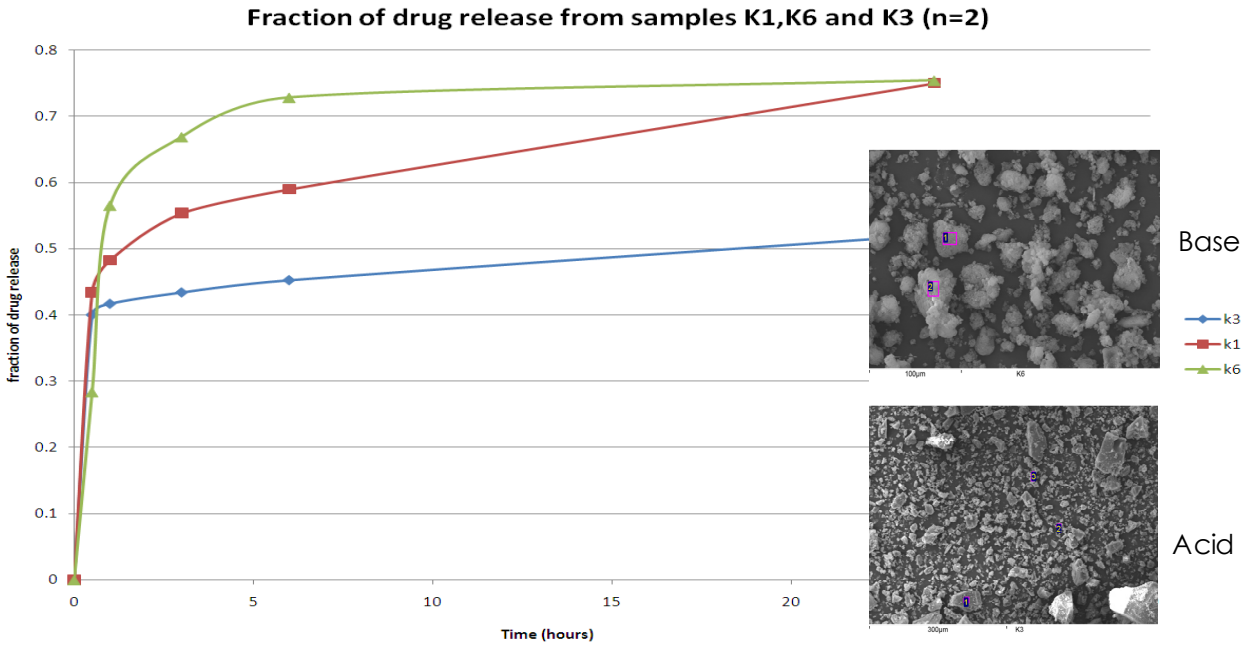


Fig 1. Effect of modifying synthesis conditions on release characteristics of API; initial fast release (to reach therapeutic levels), followed by sustained release (maintain therapeutic levels)

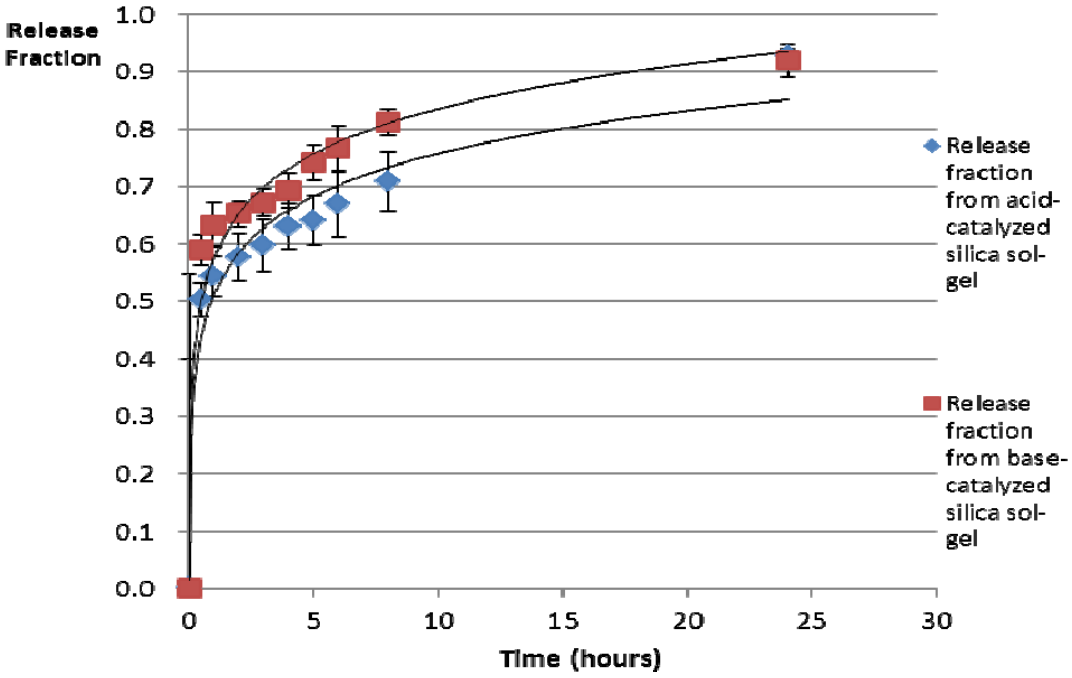


Fig 2. Effects of synthesis method on changes in “burst” whilst maintaining sustained release profile

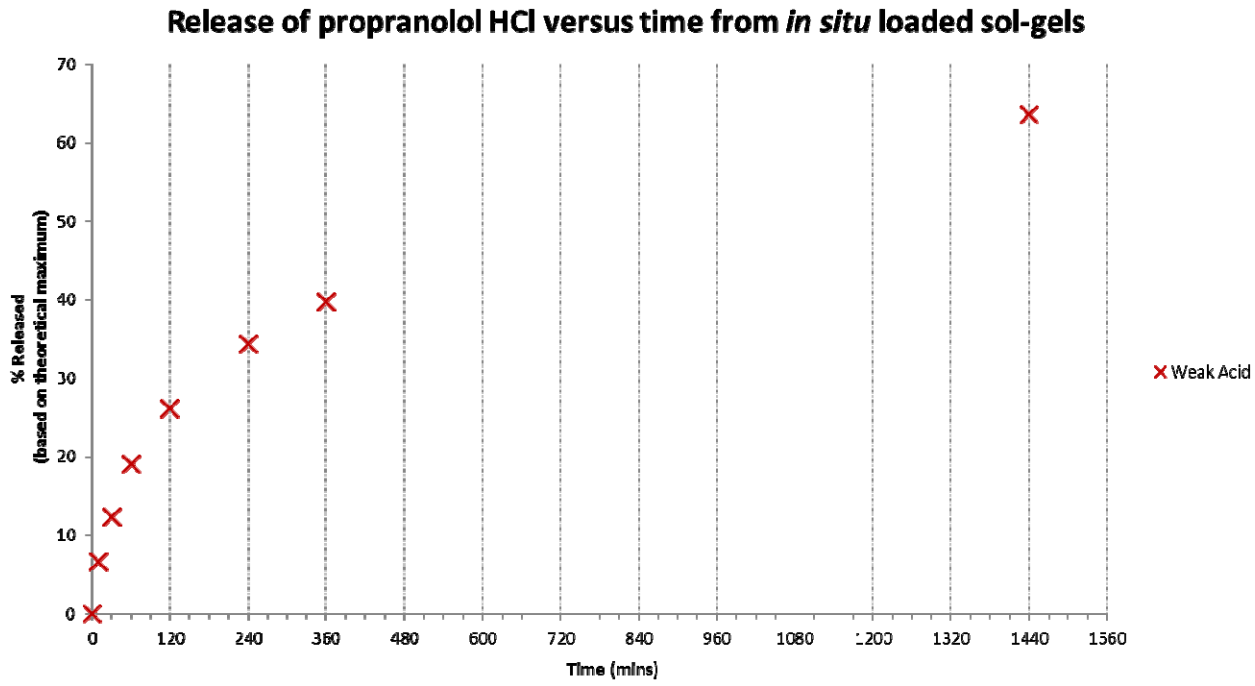


Fig 3. Effective removal of burst release (~ 6% in the first 30 minutes) whilst maintaining sustained release profile

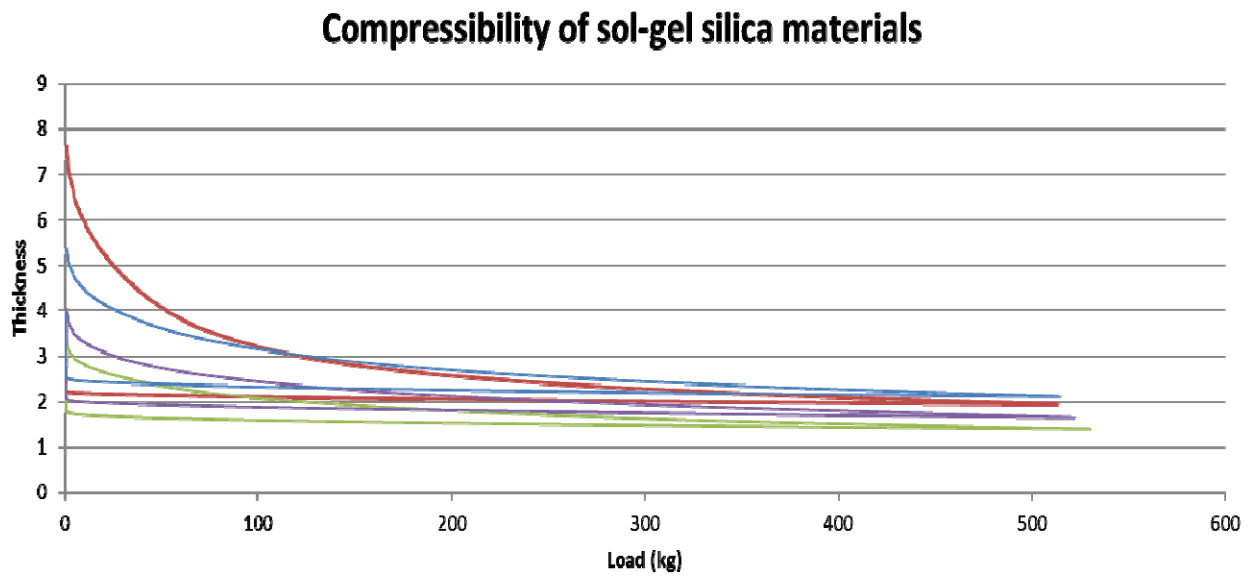


Fig 4. No granulation is required for processing to produce a firm tablet – demonstrates that powders can be processed via traditional methods using ~30% binder

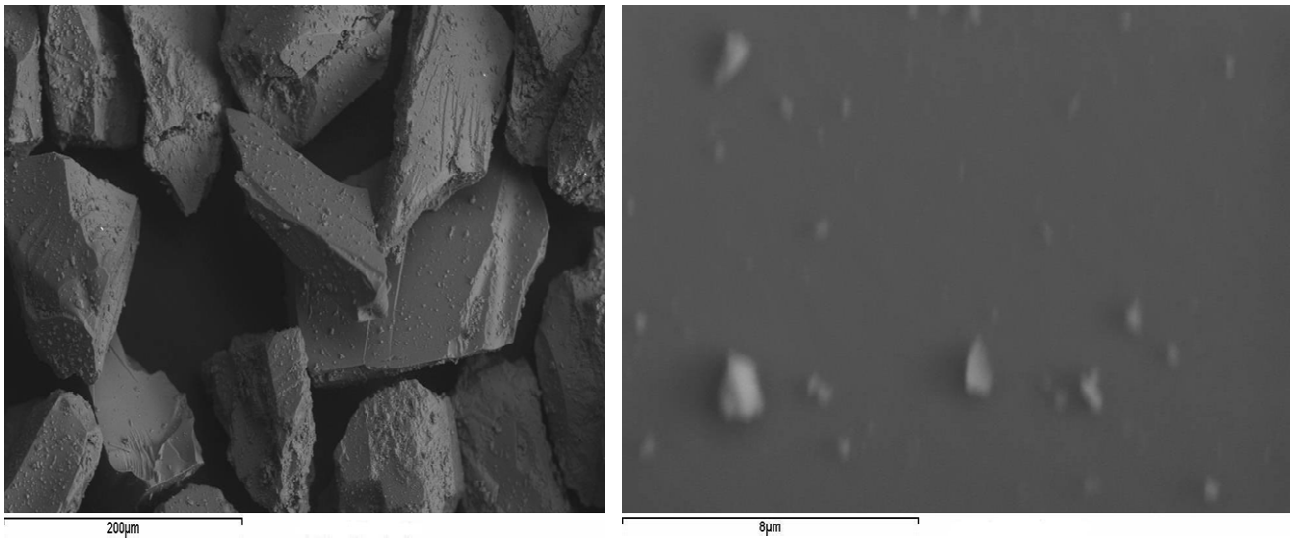


Fig 5. SEM images show no discrete, visible, drug phase, suggesting homogeneous nano-dispersion of the drug within the carrier (10 wt.% loading). N.B. small particles seen on surface are debris from breaking up the drug-loaded glassy carrier.

CURRENT RESEARCH

- Optimisation of tamper resistance
- Compatibility with large molecules/biologics
- Potential for use as a long term implant or injectable powder (achievable release profile over weeks, months… years)
- Assessment of effect of carrier on crystallinity of drug (expected to improve solubility)