Introduction

Solid dosage forms for oral drug administration are the mainstay of product formulation. Conventionally a company will look at this strategy as a convenient and reproducible method of manufacture. This does always however take into account patient needs and preferences and undoubtedly a significant number of patients find difficulty in swallowing a tablet. Convenience and palatability of the dosage form are major considerations and orally disintegrating tablets have addressed this in a number of cases. Currently available technologies for oral disintegration are based upon effervescent systems, freeze-dried matrices or rapidly-disintegrating granulated material. A major limitation of current technologies is their low mechanical strength inherent to their fast disintegration in the mouth. This results in the requirement of specialized costly packaging to protect the tablets and maintain them intact for administration.

The oral drug delivery market is a $35bn industry and expected to grow as much as 10% per year. There is a clear opportunity for new enhanced oral products arising within this market segment. With a growing elderly population and associated chronic diseases such as diabetes, cardiovascular diseases, Parkinson diseases, oral technologies and products which offer ease of administration and cost benefit are expected to stimulate the market for oral delivery. Non-invasive delivery of insulin and GLP-1 analogs for type II diabetic patients in particular an oral or buccal formulation represents a significant unmet need for these patients. The global market for diabetes therapeutics was valued at $97bn in 2008, (with over 200m people affected), and is forecast to grow to $113bn by 2013.

Technology

The School of Pharmacy at RCSI has developed a novel technology which produces mechanically strong tablets, with low friability and can withstand conventional blister-packing. The manufacture utilises existing tablet presses, is cost effective and as the manufacturing process avoids liquids, it is suitable where stability may be a consideration. The technology allows incorporation of microparticulates to produce extended-release and taste-masked, orally disintegrating tablets. Importantly RCSI has shown that the major excipient used in its ODT technology has an effect on cell membrane permeability, improving the absorption of agents administered in this way. RCSI is currently examining adding further enhancers to increase the absorption-enhancing effect of the formulation. One important consequence of this is the use of the technology in the delivery of certain large molecules, including peptide agents that are otherwise destroyed after swallowing.
Evaluation in a phase I pharmacokinetic study in human volunteers (n=18) of RCSI’s simvastatin formulation showed a 50% increase in bioavailability when administered sublingually compared to oral administration of the innovator product, Zocor™ (Figure 1).

**Figure 1.** Pharmacokinetic profiles of Simvastatin from RCSI’s simvastatin ODT formulation administered sublingually vs Zocor® tablet administered orally.

---

**Applications**

There are many opportunities to apply this approach to new actives or to extend life or add value to existing actives. This technology is especially suited to relatively potent agents for which rapid onset of action is desired, for example in providing pain relief, relief from nausea, sleep or sedation, or cardiovascular effects. In addition the technology has a niche application in the buccal delivery of therapeutic agents. Delivery through the buccal mucosa enters the systemic circulation directly thereby avoiding first pass metabolism and offering an added advantage for therapeutic agents with poor permeability and oral bioavailability.

Oral mucosal delivery has been shown to be a potential route for insulin delivery, with detectable insulin concentrations and increased glucose consumption following delivery as an aerosol to the oropharyngeal cavity [1, 2]. While oral sprays show indications of systemic delivery, this will be limited by mucosal contact time. A buccal delivery system will produce enhanced contact time. RCSI is currently seeking a partner to help bring this product to a clinical study. The increasing prevalence of type 2 diabetes makes this an area of significant value.
Advantages

- New proprietary method allows for enhanced systemic absorption of actives from buccal mucosa
- Versatile technology suitable for the development of enhanced products for veterinary medicines, OTC, Rx medicines and line extensions
- New proprietary method allows the incorporation of microencapsulated drugs for enhanced bioavailability, flexibility of dosing and immediate and/or controlled release for superior therapeutic benefit.
- Lower production, packaging and distribution costs compared to current commercially available products

References


Contacts:
Dr. Gearóid Tuohy, RCSI Technology Transfer, 123 St Stephen’s Green, Dublin 2, Ireland.
Email: gearoidtuohy@rcsi.ie  Tel: +353 1 4022362

A Method of Producing a Fast Dissolving Tablet
PCT Date: 03/04/2008

Orodispersible Tablets
PCT Date: 27/03/2010

Orodispersible Dosage Forms Containing Solid Drug Dispersions
PCT Date: 18/05/2010

Principal Investigator:
Dr. Zeibun Ramtoola, School of Pharmacy, Royal College of Surgeons, 123 St Stephen’s Green, Dublin 2, Ireland. Email: zramtoola@rcsi.ie Tel: +353 1 40228626 or +353 1 4022498