Introduction

Oral delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, most convenient and most economical method of drug delivery with the highest patient compliance. The tablet is the most widely utilised oral dose format. A novel tablet concept which offers ease of oral administration and benefits of increased patient compliance is an orodispersible tablet. This tablet format is designed to readily dissolve or disintegrate in the mouth generally within <60 seconds without chewing and without water. A number of orodispersible tablets are commercially available for human use using technologies developed by pharmaceutical companies such as Cardinal Healthcare, Jannsen Pharmaceutical, Bioavail, Cima, Eurand and Yamanouchi. These technologies produce orodispersible tablets which have purposely low mechanical strength to facilitate their fast disintegration in the mouth. A major limitation of this low mechanical strength of the tablets is the requirement of specialized costly packaging to protect the tablets and maintain robustness for administration. A second limitation of the commercialised competitor technologies is the addition of effervescent or highly water soluble disintegrants which require controlled processing environment in addition to storage and packaging constraints.

The School of Pharmacy at the Royal College of Surgeons in Ireland has addressed the above shortcomings by developing a novel formulation and a cost effective one step manufacturing process using conventional tabletting technology for the production of mechanically strong orodispersible tablets which are suitable for conventional packaging. This novel and simple formulation does not require the use of effervescent excipients or a disintegrant and yet produces rapid dissolving tablets with comparable or faster disintegration profiles relative to competitor technologies. Using RCSI’s novel formulation and process, orodispersible tablets do not require to be processed under humidity controlled environment. RCSI’s proprietary technology is applicable to a wide range of therapeutic agents including generics, thereby adding value, i.e. “supergenerics” for veterinary or human application.

RCSI’s novel orodispersible formulation may also be applied to deliver therapeutic agents through the buccal mucosa directly to the systemic circulation thereby avoiding first pass metabolism offering an added advantage for therapeutic agents which have poor permeability and oral bioavailability.

The oral drug delivery market was estimated to be worth $35bn in 2006 and forecast to reach $52bn by 2010 with a CAGR of 10%. Of this, the orodispersible tablets, taste masked and micro emulsion formulation segments constitute a 22% share with an expected CAGR of 17% to 2010. There is a clear opportunity for new enhanced oral products arising within this market segment. With a growing elderly population, oral technologies and products which offer ease of administration and cost benefit are expected to stimulate the market for oral delivery.
Technology

Approximately one-third of the population, primarily the geriatric and pediatric populations, has swallowing difficulties, resulting in poor compliance with oral tablet drug therapy which leads to reduced overall therapeutic effectiveness. A new tablet dosage format, the orodispersible tablet, has been developed to offer the combined advantages of ease and convenience of dosing in the absence of water or fluid. These tablets are designed to dissolve or disintegrate rapidly in the saliva generally within 1 minute (range of 5-50 seconds). Due to the constraints of the current technologies as highlighted here, there is an unmet need for improved manufacturing processes for rapid orodispersible tablets that are mechanically strong, allow for ease of processing, handling and packaging with production costs similar to that of conventional tablets to allow application to a wider range of actives.

Applications

Formulation advances using a conventional tabletting process have led to the development of mechanically robust tablets which readily dissolve/disintegrate within <50 seconds and can be formulated in a range of sizes from 10 - 15mm. The tablets produced are stable, and can withstand shipment in conventional tablet containers without loss of integrity. A number of orodispersible products for human and veterinary administration are currently under development at RCSI for the delivery of water soluble, lipophilic as well as poorly permeable therapeutic compounds. A number of these formulations have been scaled up and are at the stage of evaluation in a phase I pharmacokinetic study in human volunteers.

Advantages

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

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