A novel biphasic drug delivery system containing taste masked diclofenac sodium

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ABSTRACT SUMMARY
A novel formulation of taste masked diclofenac pellets has been developed for enhanced patient compliance and convenience. This drug delivery system comprises the following advantages:
- Enhanced therapeutic effects
- Reduced inter/intra patient variability
- Pleasant mouth feeling
- Easy to swallow
- Increased patient compliance
- Enhanced possibilities for taste masking

A successful feasibility study of this drug delivery system has been completed, showing excellent stability data for diclofenac sodium pellets dispersed in a gelatin matrix. Multiple formulations were investigated to evaluate and optimize the stability and release profile of the drug.

INTRODUCTION
Solid oral pharmaceutical dosage forms are typically administered in terms of tablets, pellets, granules, powders and capsules. However, some patients, particularly pediatric and geriatric patients, can have difficulty swallowing or chewing many types of conventional solid dosage forms. The challenge of the formulator is to improve patient compliance and also to potentially enhance the therapeutic effects of oral dosage forms. One possible solution is to formulate semi-solid pharmaceutical formulations, such as water soluble gels containing an active ingredient [1]. Such formulations are sufficiently viscous to be spill resistant, but also fluid enough to be readily dispensed by squeezing of the flexible packaging tube.

This novel drug delivery system is best described as a two phase delivery system based on a semisolid technology platform comprising an aqueous gel containing a dispersion of a multiparticulate solid dosage forms. These particles contain one or more pharmaceutical compounds which are either sparingly or completely insoluble in the gel. This system allows tailored doses and dose strengths to be achieved. The gel containing the particles is packed in a stick pack for easy administration.

EXPERIMENTAL METHODS
The drug delivery system has been developed on a lab scale but is expected to be readily scaled to pilot or full scale manufacture. Diclofenac sodium pellets were coated with Eudragit FS30D as gastric resistant coating in a fluid bed coater and then suspended in a prepared gelatin matrix. This gelatin matrix consists of gelatin, citric acid, colorant, flavor, a preservative agent and a buffer solution to adjust the pH value of the matrix. In this study the pH 2.5 was optimal in order to prevent the release of diclofenac through the Eudragit FS30D coating layer and into the gelatin matrix.

Unit dose packaging was developed to dispense directly into the oral cavity (Figure 1). Administration of the dose is conveniently and simply achieved by squeezing of the stick pack.

Figure 1: Solid particles dispensed in a gelatin matrix and filled into stick packs. Administration to the oral cavity.

In order to ensure the uniform distribution of the pellets in the filled stick packs, the aluminum foil of the stick pack can be removed (Figure 2).
RESULTS AND DISCUSSION

The successful feasibility of the novel drug delivery system has been demonstrated in a series of trials using diclofenac sodium pellets dispersed in a semisolid gelatin matrix. The hydrocolloid was adjusted to pH 2.5. During short term stability storage, samples were analyzed for microbial purity and for the absence of API in the gelatin matrix. Samples were analyzed immediately after manufacturing and after 1, 3 and 6 months storage intervals at 25°C/60%rH and 40°C/75%rH. No active was detectable in the matrix up to 3 month, with very small amounts of diclofenac been seen in the gelatin matrix after 6 months (0.08% at 40°C/75%rH). No microbial contamination has been found after 6 month storage.

The drug delivery system containing 10% of gelatin has been investigated on dissolution. The pellets are coated with the gastric resistant coating Eudragit FS30D. The gastric resistance is demonstrated on Figure 3.

The release of diclofenac from the drug delivery system has been tested in phosphate buffer pH 6.8 and is shown on Figure 4.

The slow drug release at pH 6.8 could be caused by the Eudragit FS30D polymer and/or by the gelatin matrix. At pH 7.2 a faster dissolution rate can be observed (Figure 5).

Two different gelatin concentrations have been analyzed for drug release profiles at pH 6.8 (figure 6). The system with a high concentration of gelatin (30%) shows very slow dissolution relative to lower concentrations (10%) which indicates that a lower viscosity formulations shows faster dissolution of diclofenac sodium at pH 6.8.

Further studies will be conducted to more fully evaluate the drug release of this novel drug delivery formulation.
CONCLUSION
The feasibility of a novel drug delivery formulation has been performed successfully. During a short term storage period of 6 months at standard and accelerated conditions, the stability of the formulation was clearly demonstrated. Additionally it was show that the drug release profile of the active compound could be modified by adjusting the viscosity of the matrix.

The benefits of this formulation include convenience of the dosage form combined with a pleasant mouth feeling. It also affords a dividable dosage form and an easy to swallow formulation, administered without water (‘on-the-go formulation’). The concept is to be further evaluated in a consumer study and different applications will be developed to fully understand the limits of this novel drug delivery system.

REFERENCES
1. Patent WO 99/62498