Introduction

Ketoprofen is a non-steroidal anti-inflammatory drug (NSAID) used in the management of pain.

Ketoprofen is rapidly metabolized in the liver with no known active metabolites.

Delivery, which bypasses first pass metabolism, may reduce side effects and improve efficacy.

Transdermal delivery has been somewhat successful but requires patch or device maintenance and relies on various methods of penetration enhancement limiting compliance.

Therefore, a drug delivery device capable of sustaining the release of an NSAID with minimal maintenance may increase patient compliance, eliminate GI related side effects and improve pain management.

NanoMedic Systems has developed a novel delivery device for Ketoprofen. The device is an assembled capsule containing a nanochannel Delivery System (nDS) chip and internal reservoir solution meant to be implanted subcutaneously within the patient.

It is designed to provide sustained release of a desired active therapeutic agent over a long period of time with no maintenance required. Release of the drug is not dependent upon the concentration of the drug solution (zero order) and is controlled by diffusion through the nanochannels of the device.

The device is not limited in the range of deliverable APIs as the size and number of nanochannels within the chip can be altered to achieve a specific release rate for a desired API. As the device relies on the use of nanochannels, particles present in the drug solution may influence the release rate of the drug.

Additionally, longer therapy regimens may require more drug in the donor solution than is possible due to solubility related issues. Therefore the use of a drug suspension may be required to ensure an adequate drug concentration in the donor solution over time.

The in vitro study has demonstrated that maximum number of particles allowed in solution according to the USP 32/NF 27 test 13b solutions for parenteral infusion or solutions for injection supplied in containers with a nominal content of less than 100 mL on diffusion through an nDS chip was assessed using ketoprofen as a model compound.

Additionally the ability to deliver drug through the device utilizing an internal drug suspension was assessed using ketoprofen as a model compound.

Materials and Methods

- Ketoprofen USP (Janssen Pharmaceutical Group, Minneapolis, MN)
- Benzalkonium Chloride (BAC) (Axxora Organics, New Jersey, USA)
- Phosphate Buffered Saline (PBS) (Becca Chemical Company, Arlington, TX)
- Aetomintride (Fisher Scientific, Pittsburgh, PA)
- Monoalumina Polyampholyte Spheres
  - 100 nm, 1 μm, 5 μm, 50 μm (Fisher Scientific)

Solution Preparation

- PBS solution contains 0.01% BAC as preservative
- Excess ketoprofen placed in 20 mL of PBS/2% BAC
- Placed on environmental shaker held at 25°C and 100 rpm for 24 hours
- Suspension filtered through 0.45 μm filter
- Fixture 1: Filtrated solution diluted to 2% original concentration
- Fixture 2: Saturated solution used following filtration

Experimental Fixtures

- Solution 1: 0.136 mg/day
- Solution 2: 0.192 mg/day

Results

Conclusions

- The nDS provides linear release of a therapeutic agent over a prolonged period of time
- The presence of particulate matter at the highest allowable amount as stated in USP 32/NF 27 in the drug solution does not influence the drug release rate or linearity thereof
- The use of drug suspensions or drug suspensions is possible with the nDS

Acknowledgements

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References

1. Matosina T. Inflammation and Regeneration. 28 (2): 100 – 104