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Novel Design of a Monolithic Controlled Release Formulation of Phenylephrine HCl for Oral Administration

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Summary

Novel oral controlled release tablet preparations of Phenylephrine HCl were developed using a monolithic self-correcting matrix delivery system. Several formulations of a therapeutically relevant Phenylephrine HCl dose were developed to provide first-order and near-linear in vitro release profiles over 12 hours.

Introduction

The objective of this work was to develop novel orally-administered controlled release tablet preparations of Phenylephrine HCl using a monolithic self-correcting matrix delivery system. Phenylephrine is a synthetic sympathomemetic agent chemically related to ephedrine and epinephrine indicated for the symptomatic relief of sinusitis, bronchitis and other symptoms associated with the common cold. The action of Phenylephrine is primarily that of vasoconstriction and its effect is more long lasting than either epinephrine or ephedrine. Phenylephrine is an especially interesting candidate for oral controlled release formulation because of the current concern over the illegal diversion of other sympathomemetic compounds such as Pseudoephedrine HCl. Controlling the release of highly-soluble compounds such as Phenylephrine HCl in a near-linear manner is difficult using traditional matrix delivery systems; the self-correcting monolithic tablet technology applied to these formulations demonstrates its capability to deliver high-solubility actives in a highly controlled manner over a prolonged period.

Experimental Methods

Tablets containing 30mg Phenylephrine HCl were dry-blended and directly compressed using both a single-station Carver hydraulic press and a ten-station Piccola rotary press. In addition to active drug, tablet preparations contained hydroxypropylmethylcellulose, an electrolyte as a channel former/release modifying agent, and tableting aids such as microcrystalline cellulose and lubricants. *In vitro* dissolution studies were conducted using a USP Type II apparatus with 900mL of deionized water at 37°C and 50 rpm paddle speed. Samples were removed every 60 minutes over 12-18 hours via peristaltic pump and analyzed via UV spectroscopy at 214nm. Robustness and ruggedness examinations were conducted, including increased hydrodynamic agitation of 75 rpm and 100 rpm paddle speeds.

Results and Discussion

Novel self-correcting monolithic tablets of Phenylephrine HCl were shown to effectively control the release of drug over a 12-hour period. Phenylephrine HCl yields similar release profiles to the same matrix formulation of Pseudoephedrine HCl *in vitro* over 12 hours, shown in figure 1. Variation in release performance can be effected by increasing or decreasing polymer load in the formulation, shown in figure 2.

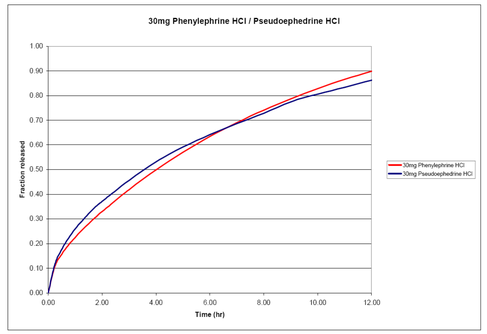

Figure 1. Release comparison of similar 30mg Phenylephrine HCl and Pseudoephedrine HCl formulations.

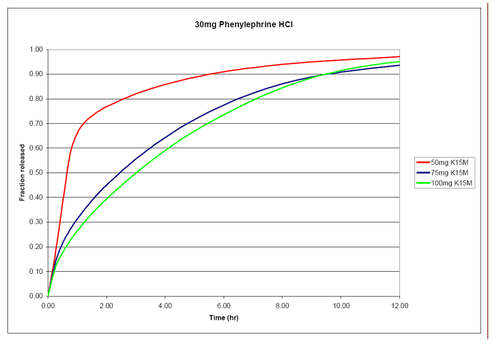

Figure 2. Effect of increased polymer load on Phenylephrine HCl release profile.

Other variations in formulation had less marked impacts on release performance. Changing polymer viscosity, type of electrolyte, and API particle size in the same ratios yielded similar release profiles, shown in figures 3-4. Increases in dissolution paddle speed have minor effect on dissolution rate, shown in figure 5.

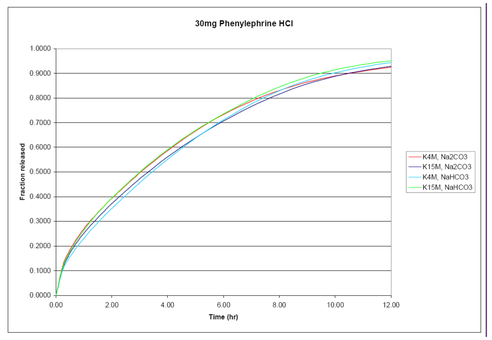

Figure 3. Effect on Phenylephrine HCl release profile of changing polymer viscosity and electrolyte within otherwise identical formulations.

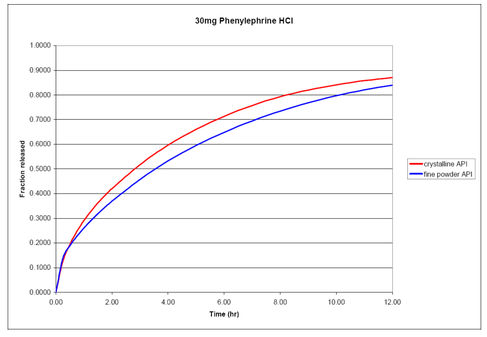

Figure 4. Effect of API particle size on Phenylephrine HCl release.

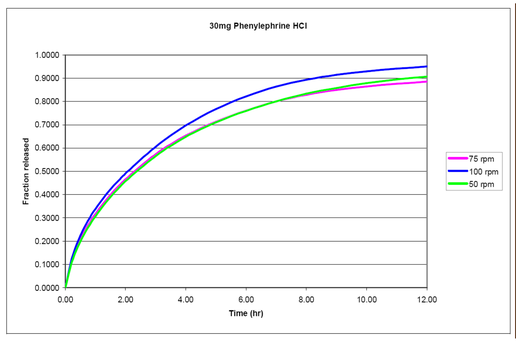

Figure 5. Effect of increased dissolution paddle speed on Phenylephrine HCl release.

Conclusion

Self-correcting monolithic tablet preparations of Phenylephrine HCl were capable of effectively controlling the release of a therapeutically relevant amount of the active drug over 12 hours, and release may be programmed to occur in a first-order or near-linear manner by modifying the amount of hydrophilic polymer. These matrix formulations can withstand changes to several formulation components without significantly impacting *in vitro* release performance.

References

-U.S. Patent 6090411 (Pillay, et al, 2001). Monolithic tablet for controlled drug release.

Acknowledgements

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