

Haiyan Zhang, Cathy Federici, Alan Brunelle

## SUMMARY

Three controlled release tablet formulations of 30 mg, 12 hour, Phenylephrine HCl were developed using a monolithic self-correcting matrix delivery system. Tablet ruggedness was investigated using a single station press and multiple rotary presses. *In vitro* results showed that similar release profiles were achieved across all manufacturing scales.

## INTRODUCTION

Phenylephrine Hydrochloride, **C<sub>9</sub>H<sub>13</sub>NO<sub>2</sub> • HCl** is a synthetic sympathomimetic agent chemically related to epinephrine and ephedrine. Phenylephrine is indicated for the symptomatic relief of sinusitis, bronchitis and other symptoms associated with the common cold<sup>1</sup>. Phenylephrine is an especially interesting candidate for oral controlled release formulation because of the current concern over the illegal diversion of other sympathomimetic compounds such as Pseudoephedrine HCl<sup>2</sup>. We developed novel orally-administered controlled release tablet of Phenylephrine HCl using a monolithic self-correcting matrix delivery system<sup>3</sup>. The objective of this project was to develop three formulations of differing release profiles and to evaluate the ruggedness of each formulation at a variety of manufacturing scales.

## EXPERIMENTAL METHODS

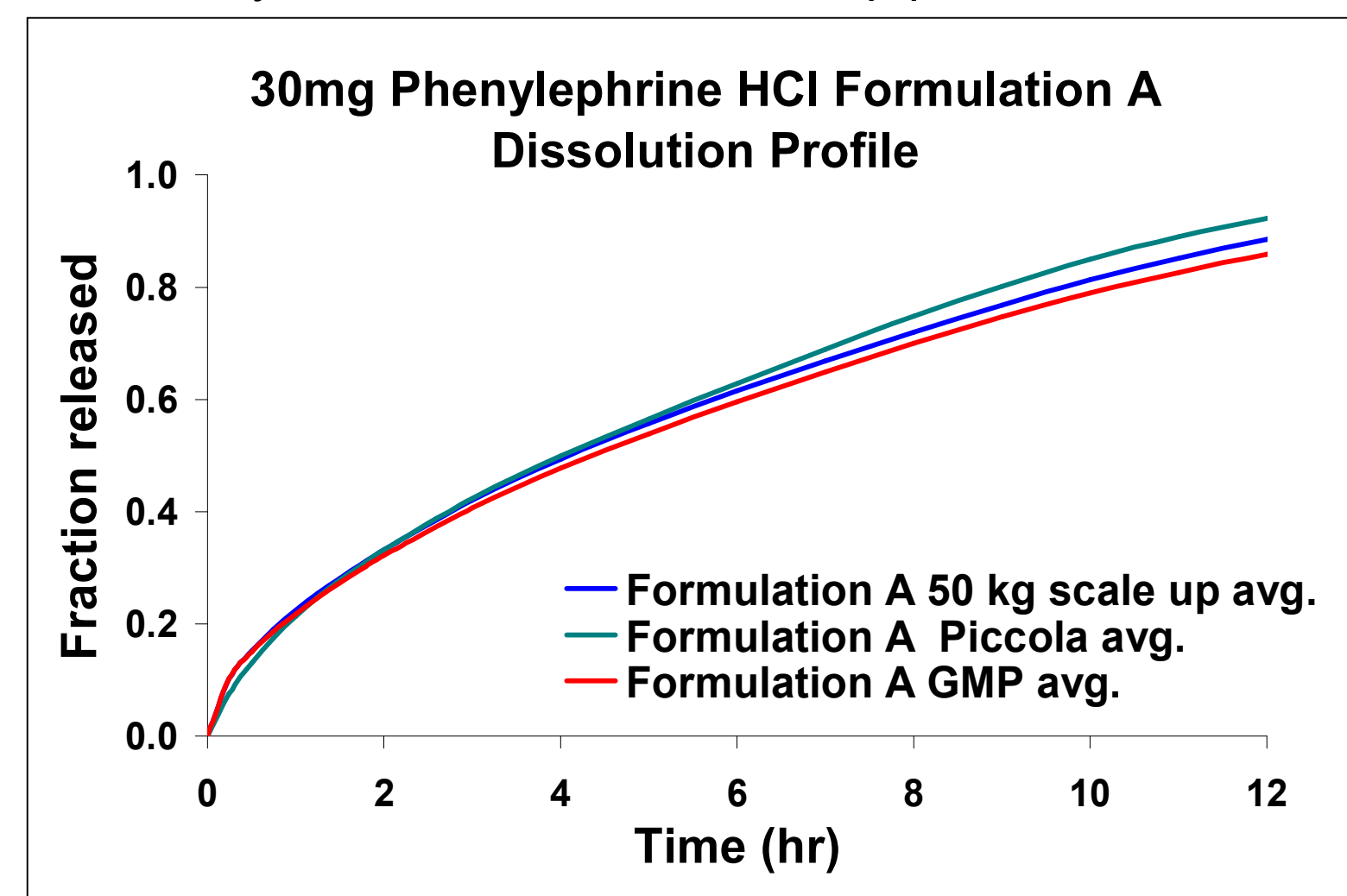
Tablets containing 30mg Phenylephrine HCl were dry-blended and directly compressed using a single-station Carver Hydraulic press, a ten-station Piccola rotary press, and a 29 stations Korsch Tablet Press. In addition to active drug, the controlled release tablet matrix formulations contained hydroxypropylmethyl cellulose, microcrystalline cellulose, an electrolyte as a novel channel forming and release modifying agent, and lubricants. *In vitro* dissolution studies were conducted using USP Type II apparatus with 900mL of deionized water at 37°C ± 0.5 and 50 rpm paddle speed. Samples were withdrawn every 60 minutes over 12-18 hours via peristaltic pump and analyzed via UV spectroscopy at 214 nm.

## RESULTS AND DISCUSSION

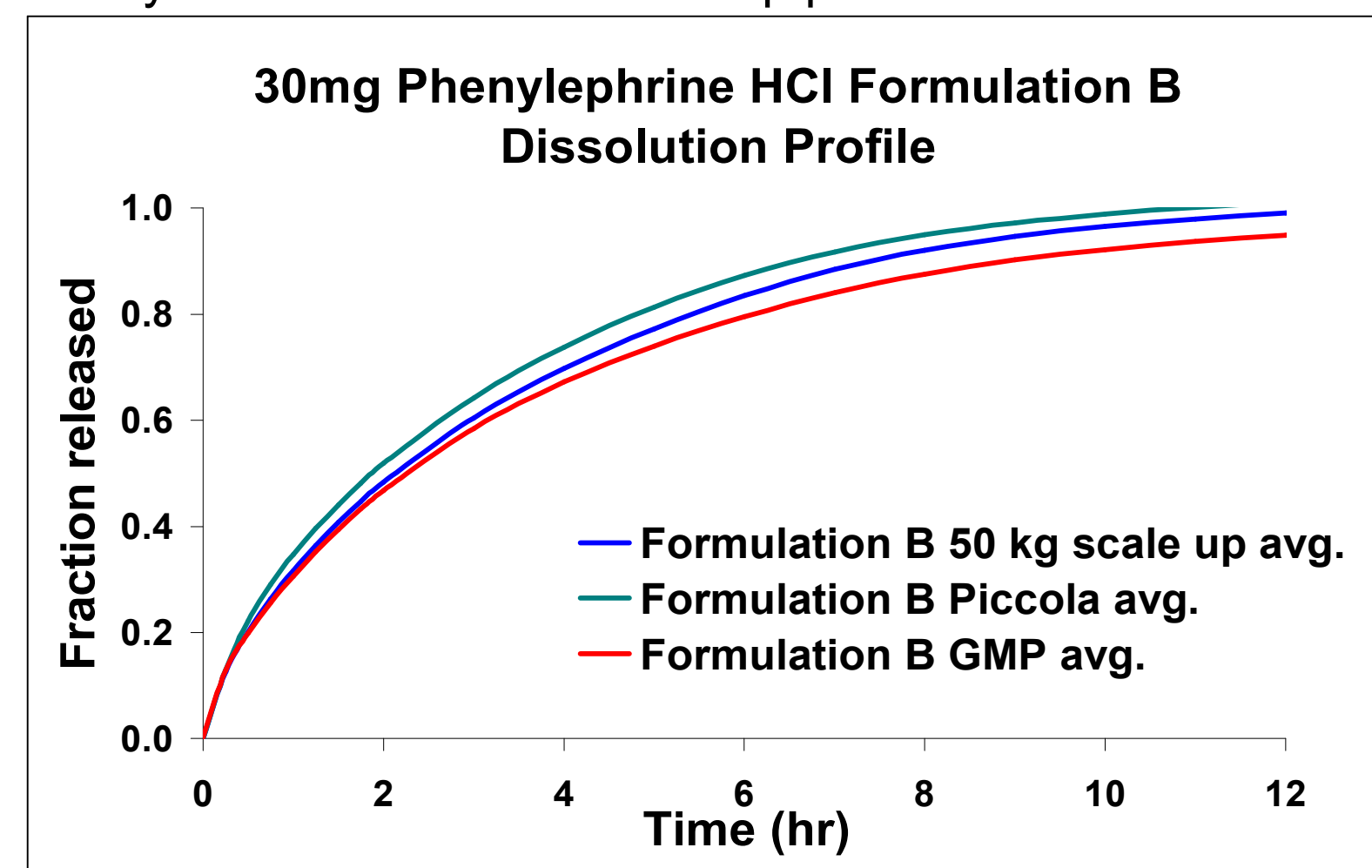
Three controlled release formulations of Phenylephrine HCl were shown to effectively control the release of drug over a 12 hour period and demonstrated excellent ruggedness at a variety of manufacturing scales (as shown in Figures 1, 2 and 3). As is evident from the dissolution profiles, the controlled release matrix technology allows for the development of a variety of release profiles: formulation A displays a near-linear rate of release, formulation B displays a first order rate, and formulation C displays a hybrid profile of near-linear and first order

rates. The variation in release was achieved by varying the amount of the electrolyte present in the tablet matrix. The three formulations also demonstrated very reproducible physical characteristics across all manufacturing scales (as shown in Table 1).

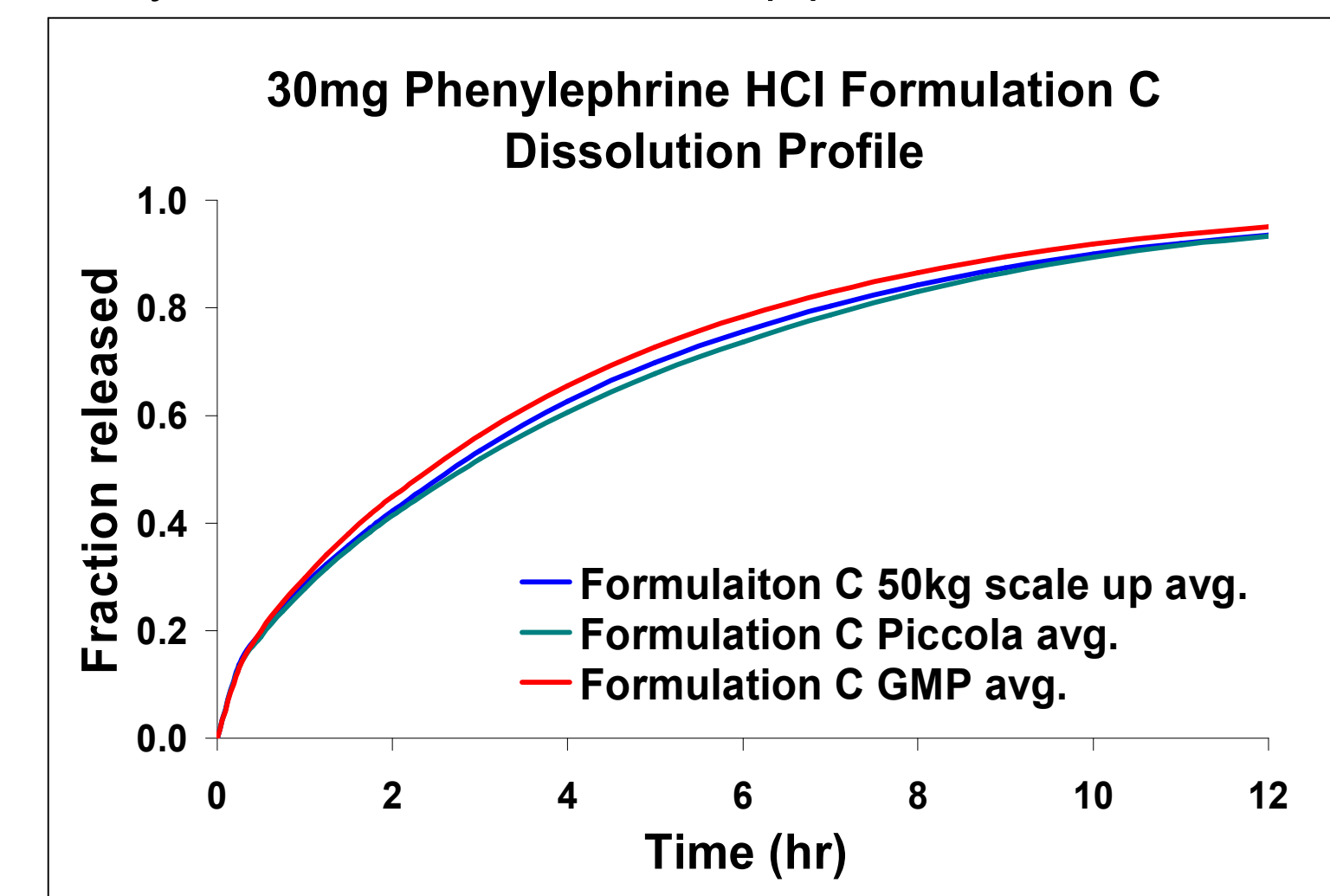
**Figure 1.** 30 mg Phenylephrine HCl formulation A *in vitro* study results in different scale up performance.



**Figure 2.** 30 mg Phenylephrine HCl formulation B *in vitro* study results in different scale up performance.



**Figure 3.** 30 mg Phenylephrine HCl formulation C *in vitro* study results in different scale up performance.



**Table 1:** Phenylephrine HCl physical characteristics at different manufacturing scales.

	Batch size (g)	Hardness average (kp)	Thickness average (inch)
Formulation A	500	16	0.23
Formulation B	500	12	0.19
Formulation C	500	18	0.17
Formulation A	50,000	16	0.23
Formulation B	50,000	12	0.18
Formulation C	50,000	18	0.17

## CONCLUSION

Three oral controlled release formulations of Phenylephrine HCl were successfully developed. By varying the amount of a novel controlling excipient, an electrolyte, programmable release was demonstrated using otherwise similar monolithic polymer matrices. All three formulations demonstrated excellent reproducibility in terms of physical characteristics and dissolution performance at various scales of manufacture.

## REFERENCES

1. Phenylephrine HCl. RxList the Internet Drug Index. (On line) <<http://www.rxlist.com>> Copyright © 2006 by RxList Inc.
2. Federici, C. and Brunelle, A., *et al.*, Novel Design of a Monolithic Controlled Release Formulation of Phenylephrine HCl for Oral Administration. SCOLR Pharma, Inc.(2005)
3. Pillay, *et. al.* Monolithic tablet for controlled drug release. U.S. Patent 6090411. (2001)

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