

Department of
Pharmaceutics
Bonn

3D molded carbidopa stoppers for fix dose levodopa gastro retentive tube delivery system

UNIVERSITÄT **BONN**

Excipients
NISSO HPC

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Introduction:

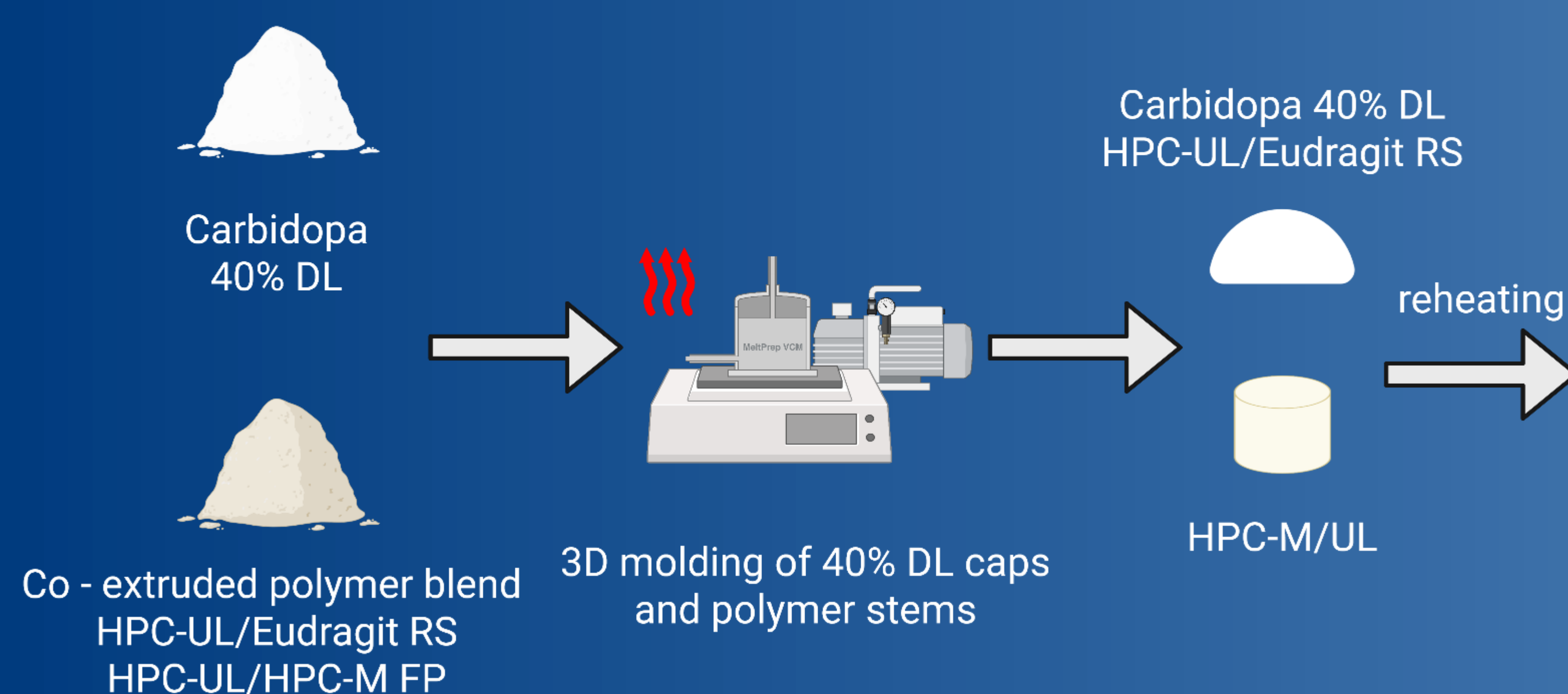
Starting from a floating levodopa gastroretentive system a 3D-molded plug was developed to incorporate an DDC inhibitor (carbidopa) with a faster release profile into an extended release levodopa formulation.^[1]

Highlights:

- Floating gastroretentive tube system, containing two different APIs with individual release kinetic.
- Floating over 6-12 hours.
- Tunable exiting time from the stomach to the gut (here from 6-12 hours).
- pH independent sinking time due to pH independent swelling of HPC.

Methods:

3D molding of plugs



Release and sinking controlling plug

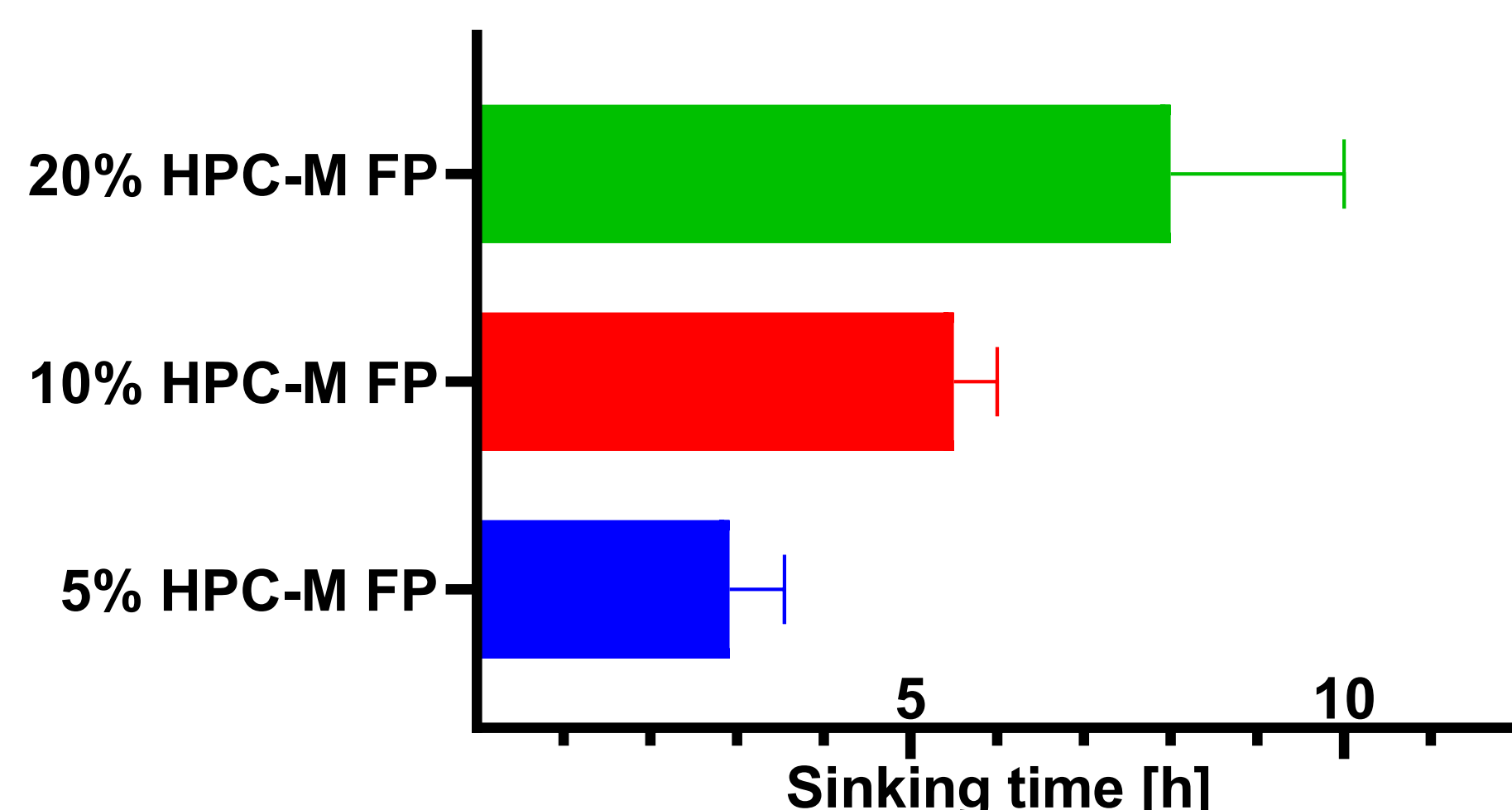
- Head controls Carbidopa release
- Stem controls exiting time out of the stomach

Swimming gastroretentive tube

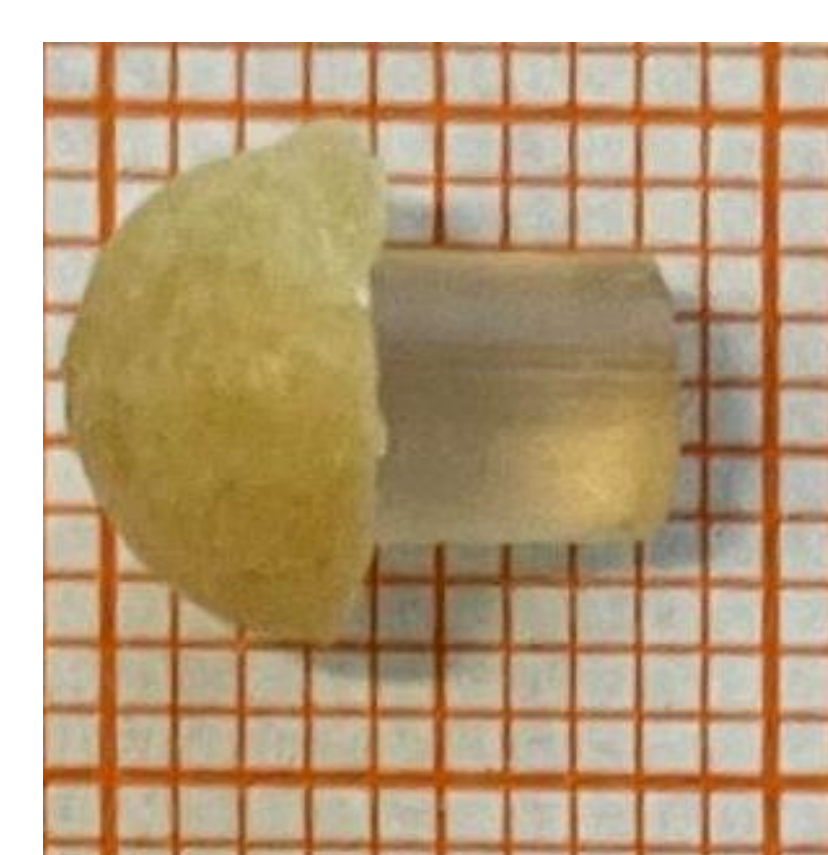
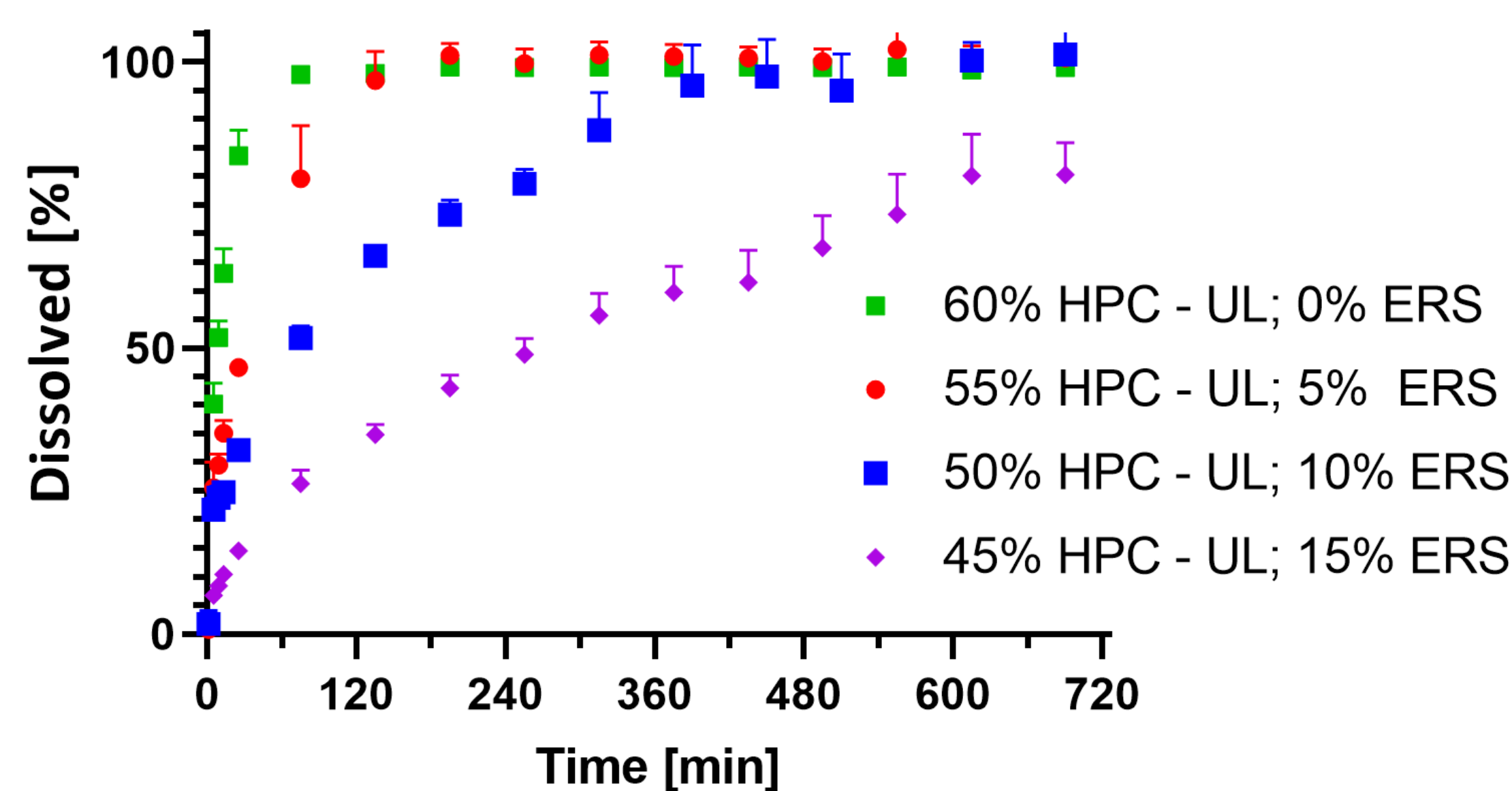
- Head controls Carbidopa release and exiting out of the stomach
- Hollow tube controls Levodopa release and ensures swimming

Results:

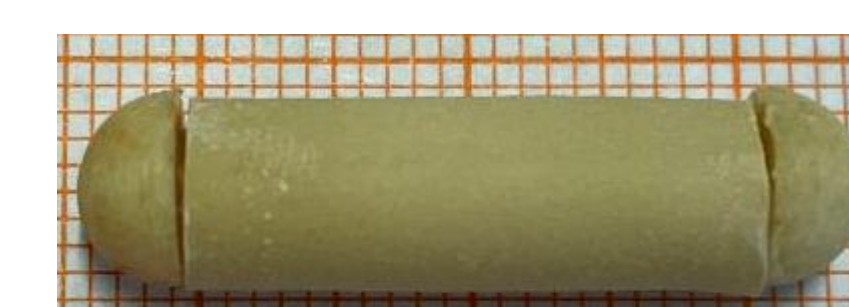
Sinking time of Levodopa tube with different stoppers (containing different HPC-UL/M FP ratios), (0.1 N HCl, USP 1, 37° C, 75 RPM)



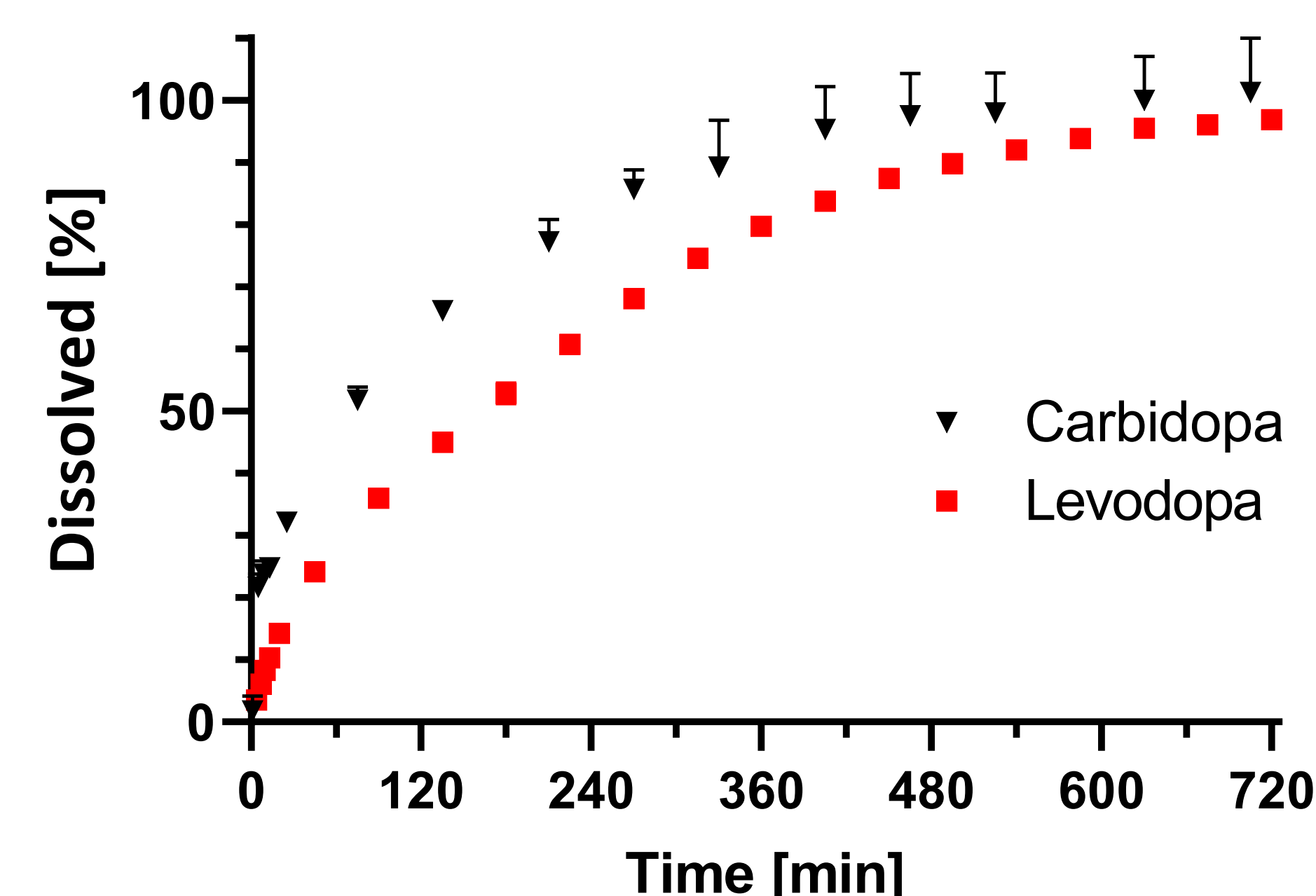
Dissolution study of the plugs containing 40% DL Carbidopa



Picture of a carbidopa containing plug and closed (floating) tube



Dissolution study of the final Carbidopa plug with previously developed Levodopa dosage form^[1]



Conclusion:

- Floating gastro retentive drug delivery system containing a combination of levodopa and carbidopa
- Optimized, faster release profile of carbidopa in combination with levodopa^[2]
- Optimized safe exiting out of the stomach preventing accumulation using HPC-M FP/UL
- Production of extended release plugs using the 3D-molding manufacturing technique by MeltPrep® as small scale surrogate for later on injection molding processing

References:

- [1] P. Bebernik, J. Frenzel, L. Beck, K. Dauer, K.G. Wagner, Rational design and DoE based prediction model for levodopa gastroretentive systems based on hot-melt tube extrusion, *Journal of Drug Delivery Science and Technology*, <https://doi.org/10.1016/j.jddst.2025.107201>.
- [2] Nyholm, D., Odin, P., Johansson, A. et al.: Pharmacokinetics of Levodopa, Carbidopa, and 3-O-Methyldopa Following 16-hour Jejunal Infusion of Levodopa-Carbidopa Intestinal Gel in Advanced Parkinson's Disease Patients. *AAPS J* 15, 316–323 (2013). <https://doi.org/10.1208/s12248-012-9439-1>