Calcium phosphate microcapsules for paediatric drug delivery

J. Kost[1], J. Huwyler[2], M. Puchkov[2]

[1]*Galvita AG, Mattenstrasse 22, 4058 Basel, Switzerland*

[2]*University of Basel, Klingelbergstrasse 50, 4056 Basel, Switzerland*

Introduction

Modern drug delivery needs to use novel multifunctional materials for developing medicinal products and new therapies.[1] Porous particles attract a lot of attention as promising drug delivery systems. Functions of porous particles are directly related to their surface properties, specific surface area, morphology, size and pore size distribution.[2] Our previous works have shown that porous functionalized calcium carbonate particles are a prototype material with several functions, i.e., they can be used as filler, disintegrant, tablet hardness enhancer, and encapsulation carrier at the same time. Besides the multifunctionality, it is a biocompatible, biodegradable, and non-toxic compound. On the other hand, we have identified some downsides, such as a limited encapsulation efficiency.[3-4] The latter results in drug depositions on the carrier's surface, which leads to a loss of material multifunctionality as the physicochemical properties change.

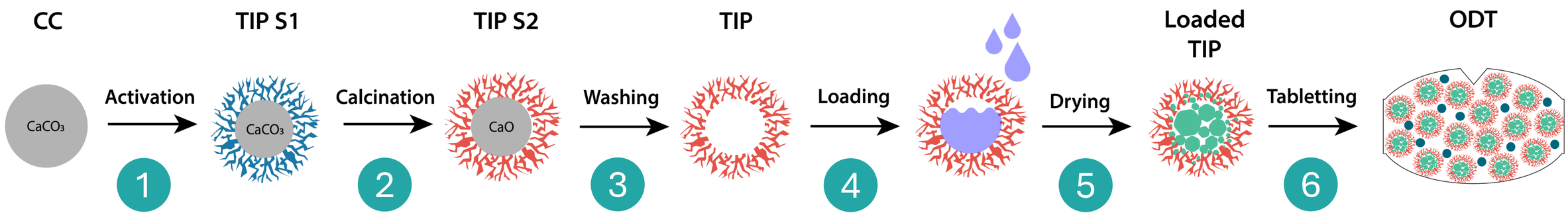
Aim

Galvita provides a novel easy-loadable inorganic carrier material for paediatric drug delivery:

Template-Inverted Particles (TIP).

Concept

- ☑ Hard Tablets
- ☑ Fast Disintegration
- ☑ Biodegradable
- ☑ Broad applicability



Activation: CC is activated with H_3PO_4 to TIP stage 1 (TIP S1) forming a porous shell

Calcination: Temperatures > 700 °C are used to degrade the CC core to CaO

pH controlled Washing: The degraded template core is removed by washing with water

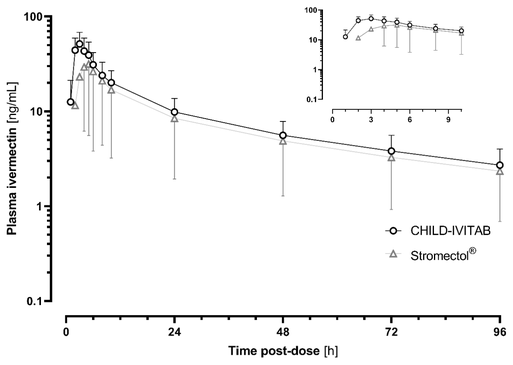
Loading: Dissolving drug of interest in a solvent

Loading: Solvent evaporation using a fluidized bed or rotary evaporator approach

Tabletting: Loaded particles are blended with disintegrants and compacted into Orally dispersible tablets (ODT)

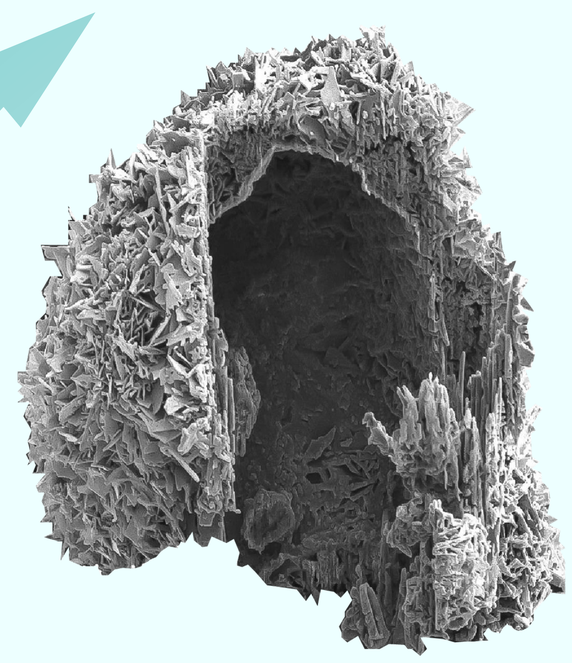
Clinical evaluation

Ivermectin loaded TIP



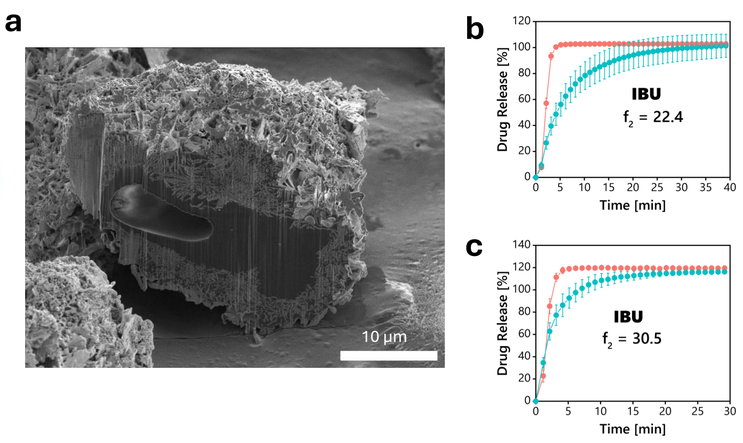
Dao et al. *J Clin Pharmacol 2024*

- Less intersubject variability in drug exposure [5]
- Excellent palatability and acceptability
- Ongoing clinical studies: NCT05894057, NCT04716335 and NCT04508166



Drug loading

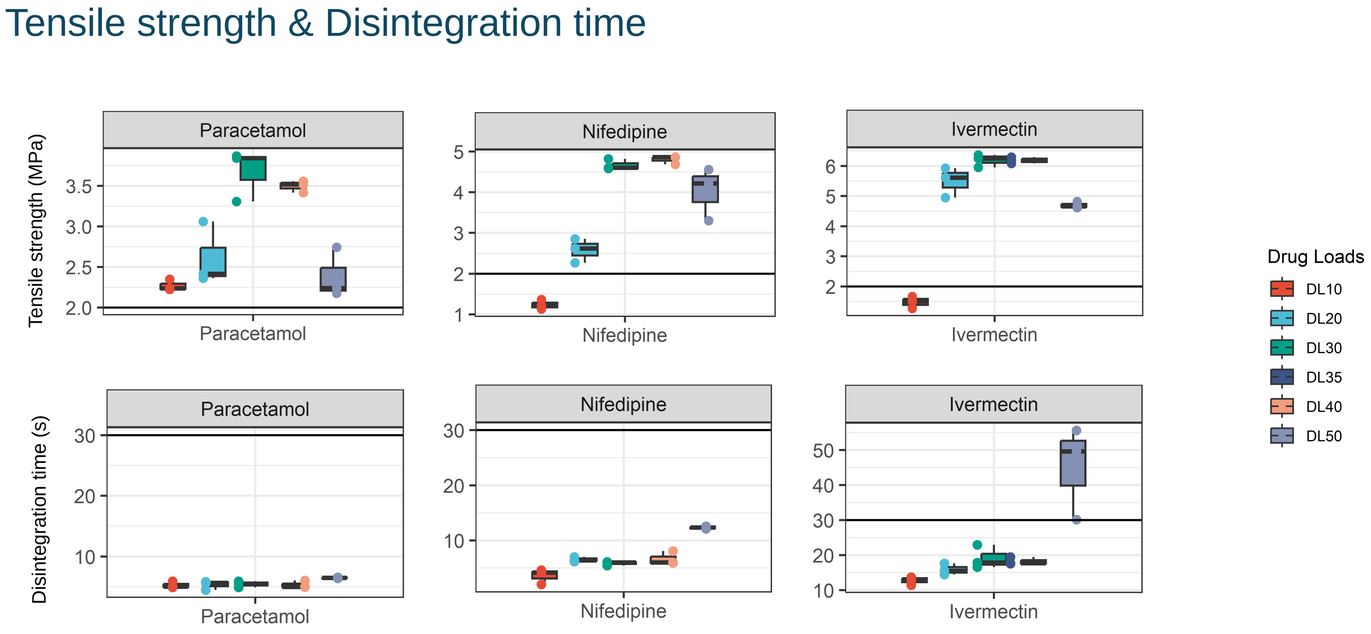
The cavity of TIP is loaded with API using a solvent evaporation approach. Loading is preferably performed using a fluidized bed equipment or a rotary evaporator.



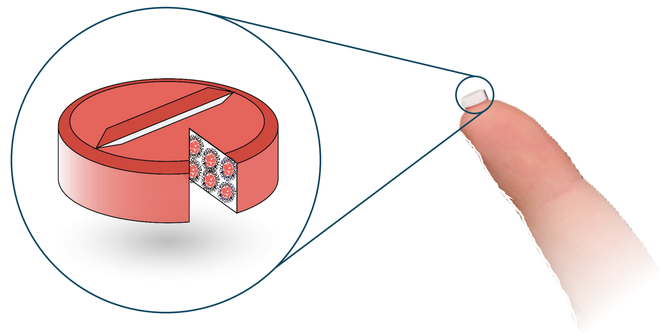
Characterization of drug-loaded TIP. a) FIB-SEM cross-section of ibuprofen (IBU) loaded TIP. Drug load 45% (v/v). **b)** Drug release from drug-loaded TIP (red) comparfed to drug TIP mixtures in artificial saliva. **c)** Drug release from drug-loaded TIP (red) compared to drug TIP mixtures in simulated gastric fluid.

Tablet characterization

Tensile strength & Disintegration time



Tablet features



Tablet features

- Disintegration time: < 30 sec.
- Hardness: > 40 N
- Drug loading capacity: 45% (v/v)

Conclusion

- TIP is a monomaterial, consisting of pure tricalcium phosphate in the form of hydroxyapatite
- Template Inverted Particles (TIP) microcapsules are a platform technology for the development of ODTs
- Drug-loaded TIP microcapsules have an excellent compactability
- The maximal drug loading capacity is 45% (v/v)
- TIP tablets are well accepted in patients, particularly in paediatrics, and have less intersubject variability in drug exposure

References

[1] T. Stirnimann, et al., Pharm. Res. 2013, 30, 1915–1925
[2] M. Zhou, et al., RSC Adv. 2017, 7, 39490–39501
[3] T. Stirnimann, et al., Int. J. Pharm. 2014, 466, 266–275
[4] D. Preisig, et al., Eur. J. Pharm. Biopharm. 2014, 87, 548–558
[5] K. Dao, et al., J. of Clin. Pharmacol. 2024, 0, 1-9