Gel Forming Tablets: Formulations with different gel former combinations and their characterization

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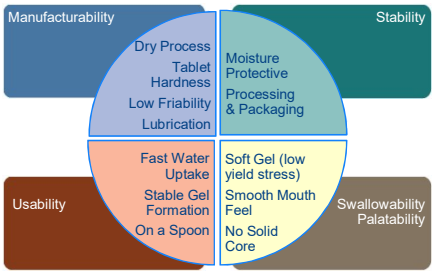
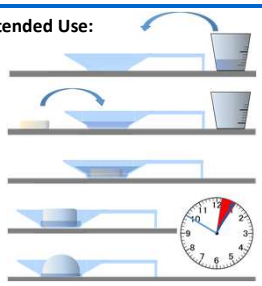
INTRODUCTION

Gel forming tablets are attractive, alternative dosage forms for children that have difficulties in swallowing monolithic solid dosage forms [1]. Such formulations combine advantages of oral solids with those of semi-solids. Rapidly gelling systems are known from gel forming system Parvulet™[2] containing gel former gellan gun, but have not been further explored with other gelling agents. Fast water uptake and a stable gel body need to be reconciled with each other during development.



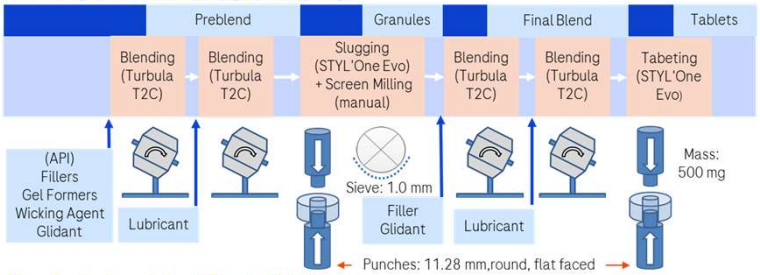
Intended Use:



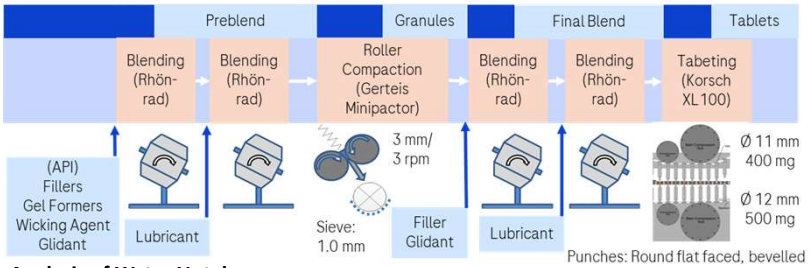
METHODS AND MATERIALS

Manufacture:

Screening Trials at Benchtop Scale (100g)



Manufacturing at Small Scale (1 kg)



Investigations:

- Screening of different water-soluble fillers in combination with MCC
- Screening of gelling agent combinations and concentrations
- Comparison of wicking agents
- Manufacture of selected formulations as placebo and with model drugs ibuprofen and acetaminophen

Excipients:

Functional Group	Ph.Eur. name	Trade name	Supplier
Filler	Mannitol	Parteck® M 100	Merck Sigma
	Isomalt	GalenIQ™ 801	BENEO
	Lactose monohydrate	Tablettose® 70	MEGGLE Pharma
	Microcrystalline Cellulose	Avicel® PH102	IFF Pharma
Gelling agent	Kappa-Carrageenan	Gelcarin® PH-911	FMC Biopolymer
	Polyethylene oxide	Polyox® WSR N10	DUPONT
	Sodium alginate	Manucol® LKX USP	FMC Biopolymer
	Pectin	Vivapharm® Pectin USP	JRS Pharma
Wicking agent	Calcium Silicate	Florite® R	Tomita Pharm.
	Magnesium Aluminium Silicate	Neusilin® US2	Fuji Chemical Ind.
Glidant	Colloidal Silicon Dioxide	Aerosil® 200	Evonik Ind.
Lubricant	Sodium stearyl fumarate	PRUV®	JRS Pharma
Drug substance	Ibuprofen	Ibuprofen 25 US Quality	BASF
	Paracetamol	Paracetamol Ph Eur micronized	Mallinckrodt Pharm.

Combination of Gelling agents investigated based previous screening studies [3] :

- Kappa carrageenan: 3-5% / Polyethylene oxide: 3-5% (CA/PO)
- Kappa carrageenan: 3-5% / Sodium alginate: 0.1% (CA/SA)
- Polyethylene oxide 3-5% / Sodium alginate: 0.1% (PO/SA)
- Polyethylene oxide: 3-5% / Pectin: 3-5% (PO/PE)

Analysis of Water Uptake

Tensiometer:
KRÜSS K100 Mk2, 80mL potable water (Evian®) at 20°C

Optimized 3DP tablet holder with an aluminum base

Weight increase recording

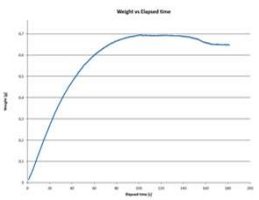


Image Analysis

KEYENCE VHX-7000 Digital Microscope

3 mL potable water (Evian®)

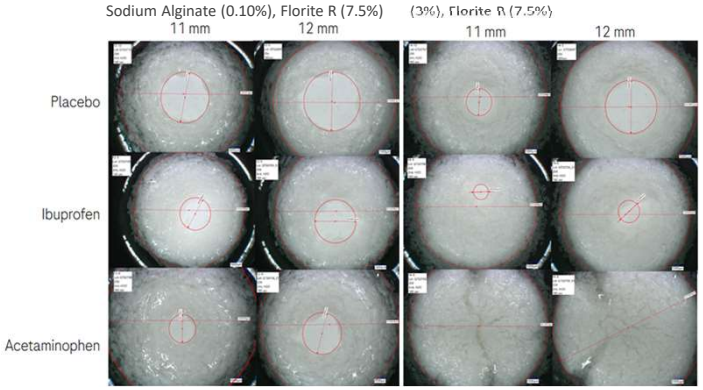
Video recording for 3 min.

RESULTS

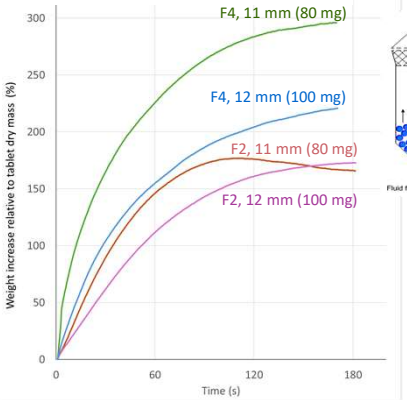
Water Ingress after 180 sec.

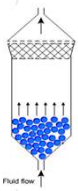
F4 Gelling System: κ-Carrageenan (3%), Sodium Alginate (0.10%), Florite R (7.5%)

F2 Gelling System Pectin (3%), Polyox (3%), Florite R (7.5%)

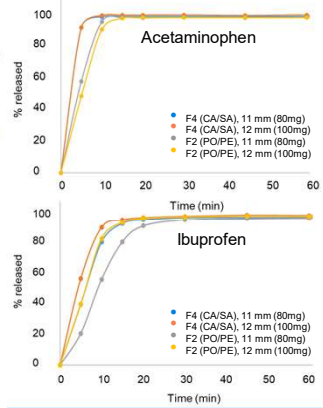


Tablets with Acetaminophen: Weight increase over 180 sec.





Dissolution (USP4) in 15mM Citrate/46 mM NaCl pH 6.8, Flow rate: 15 mL/min



CONCLUSIONS

Gel forming tablets are manufacturable at targeted properties and performance. Applied characterization methods were able to guide the development in optimization. Drug properties and dose will drive the selection of the best gel former combination and will determine the optimal tablet dimensions. Tailor-made, optimized formulations depending on the drug are necessary. Placebo tablets may be developed as gel forming carrier system for sprinkle of granules and capsule content.

REFERENCES

(1) Strickley, R.G., *Pediatric Oral Formulations: An Updated Review of Commercially Available Pediatric Oral Formulations Since 2007.* Journal of Pharmaceutical Sciences, 2019. 108(4): p. 1335-1365.
(2) Bar-Shalom, D., Slot, L., Fischer, G., Hemmingsen, P.H., *Swellable Dosage Form Comprising Gellan Gum.* United States Patent: US 8,383,155 B2, Feb. 26, 2013
(3) Si Ying Lai, Oral Gel Forming Tablets as Generic Vehicles in an age-appropriate approach for easily swallowable medicine, Master Thesis, 2023, EPFL Lausanne, Prof. F. Stellacci