

Difficult to tablet,
high dose drug

PARACETAMOL

Mallinckrodt code 6375, formerly 6088



**PARACETAMOL MILLED GRADES
TYPICAL PROPERTIES AND APPLICATIONS**

Description		Standard Powder		Semi-Fine Grade		Fine Powder		Micronised	
Application		Granulation For Tablets		Granulation For Tablets		Liquid Products/ Granulation		Suppositories	
Code/Container Size (*Other pack sizes available)		6088 0048	50kg 100kg*	0081 0084	50kg 100kg*	7845	50kg*	0422	50kg
Particle Size Analysis		% Retained		% Retained		% Retained		% Retained	
Mesh	Micron	Specification	Typical	Specification	Typical	Specification	Typical	Specification	Typical
+20	+850		0.1						
+40	+425	1.0 max.	0.5		0		0		
+60	+250	7.0 max.	4	2.0 max.	1		0.3		0
+80	+180		10		3		1		
+100	+150	5.0 -19.0	11		5		2	1.0 max.	0.1
+140	+105			12.0 max.		9.0 max.	2		
+200	+75		32		17		9		0.1
+270	+53						16		0.3
+325	+45		47		34		21		0.4
+400	+38		56	22.0 – 44.0	37	11.0 -32.0	23	5.0 max.	1
+500	+26		65		52		38		38
+635	+20		84		68		59		67
Typical Bulk Density (g/ml)		0.41		0.31		0.26		0.24	

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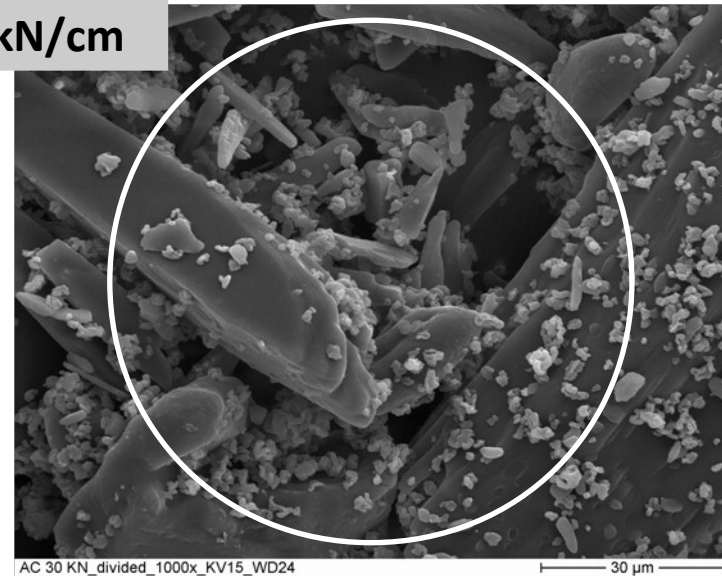
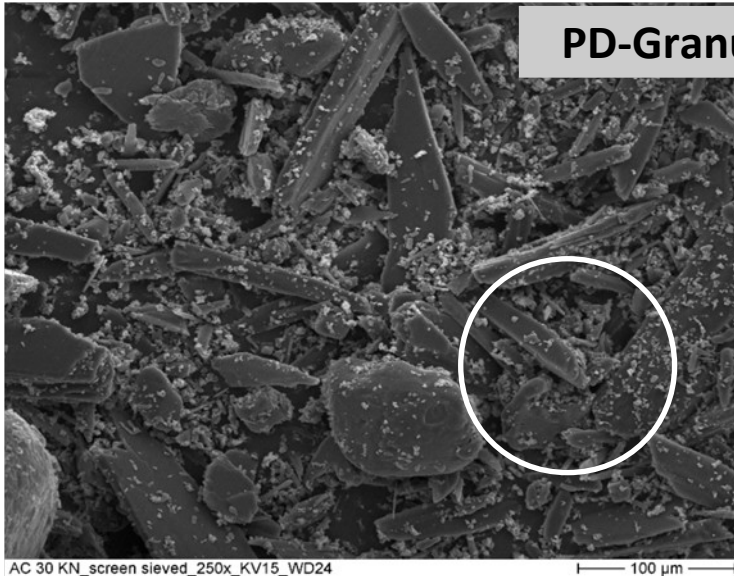
Reviewed August 2008

Paracetamol trial set-up

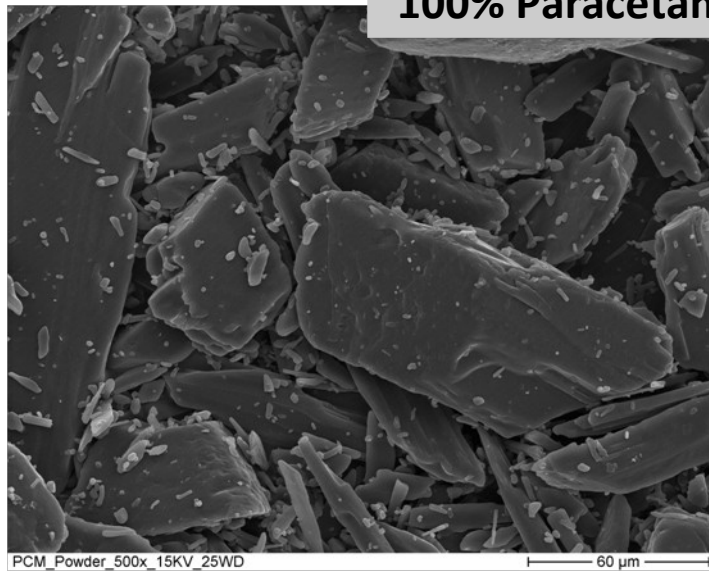
Pre-blend (to be PD-Granulated)

- 94.1% Paracetamol (80 parts)
- 5.9% Kollidon CL-M (5 parts)

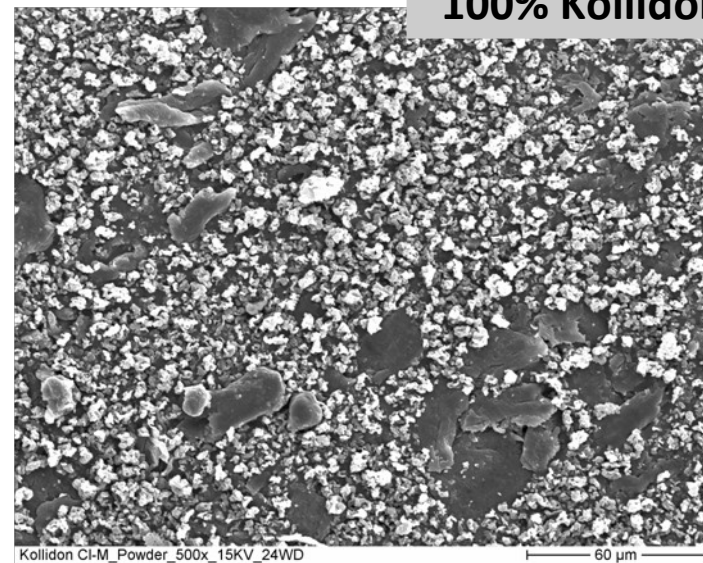
PD-Granulate 5kN/cm



100% Paracetamol



100% Kollidon CL-M



Paracetamol trial set-up

Pre-blend (to be PD-Granulated)

- 94.1% Paracetamol (80 parts)
- 5.9% Kollidon CL-M (5 parts)

Final blend

- 85.0 % Pre-blend
- 9.5 % PD-Granulated Avicel (PH105)
- 5.0 % Klucel EXF
- 0.5 % Magnesiumstearate

Final tablet contains 80% of Paracetamol

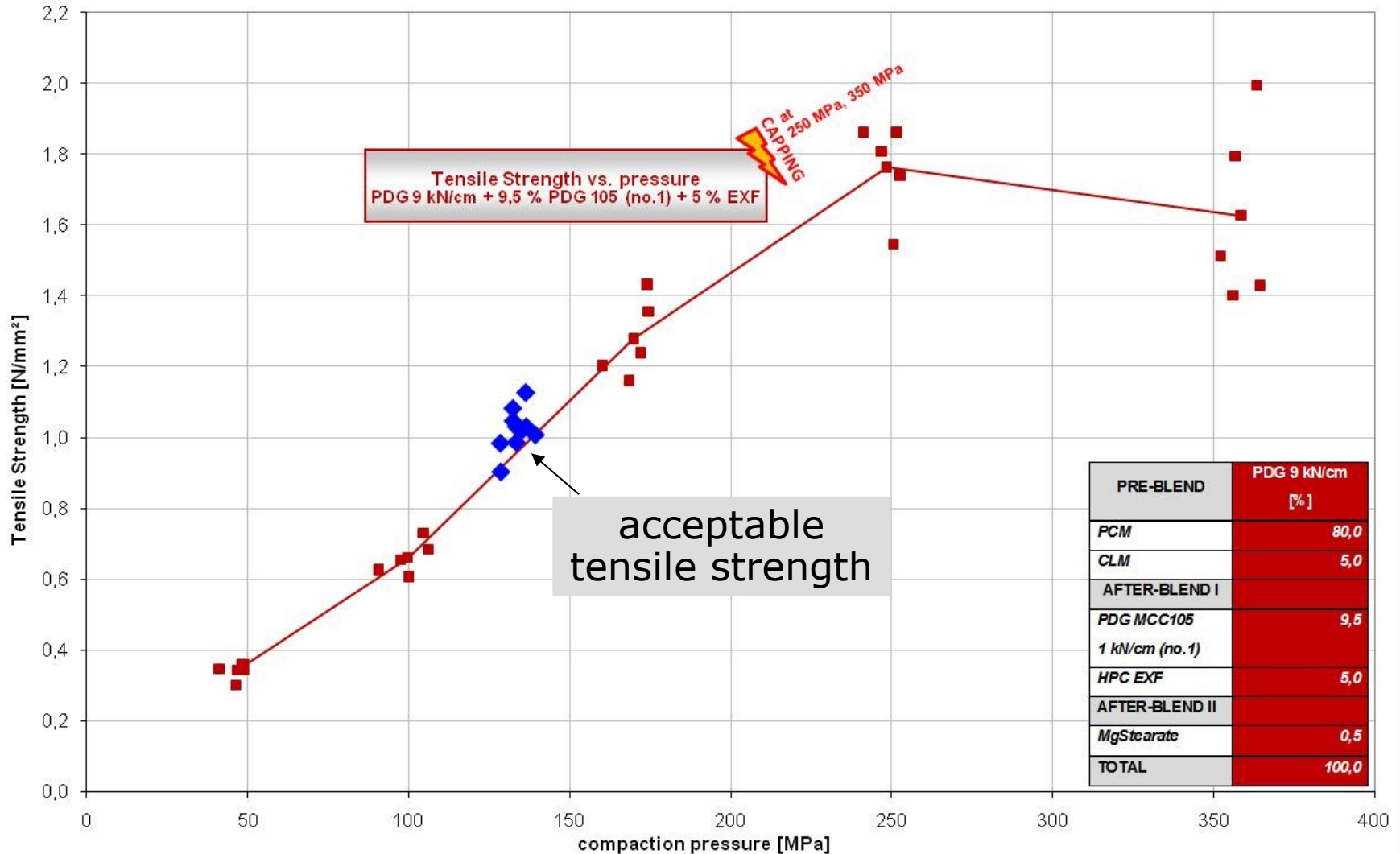
PDG granules: flowability



Avicel 102 AC 45 AC FB.mov

PDG granules: compactibility

Tensile Strength - compaction pressure - profile



PDG granules: no capping

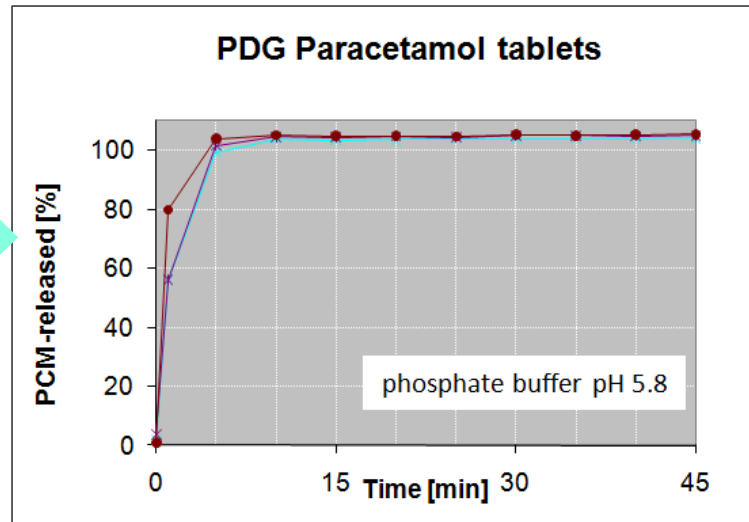
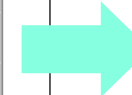
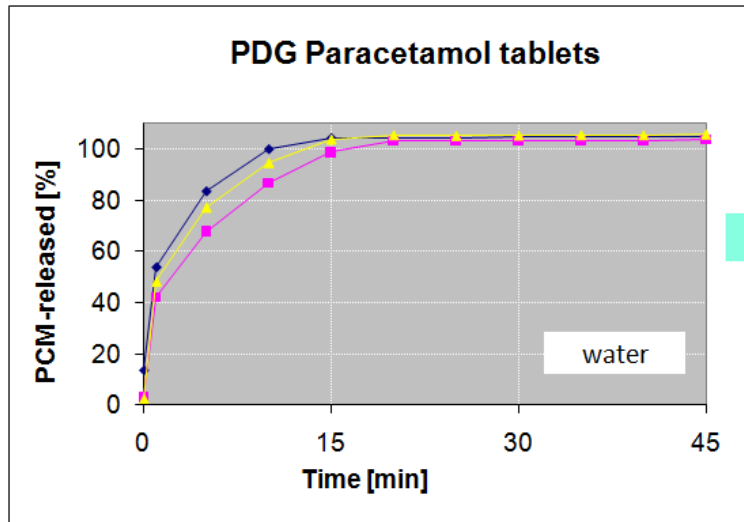
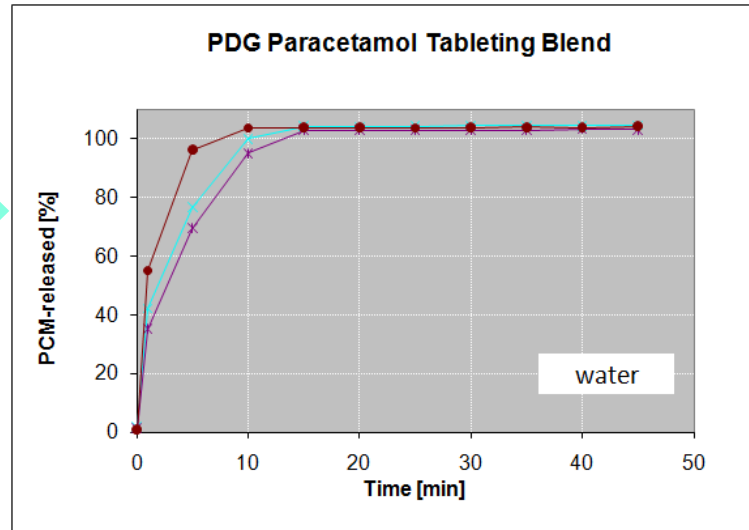
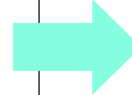
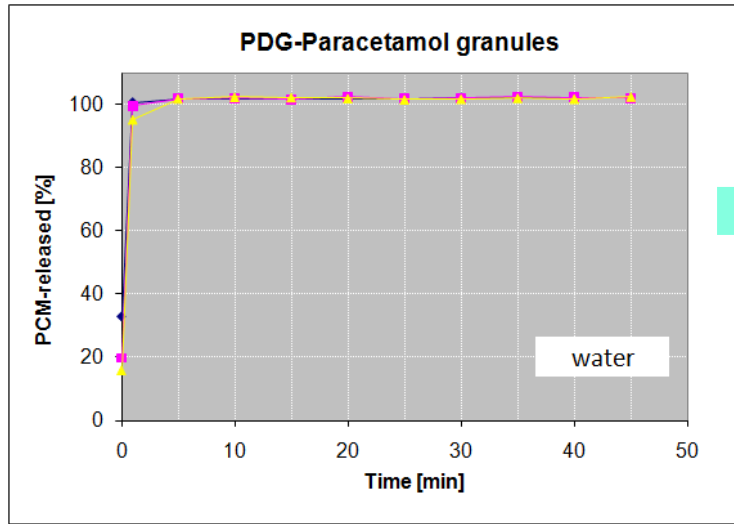


Friability: 0.27 %

No capping at all



PDG granules: dissolution



PDG tablet properties:

aspect		
Crushing Force (9mm concave tablets (rc=15 mm), 312.5 mg)		62 N (no capping)
Tensile Strength		1.02 MPa
Friability		0.27 %
Disintegration		< 60 s
Dissolution	(phosphate buffer) (water)	100% within 5 -10 min 100% within 15-20 min

simulated tableting speed: 43000 tablets/hr (Fette 102i, 30 rpm), no sticking to punches observed

Conclusion PDG Paracetamol

Even a difficult-to-tablet material like Paracetamol results in

a well flowable granulate/tableting mix

and tablets, which

are strong enough: 60N, low friability, no capping

disintegrate rapidly: < 60 s

dissolve rapidly: within 5 to 10 min
(phosphate buffer)

have high drug load: 80% (vs. max. 50% in RC)