Wet Granulation of Acetaminophen with Starch 1500®

OBJECTIVE

To demonstrate the combined binding and disintegration properties of Starch 1500 in a low shear wet granulation process. Acetaminophen powder was chosen as the example active due to its high dose, poor flow, and compaction properties. The use of Starch 1500 in the granulation was examined in two ways: As a dry mix with the acetaminophen using water as the granulation binder (Formula A), and with some of the Starch 1500 dispersed in the water to be used as the binder liquid (Formula B). The binding properties of Starch 1500 were also compared to PVP (Polyvidone), a commonly used wet granulation binder (Formula C).

GRANULATION PROCESS

The granulations were conducted on a laboratory scale using an 8 qt. Hobart Planetary Mixer.

Formulation	**A**	**B**	**C**
Acetaminophen	85.10	85.10	85.10
Starch 1500 (dry)	14.65	11.73	9.65
Starch 1500 (in water)	-	2.92	-
PVP K 29/32 (in water)	-	-	5.00
Magnesium stearate	0.25	0.25	0.25

Granulation Conditions

Hobart speed setting	1	1	1
Dry mix time (min.)	4	4	4
Wet mass time (min.)	5	5	5
Binder used	water alone	water + Starch 1500	water + PVP
Binder concentration (% solids)	-	20.0	18.2
Wet screening (mesh)	12	12	12

Drying conditions

Glatt GPCG-3 Inlet air (deg.C.)	65	65	65
Drying time (min.)	21	27	35
Final product temperature (deg.C.)	40	40	40
Final granulation % L.O.D.	1.4	1.2	1.2

Blending - 8 qt. "V" blender

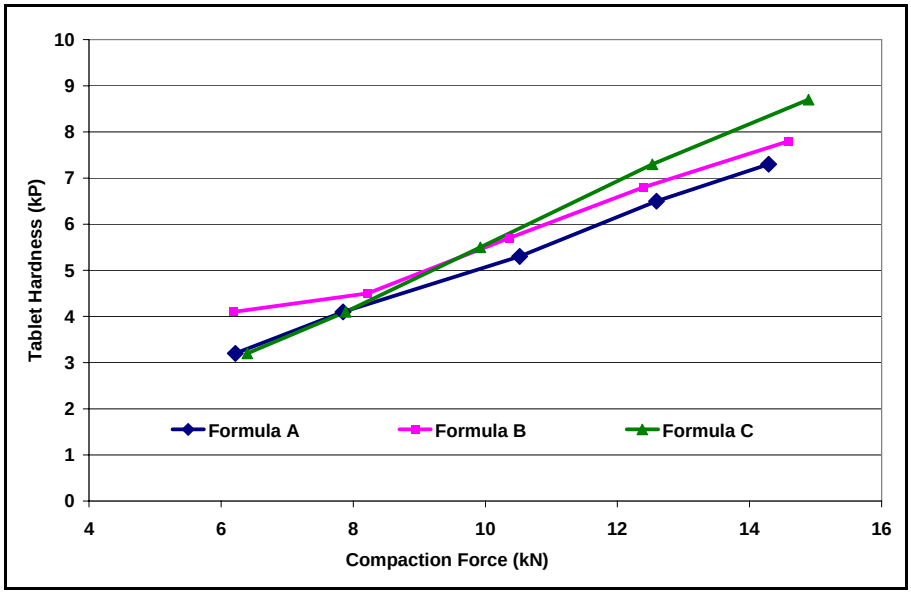
Magnesium stearate blend time (min.)	3	3	3

COMPACTION PROCESS

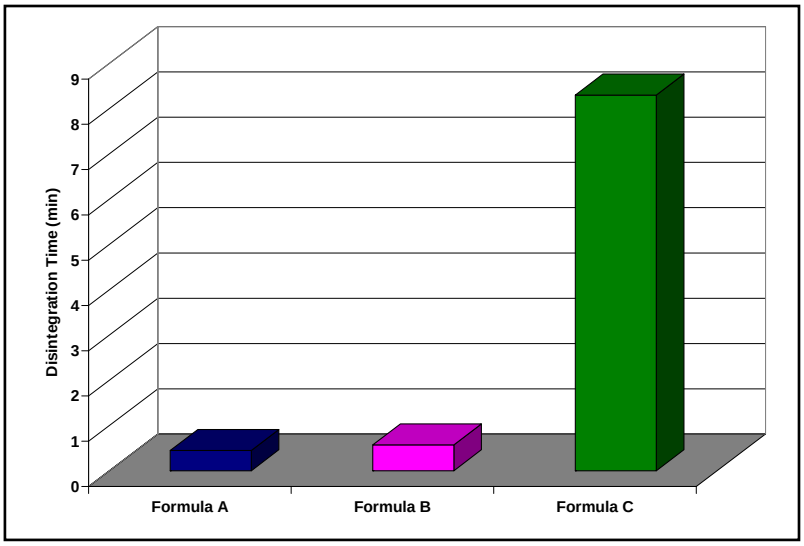
Each of the granulations were compressed on a 10 station rotary tablet press using size B, 3/8" standard concave tooling, to a total tablet weight of 382.0 mg. Tablet samples were taken at 6 different compaction forces between 6 and 15 kN of force.

COMPACTION PROFILES

The compaction profiles for the three granulations were very similar and each of the three formulations produced robust tablets. Adding some of the Starch 1500 to the water for granulation (Formula B) slightly increased the overall tablet hardness. The batch with PVP as the binder (Formula C) produced slightly harder tablets. However, upon disintegration testing in water the clear advantage of Starch 1500 as a binder was seen.



DISINTEGRATION RESULTS



CONCLUSIONS

Starch 1500 exhibited dual functionality in this formulation. As a wet granulation binder it produced tablets with similar hardness to PVP. As a disintegrant it significantly outperformed PVP, which acutally caused a delay in disintegration.

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