Issue 17: June 2009

Blending and Content Uniformity of Micronized Low Density Acetaminophen - Comparison of Fujicalin® with other DCPA's

Greetings!

Welcome. This issue of Fuji's newsletter presents preparation of acetaminophen with Fujicalin® and comparison with other commercially available DCPA's.

Blending of micronized and low dose drugs can be a big challenge due to problems related to segregation, content uniformity and physical stability. The micronized drug substances may exhibit increased cohesiveness and have a tendency to segregate in blend. Choice of excipients with narrow particle size variation, appropriate bulk density, selection of suitable equipment and technique are some of the factors that contribute to easy and stable blending of powders with different particle size.

Fujicalin® is an innovative Dibasic Calcium Phosphate Anhydrous (DCPA) that provides significantly improved compressibility and flowability when compared to other DCPA's.

Table 1. Comparison of powder properties- Fujicalin® with other DCPA's

	Acetaminophen	Fujicalin®	DCPA 1	DCPA 2	DCPA 3
Mean particle size (μm)	14	**120**	45	154	81
Bulk density (g/ml) loose	0.28	**0.46**	0.84	0.69	0.59
Bulk density (g/ml) Tapped	0.36	**0.54**	1.08	0.83	0.67
Oil adsorption capacity (ml /100g)	-	**110**	63	70	84
BETSSA (m^2/g)	-	**36.9**	0.74	16.2	19.6
Angle of repose (°)	-	**29.5**	39.6	38.2	30.5

Fujicalin has distinct advantages with respect to specific surface area, angle of repose and oil adsorption capacity when compared to other DCPA's.

Experimental Methods:

Acetaminophen tablets were prepared by direct compression technique with **Fujicalin®** and three other DCPA's. Micronized acetaminophen (14 μm) was blended with DCPA's and the powder as well as tablet properties were compared with **Fujicalin®.**

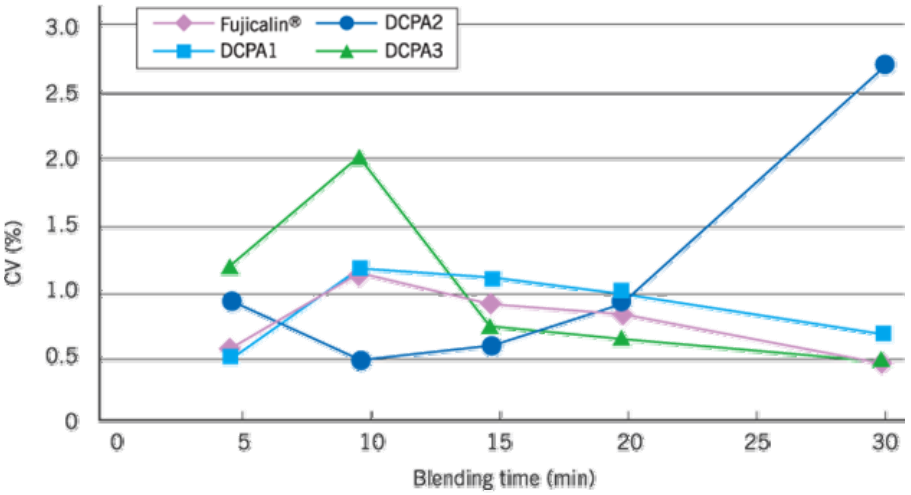
Table. 2 Formulation summary

Formulation	i	ii
Micronized acetaminophen (14 μm)	10.0	10.0
Fujicalin®	84.0	-
DCPA's (1, 2 and 3)	-	84.0
Croscarmellose sodium	5	5
Mg-St	1	1

Croscarmellose sodium was used as a disintegrant and Magnesium stearate (Mg-St) as lubricant.

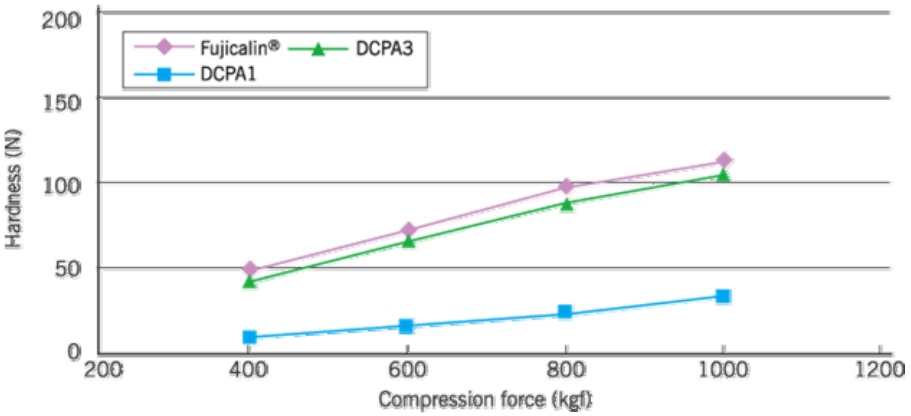
Results:

Fig. 1. Content uniformity of powder blend of micronized acetaminophen with Fujicalin® and other DCPA's



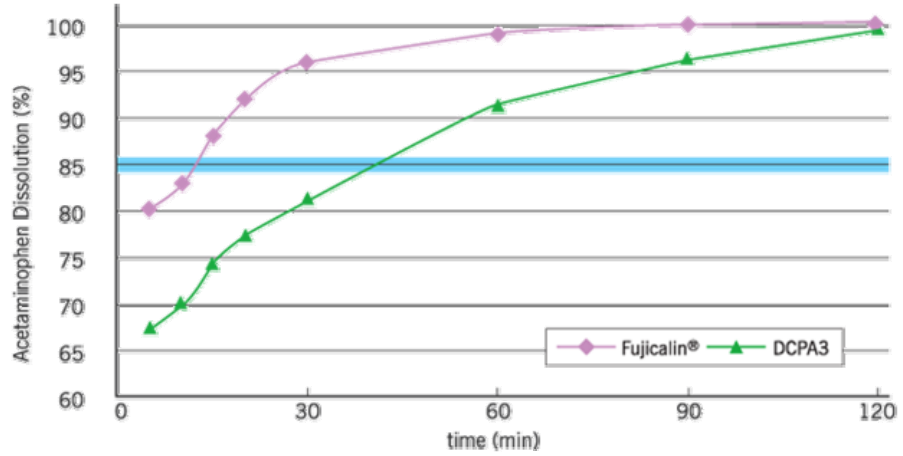
Blending of micronized acetaminophen powder and DCPA's were carried out for 30 minutes in a 2 Litre V shaped low shear blender at 40 rpm. Samples were chosen from three predefined locations in the blender at 5 minute intervals and checked for content uniformity using spectroscopic assay. Fujicalin® showed easy blending character when compared to other DCPA's. DCPA 2 tends to segregate after 20 minutes of blending. The extended blending was carried out to check the stability of tabletting operations like transfer to hopper prior to tabletting.

Fig 2. Tablet hardness of acetaminophen tablets directly compressed with Fujicalin® and other DCPA's



Tabletting was carried out in a rotary tabletting machine (2 HT AP18SS) manufactured by Hata Iron Works, at 400 to 1000 Kgf. Tablet dimensions (Ø8mm x 9mmR); Tablet weight (275 mg). **Fujicalin®** and DCPA3 showed similar tabletting properties with respect to hardness. DCPA1 showed poor moldability and DCPA2 was not considered for tabletting due to segregation of blends.

Fig 3. Dissolution profile of directly compressed acetaminophen tablets and DCPA 3



Dissolution was carried out as per JPC in purified water at 37°C at a paddle speed of 50 rpm. The acetaminophen content was determined spectrophotometrically. More than 85% of the drug was released within 15 minutes of dissolution. DCPA 1 was not tested due to poor hardness of tablets.

Conclusions:

Among the DCPA's tested, **Fujicalin®** showed superior powder and tabletting properties after blending with low density micronized acetaminophen. **Fujicalin®** is spherically granulated, and has high specific surface area when compared to other available DCPA's.

Summary:

Tablet Characteristics	Fujicalin®	DCPA 1	DCPA 2	DCPA3	Quality parameters
Content uniformity	Good	Good	Poor	Good	Uniform Blend
Hardness	Good	Poor	Below spec	Good	High quality
Drug Release in 15 min	>85%	Below spec	-	>75%	Release

Fujicalin® was the best performer giving higher tablet hardness at low compression forces and improved dissolution profile when

compared to other DCPA's.

Dosage and Safety:

Fujicalin® is manufactured under strict quality control at our FDA-GMP certified facilities. Dibasic calcium phosphate anhydrous is widely used in oral pharmaceutical products and food products. It is generally regarded as relatively nontoxic and nonirritant material.

Fujicalin®:

Chemical formula : $CaHPO_4$
Chemical Abstract Service (CAS) Number: 7757-93-9
U.S. Patent No. 5,486,365, Jan 1996
U.S. Drug Master File (DMF) filed, Conforms to USP/NF, EP and JP; and listed as GRAS

To obtain a sample or to find your local distributor, please contact us.
For more technical information on Fujicalin®, click here.
To read Fuji's technical newsletter back numbers, click here

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