Fuji Chemical Industries

PHARMACEUTICAL TECHNICAL NEWSLETTER

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F-MELT®: THE COST-EFFECTIVE SOLUTION FOR PRODUCING HIGH-QUALITY ORALLY DISINTEGRATING TABLETS (ODTs).

NEWSLETTER HIGHLIGHT

Directly compressible excipient system for fast-Disintegrating oral tablets*, F-MELT® formulations are designed with a focus on three important characteristics of ODTs: tablet hardness, mouthfeel, and acceptable oral disintegration times.

ODT is a rapidly developing market, with new technologies emerging that offer distinct advantages. However, direct compression remains the preferred choice due to its use of conventional equipment and materials, which help to maintain lower manufacturing costs.

F-MELT® is a spray-dried granulation composed of five pharmaceutical grade excipients, including carbohydrates, inorganic ingredients, and disintegrants. It is available in two grades, F-MELT® Type C and F-MELT® Type M. The individual excipients which are contained in F-MELT® conform to either USP-NF, EP or JP standards.

**Patented in Japan, U.S., EU and India*

Physical Properties of F- MELT®**

Physical Parameters	Type M	Type C
Appearance	White to pale yellow powder	
Loss on Drying (%)	1.80	1.30
Loose Bulk Density (g/mL)	0.56	0.54
Tapped Bulk Density (g/mL)	0.65	0.65
Angle of Repose (°)	**32.9**	34.2
Mean Particle Size (μm)	122.3	120.8

**Reference Data

While F-MELT® can provide the desired tablet hardness and mouthfeel, in many cases, additional organic or inorganic excipients may be necessary to achieve the desired outcome. The following examples illustrate how F-MELT® can be combined with other excipients to maintain a higher tablet hardness and improve the overall mouthfeel.

FORMULATION EXAMPLE

Example 1. F- MELT® Type C - Acetaminophen and Aspirin ODT formulations with focus on tablet hardness, mouthfeel and acceptable oral disintegration times.

	Acetaminophen			Aspirin		
(wt %)	**30**	**30**	**40**	**40**	**40**	**40**
F-MELT® Type C (wt%)	49.6	64.6	34.6	49.6	49.6	39.6
Other Excipients (wt%)	20	5	25	10	10	20
	CMC	**Kollidon CL**	**MCC**	**CMC**	**Kollidon CL**	**Corn Starch**
Lubricant (Mg-St) (wt%)	0.4	0.4	0.4	0.4	0.4	0.4
Compression Force (kN)	12-13	11-12	6-7	7-8	6-7	9-10
Tablet Hardness (N)	**44.7**	**50.4**	**58.2**	**43.6**	**41.6**	**49.2**
Oral Disintegration Time (sec)	**24.7**	**21.4**	**21.1**	**21.2**	**19.1**	**22.8**
Mouth Feel	**Very Good**	**Very Good**	**Fair**	**Very Good**	**Good**	**Good**

CMC - Carboxymethyl Cellulose, **MCC** - Microcrystalline Cellulose, **Mg-St** -Magnesium Stearate. Tablet of 200 mg with 8 mm diameter were manufactured on a rotary tabletting machine.

In case of acetaminophen and aspirin as API, a combination of CMC or Kollidon CL with **F-MELT® Type C** provided hard tablets with very good mouth feel and satisfactory oral disintegration times.

Example 2. F- MELT® Type M - Acetaminophen ODT formulations with focus on tablet hardness, mouthfeel, and acceptable oral disintegration times.

Acetaminophen (wt%)	**30**	**30**	**30**	**40**	**40**	**40**
F-MELT® Type M (wt%)	**49.6**	**49.6**	**49.6**	**29.6**	**39.6**	**34.6**
Other Excipients (wt%)	20	20	20	30	20	25
	Corn Starch	**CMC**	**HPS**	**CMC**	**MCC**	**MCC**
Lubricant (Mg-St) (wt%)	0.4	0.4	0.4	0.4	0.4	0.4
Compression Force (kN)	10-11	14-15	10-11	21-22	9-10	7-8
Tablet Hardness (N)	**45.6**	**43.9**	**48.6**	**46.6**	**54.0**	**55.2**
Oral Disintegration Time (sec)	**14.1**	**26.6**	**26.2**	**23.5**	**36.2**	**18.3**
Mouth Feel	**Good**	**Very Good**	**Very Good**	**Fair**	**Good**	**Fair**

At a higher drug load of 40%, MCC in combination with **F-MELT® Type M** allowed working at relatively low compression forces and yielded tablets with good hardness and a relatively low disintegration time. When used in combination with corn starch, **F-MELT® Type M** provided hard tablets with good mouthfeel and excellent oral disintegration time for acetaminophen.

Example 3. Working with sticky, sour APIs: L-Ascorbic Acid formulations with focus on tablet hardness, mouthfeel, and acceptable oral disintegration times.

L-Ascorbic Acid (wt%)	30	30	30
F-MELT® Type C (wt%)			39.6
F-MELT® Type M (wt%)	70.0	39.6	
Other Excipients			
CMC (wt%)		10	10
MCC (wt%)		19.5	19.5
Talc (wt%)		0.5	0.5
Lubricant (Mg-St) (wt%)	*	0.4	0.4
Compression Force (kN)	5	5-6	6-7
Tablet Hardness (N)	**52.9**	**44.4**	**42.0**
Oral Disintegration Time (sec)	**19.1**	**27.7**	**30.0**
Mouth Feel	**Best**	**Good**	**Good**

Ascorbic acid is a difficult API to tablet due to its sticky nature. However, F-MELT® has been successfully used in formulations to achieve ODT of ascorbic acid. Utilizing F-MELT® in the ascorbic acid ODT yielded harder tablets demonstrating DT < 20 seconds when formulated without an external lubricant system at an API load of 30%".

Commercialized ODT tablet Examples with F-MELT®

F-MELT®	Commercialized ODT Tablet
Type C	Vitamin B12 (supplements)
Type C	Probiotics (supplements)
Type C	Melatonin (supplements)
Type C	Lansoprazole
Type C	Cilostazol
Type C	Voglibose
Type C	Pitavastatin
Type C	Donepezil
Type C	Telmisartan
Type C	Montelukast
Type C	Sildenafil
Type C	Tamsulosin
Type C	Olanzapine
Type C	Entecavir
Type C	Amlodipine
Type M	Ebastine
Type C	Anti-retroviral ODT- under development (Abacavir/Dolutegravir/Lamivudine)

Fuji Chemical's F-MELT® offers formulators multiple options for their final formulation, as it depends on the type and characteristics of the API being used.

In the examples cited above, a tablet hardness of over 40N and an oral disintegration time of less than 30 seconds were achieved by effectively utilizing other excipients and lubricants in combination with F-MELT®.

F-MELT®

Suitable processes: Direct compression, wet granulation

Pharmacopoeia and regulatory information
Type C: Conforms to Japanese Pharmaceutical Excipients. All components meet USP-NF, JP, and EP.
US DMF Type IV No. 20084

Type M: Conforms to Japanese Pharmaceutical Excipients. All components meet USP-NF and JP/JPC.

Safety
F-MELT® Type C and Type M
The components of F-Melt Type C and M are safe with no reports of adverse reactions when used as excipient in pharmaceutical applications. Type C is also suitable for nutraceutical*/ food applications. The components of Type C have E-numbers (EU Food Directive) and are listed in USFDA's CFR-Title 21 as well as list of Acceptable Non-Medical Ingredients in Canada.

The maximum daily dosage of Types C and M is 5.875 g per day.

*Please check the regulatory status of each component in respective countries.

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