Fuji Chemical Industries

PHARMACEUTICAL TECHNICAL NEWSLETTER

ISSUE: 02

IN THE MARCH ISSUE TECHNICAL NEWSLETTER, WE FOCUSED ON ACHIEVING HIGHER TABLET HARDNESS WITH PLEASANT MOUTH FEEL AT GOOD ORAL DISINTEGRATING (OD) TIMES BY ADDITION OF OTHER COMMON EXCIPIENTS. F-MELT® FAST MELT TABLET MADE EASY!

NEWSLETTER HIGHLIGHT

Effect of replacing Magnesium Stearate with Sodium Stearyl Fumarate on tableting of Fast-Disintegrating Oral Tablets with F-MELT®

F-MELT® is a spray-dried powder of five pharmaceutical excipients consisting of carbohydrates, inorganic ingredients and disintegrants.
It is available in two grades, **F- MELT®** Type C and **F-MELT®** Type M. **F-MELT®** *Type C* conforms to USP-NF, EP, and JP, and *Type M* conforms to USP-NF and JP. An U.S. Drug Master file is available for Type C.

In this issue, we demonstrate that ***higher tablet hardness with pleasant mouth feel and good OD times can be achieved with F-MELT®*** alone or by adding minimum amount of Talc. Also, the lubricant was changed from magnesium stearate to sodium stearyl fumarate in order to take advantage of the superior qualities of this lubricant. PRUV is relatively inert and it overcomes problem associated with magnesium stearate like film formation and over lubrication.

**Patented in Japan and patent pending in U.S. , Europe and India*

Table 1. F- MELT® Physical Properties*

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 distribution (µm)	122.3	120.8

**Reference Data*

FORMULATION EXAMPLE

Although we achieved our objectives, the formulations were a bit complex for the formulators who want to keep the formulations simple.

Formulation Example 1) F-MELT® Type C –Acetaminophen ODT formulations with focus on tablet hardness, mouth feel and acceptable oral disintegration times.

Acetaminophen (wt %)	30	30	30	40	40	50
F-MELT® Type C (wt %)	69.1	69.0	69.0	59.0	59.0	49
Talc (wt %)	0.5	-	-	-	-	-
Lubricant (Fu-Na) (wt %)	0.4	1.0	1.0	1.0	1.0	1.0
Compression Force (kN)	6.0	4.6-4.9	6.5-7.0	5.9-6.4	8.4-9.6	7.8-8.8
Tablet Hardness (N)	52.0	34.1	58.0	37.6	59.4	41.2
Oral disintegration time(sec)	19.5	10.5	25.1	11.5	27.8	14.2
Mouth feel	VERY GOOD	VERY GOOD	VERY GOOD	VERY GOOD	VERY GOOD	VERY GOOD

Fu-Na: Sodium Stearyl Fumarate. Tablets of 200 mg with 08mm diameter were manufactured on a rotary tabletting machine.

ODT with optimum hardness, a pleasant mouth feel and satisfactory oral disintegration times were achieved with acetaminophen and **F-MELT®** Type C when sodium stearyl fumarate was used as lubricant. The hardness improved either by adding 0.5% talc or by increasing the compression pressures.

Formulation Example 2) F-MELT® Type M –Acetaminophen ODT formulations with focus on tablet hardness, mouth feel and acceptable oral disintegration times

Acetaminophen (wt %)	30	40	30	30	40	40	50
F-MELT® Type M (wt %)	69.1	59.1	69.0	69.0	59.0	59.0	49.0
Talc (wt %)	0.5	0.5	-	-	-	-	-
Lubricant (Fu-Na)(wt %)	0.4	0.4	1.0	1.0	1.0	1.0	1.0
Compression Force (kN)	6.0	9.0	4.7-5.0	6.7-7.0	5.7-6.5	8.4-9.2	7.0-8.0
Tablet Hardness (N)	53.4	55.6	39.2	63.1	44.7	63.8	35.3
Oral disintegration time (sec)	17.0	29.2	13.3	25.1	15.3	25.8	13.1
Mouth feel	VERY GOOD	VERY GOOD	VERY GOOD	VERY GOOD	VERY GOOD	VERY GOOD	VERY GOOD

Fu-Na: Sodium Stearyl Fumarate. Tablets of 200 mg with 08mm diameter were manufactured on a rotary tabletting machine.

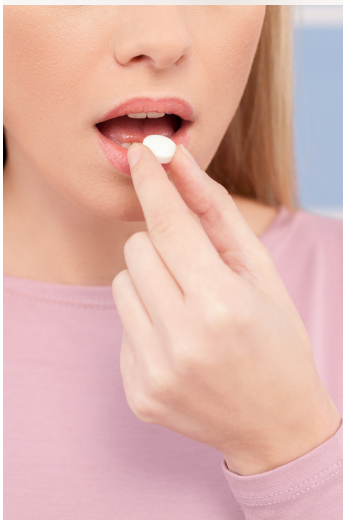
ODT with optimum hardness, a pleasant mouth feel and satisfactory oral disintegration times were achieved with acetaminophen and **F-MELT® Type M** when sodium stearyl fumarate was used as lubricant. The hardness improved either by adding 0.5% talc or by increasing the compression pressures.

Formulation Example 3) F-MELT® Type C –Ascorbic acid ODT formulations with focus on tablet hardness, mouth feel and acceptable oral disintegration times

Ascorbic acid (wt %)	30	40	40	40
F-MELT® Type C (wt %)	69	58.5	59	59
Talc (wt %)	-	0.5	0.5	0.5
Lubricant (Fu-Na) (wt %)	1	1	0.4	0.4
Compression Force (kN)	4.8-5.2	8.0-8.6	5.1-5.4	7.0-7.4
Tablet Hardness (N)	30.8	49.5	32.1	45.8
Oral disintegration time (sec)	16.4	38.5	16.2	20.5
Mouth feel	VERY GOOD	VERY GOOD	VERY GOOD	VERY GOOD

Fu-Na: Sodium Stearyl Fumarate. Tablets of 200 mg with 08mm diameter were manufactured on a rotary tabletting machine.

ODT with optimum hardness, a pleasant mouth feel and satisfactory oral disintegration times were achieved with Ascorbic acid and F-MELT® Type C when sodium stearyl fumarate was used as lubricant.



Formulation Example 4) F-MELT®Type M –Ascorbic acid ODT formulations with focus on tablet hardness, mouth feel and acceptable oral disintegration times

Ascorbic acid (wt %)	30	30	40	40
F-MELT® Type M (wt %)	69	69	59.1	59.1
Talc (wt %)	-	-	0.5	0.5
Lubricant (Fu-Na) (wt %)	1	1	0.4	0.4
Compression Force (kN)	4.6-4.9	6.5-6.9	5.4-5.7	7.4-7.8
Tablet Hardness (N)	32.6	52.4	35.3	53.1
Oral disintegration time (sec)	17.4	27.7	13.8	24.3
Mouth feel	VERY GOOD	VERY GOOD	VERY GOOD	VERY GOOD

Fu-Na: Sodium Stearyl Fumarate. Tablets of 200 mg with 08mm diameter were manufactured on a rotary tabletting machine.

ODT with optimum hardness, a pleasant mouth feel and satisfactory oral disintegration times were achieved with acetaminophen and F-MELT® Type M when sodium stearyl fumarate was used as lubricant. Ascorbic acid is a difficult to tablet API and occasionally slight adhesion to the punches were observed while tableting. If problem of stickiness persist, an external lubrication system or addition of other common excipients as described in the previous newsletter could overcome the problem.

Pharmacopoeia and regulatory information
Type C: Conforms to Japanese Pharmaceutical Excipients. All components meet USP-NF, JP, and EP. US DMF Type IV filed.

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 USA CFR 21 and list of Acceptable Non-MedicalIngredients in Canada.

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

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

F-MELT®

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