

Fast Melt Tablets Made Easy!

F-MELT®

Ready to use, blend and punch, excipient system for Orally disintegrating tablets for pharmaceutical, nutraceutical and dietary supplement applications – A proprietary product from Fuji Chemical.



Fuji Chemical Industries

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F-MELT® - Fast Melt Tablets Made Easy!



F-MELT® is a proprietary co-spray dried excipient launched by Fuji in 2005. F-MELT® is designed not only for manufacturing orally disintegrating tablets (ODTs) and tablets that dissolve fast in the oral cavity without the need of water, but is also an excellent excipient for soft chewable tablets. It is suitable for manufacturing directly compressible ODTs simply by blending with active pharmaceutical ingredients (APIs) and lubricants.

The challenges and opportunities of ODTs

A patient-centric drug delivery system to deliver specialized medicines to the aging population is very critical to any pharmaceutical drug development program. Difficulty in swallowing is a major problem of the aged patient populations with specific diseases. One of the best choices to overcome the problem associated with swallowing difficulties is an ODT drug delivery system. For ODTs, the key challenges are producing tablets with optimum tablet hardness, rapid disintegration and overcoming the bitter taste exhibited by many actives. F-MELT® addresses these challenges with ease and offers the pharmaceutical companies opportunity to take the product to market quickly.

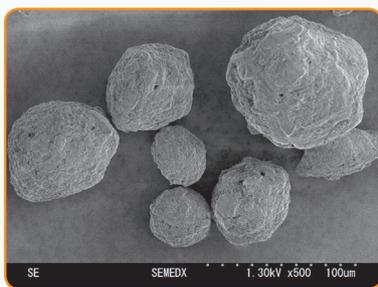
Features of F-MELT®

1. Ready to use excipient system for ODTs
2. Oral disintegration time less than 30 seconds
3. Spherical particle with high flowability
4. Directly compressible
5. API loading more than 50% possible
6. Tablet hardness more than 50 N possible with little or no sticking/capping
7. Pleasant mouth feel
8. Easy handling and storage of ODTs with low friability
9. No special equipment required for tableting
10. No royalty or license fees required

F-MELT[®] grades and general properties

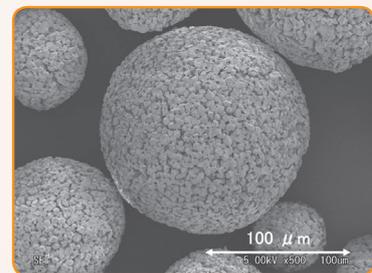
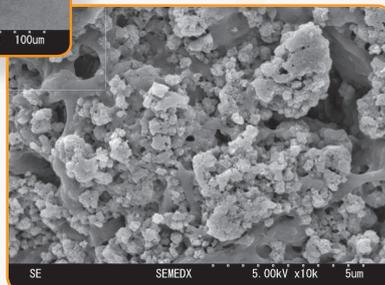
Type	Type C For pharmaceutical and nutraceutical applications	Type M For pharmaceutical applications	F1 For dietary supplement applications
Appearance	White to pale yellow powder		
Loss on Drying (%)	1.3	1.8	5.9
Loose Bulk Density (g/ml)	0.54	0.56	-
Tapped Bulk Density (g/ml)	0.65	0.65	-
Mean Particle Size Distribution (µm)	120.8	122.3	139.0
Angle of Repose (°)	34	33	31
Ingredients	D-Mannitol Xylitol MCC Crospovidone Fujicalin [®]	D-Mannitol Xylitol MCC Crospovidone Neusilin [®]	Waxy Rice Starch MCC Fujicalin [®]

Electron micrographs of F-MELT[®]



F-MELT[®] co-spray dried powder
(x 500)

F-MELT[®] co-spray dried powder
(x 10,000)

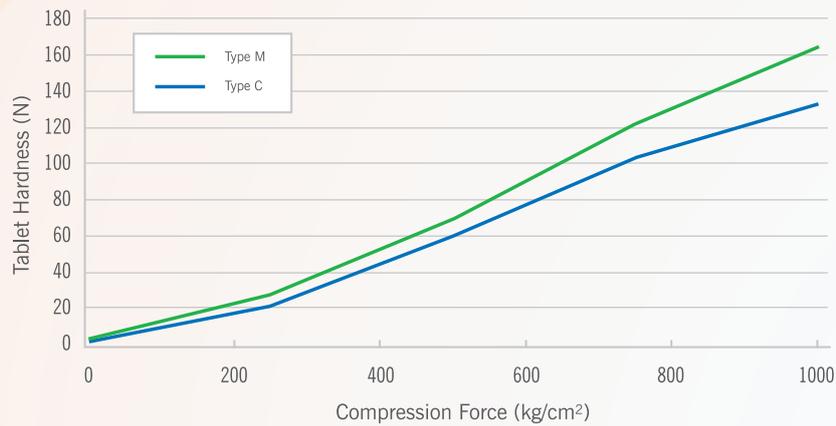


F-MELT[®] F1 co-spray dried powder
(x 500)

Performance of F-MELT[®] placebo tablets

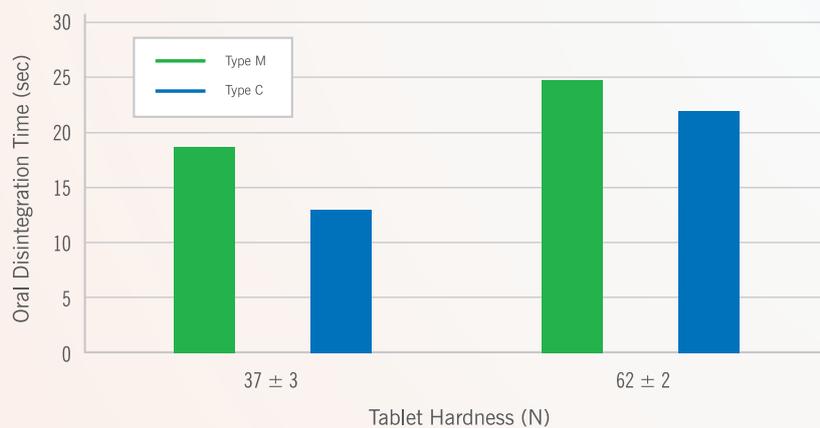
1. Type C and M

I. Optimum tablet hardness at low compression forces



F-MELT[®] Type C, M
Formulation: F-MELT[®] 99.5% + Mg-St 0.5% (Dry Blending)
Tablet size: ø 11.3 mm, 450 mg/Tab
Tablet machine: Tableting tester SK-02 (Sankyo Pio-tec)

II. Excellent disintegration time even with higher tablet hardness (<25 sec)



Excipient: F-MELT[®] Type C, M
Formulation: F-MELT[®] 99.6% + Mg-St 0.4%
Conditions: 20 rpm, ø 8 mm, 200 mg/Tab
Tableting after blending F-MELT[®] and lubricant

2. F1

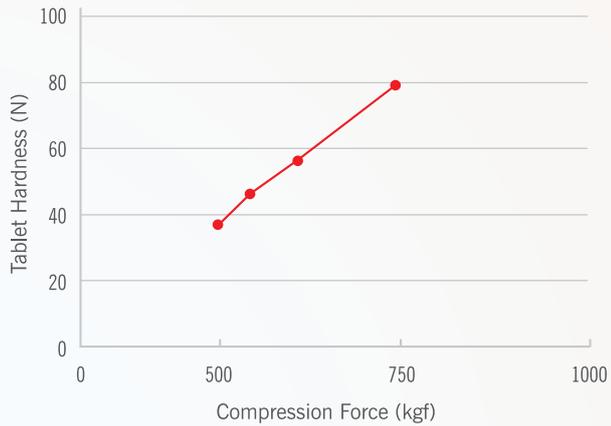
Tabletting condition:

Lubricant: Sucrose esters S-370F

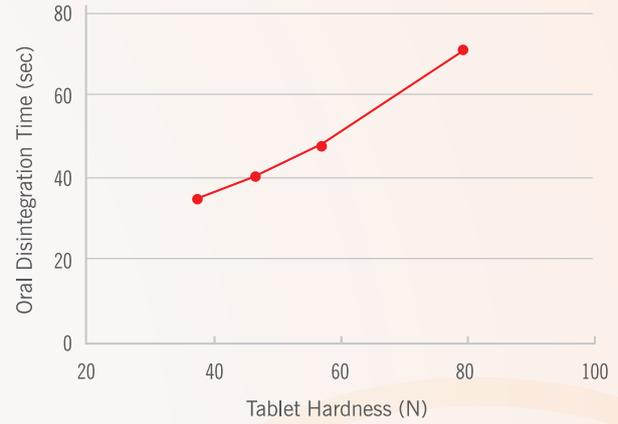
Formulation: F-MELT® 99.5% + lubricant 0.5%

Tabletting condition: \varnothing 8 mm x 9R, 200 mg/Tab, 15 rpm

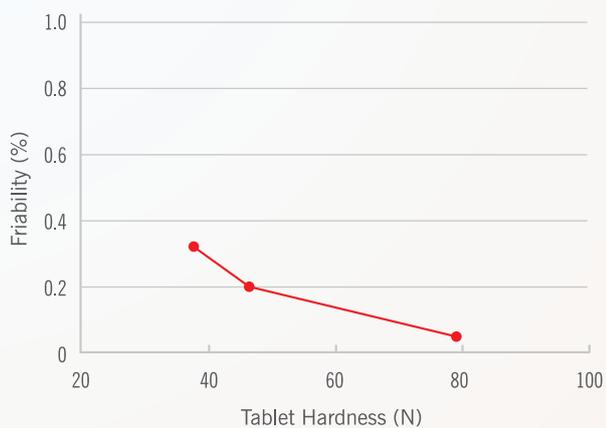
I. Optimum tablet hardness at low compression forces



II. Maintaining optimum disintegration time at higher tablet hardness

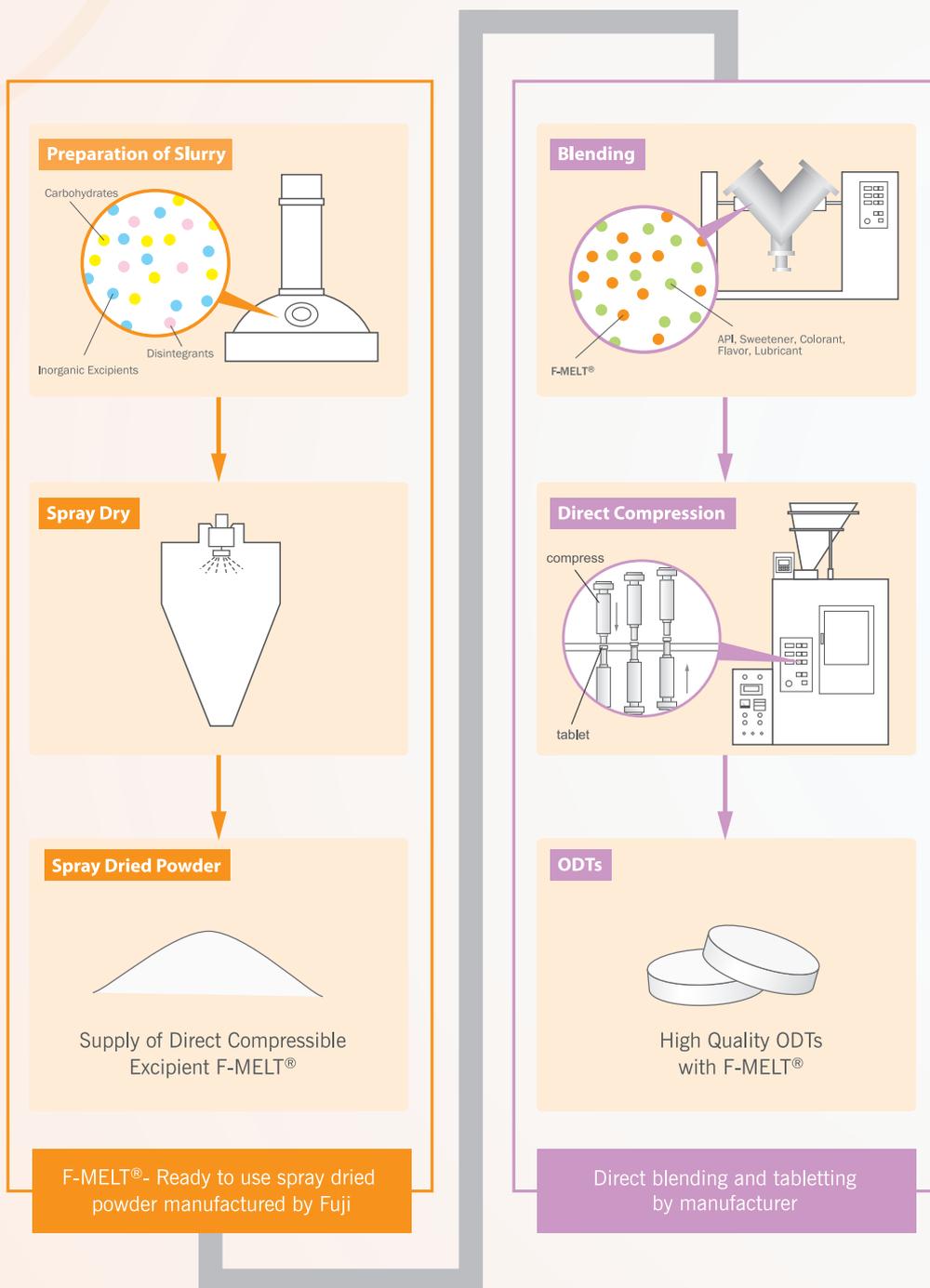


III. Friability decreases rapidly with increased tablet hardness



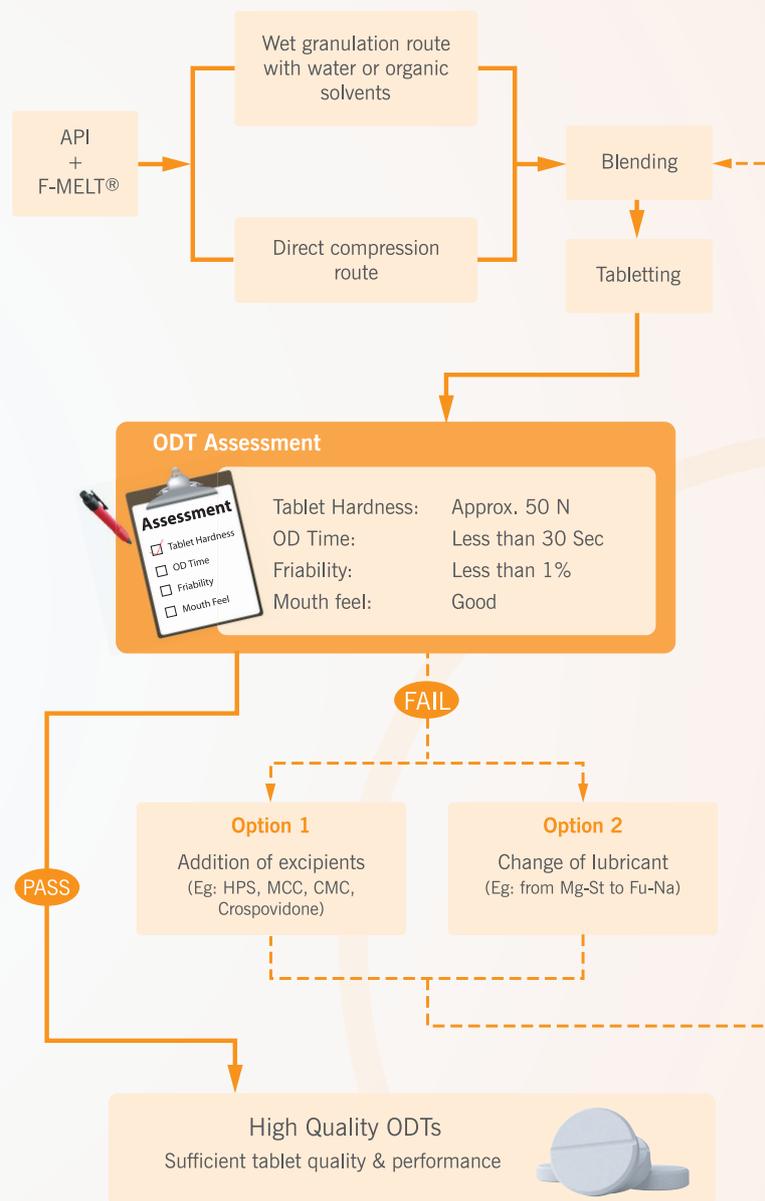
Manufacturing process of ODT with F-MELT®

Manufacturing ODTs using F-MELT® is simple - Blend F-MELT® and prepare tablets by direct compression. Flavors, colorants, sweeteners etc. could be incorporated for improved patient compliance.



Strategy for preparing high performance F-MELT® tablets

F-MELT® is a directly compressible excipient. Depending on the actives, ODTs can also be prepared through wet granulation with F-MELT® and suitable solvents. Furthermore, if ODT quality does not meet requirement, formulators can improve the quality by adding other excipients and/or changing the lubricant. This flow chart helps the formulator to choose the appropriate route for preparing high performance ODTs with F-MELT®.



HPS: Hydroxypropyl Starch, MCC: Microcrystalline Cellulose, CMC: Carboxymethyl Cellulose

Stability

F-MELT® has a shelf life of 3 years from the date of manufacture.

F-MELT® Type C and M

Formulation: F-MELT® 99.6% + Mg-St 0.4%

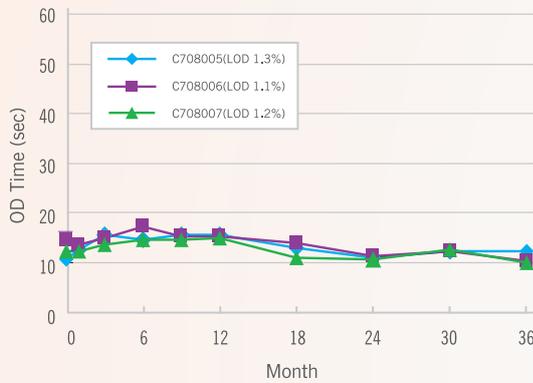
Tabletting condition: ø8 mm, 200 mg tablet, 15 rpm, 33 N

Tabletting machine: HT-AP18SS-II (Manufacturer: Hata Iron Works Co., Ltd.)

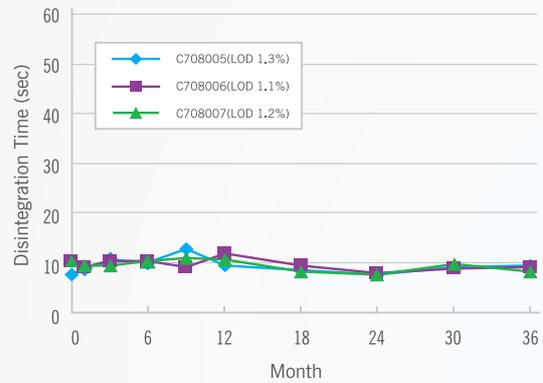
Storage: In aluminum bag with heat seal at 30°C & 65% RH

Type C

Oral Disintegration Time (OD Time) at 33N



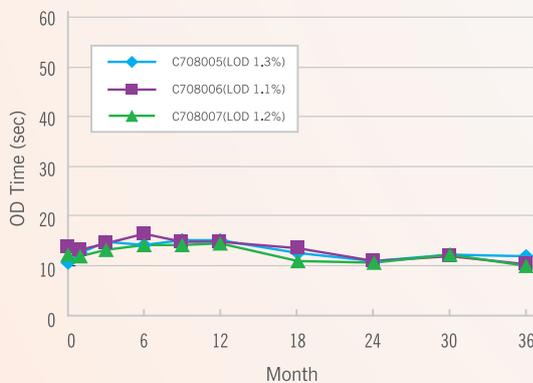
Pharmacopoeia Disintegration Time at 33N



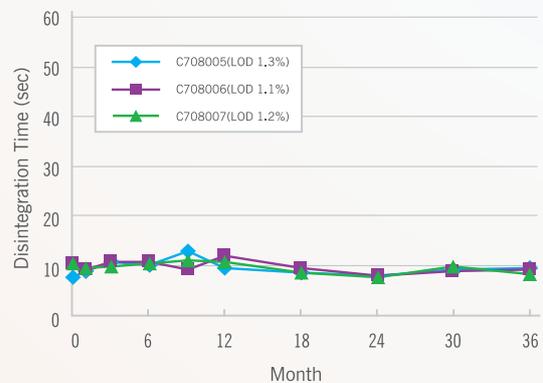
After specified storage time, placebo tablets were prepared and oral disintegration time as well as pharmacopoeia disintegration time were recorded.

Type M

Oral Disintegration Time (OD Time) at 33N



Pharmacopoeia Disintegration Time at 33N



After specified storage time, placebo tablets were prepared and oral disintegration time as well as pharmacopoeia disintegration time were recorded.

Pharmaceutical application – F-MELT® Type C and Type M

I. Formulation Examples – Direct Compression

1. Famotidine formulations with F-MELT® Type C and M

Famotidine (wt%)	10	10	10	10
F-MELT® Type C (wt%)	89.6	87.9	87.2	-
F-MELT® Type M (wt%)	-	-	-	89.6
Flavors, Sweeteners (wt%) Contains Sucralose, Menthol Acesufame potassium	-	1.7	2.4	-
Magnesium Stearate (wt%)	0.4	0.4	0.4	0.4
Compression Force (kN)	4.3-4.5	4.4-4.8	4.3-4.4	4.3-4.5
Tablet Hardness (N)	51.0	50.7	50.0	50.2
Oral Disintegration Time (sec)	20.9	21.3	24.3	22.3

Tabletting conditions: ø8mm × 9R, 200 mg/tablet, Rotary:15rpm

Famotidine belongs to histamine (H2) blockers. Famotidine is bitter in taste and need taste masking in order to be acceptable to patients.

2. Acetaminophen formulation with F-MELT® Type C and M

Acetaminophen (wt%)	30.0	40.0	30.0	30.0	40.0	30.0
F-MELT® Type C (wt%)	-	-	-	69.6	59.6	69.6
F-MELT® Type M (wt%)	69.6	59.6	69.6	-	-	-
Magnesium Stearate (wt%)	0.4	0.4	0.4	0.4	0.4	0.4
Compression Force (kN)	5.4-5.7	5.9-6.4	7.5-8.0	5.5-5.8	8.1-8.7	9.0-9.5
Tablet Hardness (N)	36.4	30.2	59.8	31.7	36.6	49.1
Oral Disintegration Time (sec.)	20.2	20.8	45.5	14.6	21.5	66.5
Mouth Feel	Very Good					

A 30-40% load of acetaminophen may bring down the tablet hardness to a region between 30 and 35 N while maintaining the oral disintegration time of 30 seconds. At higher compression forces, one can achieve a tablet hardness above 50 N. However, the oral disintegration time tends to increase slightly.

A strategy to overcome this limitation was developed by Fuji scientists to maintain tablet hardness of 50 N and an oral disintegration time of 30 seconds.

3. F-MELT® sample formulations with acetaminophen (AA) and additional pharmaceutical excipients, to achieve a higher tablet hardness and shorter oral disintegration time

Example 1.

F-MELT® Acetaminophen formulations with additional excipients like corn starch, carboxymethyl cellulose (CMC), crospovidone and hydroxypropyl starch (HPS) and magnesium stearate was used as lubricant.

Acetaminophen (wt%)	30.0	30.0	30.0	30.0
F-MELT® Type C (wt%)	49.6	49.6	64.6	49.6
Other excipients (wt%)	Corn Starch	CMC	Crospovidone	HPS
	10	20	5	10
	MCC	-	-	MCC
	10	-	-	10
Magnesium Stearate (wt%)	0.4	0.4	0.4	0.4
Compression Force (kN)	6.2-6.6	11.3-11.8	6.9-7.4	6.2-6.7
Tablet Hardness (N)	50.0	50.7	53.0	59.0
Disintegration Time JP (sec.)	17.4	22.5	12.5	19.3
Oral Disintegration Time (sec.)	16.8	21.2	9.0	20.1
Friability (%)	0.25	0.14	0.10	0.18

The F-MELT® acetaminophen tablets achieved a tablet hardness of 50 N and a disintegration time of less than 30 seconds with low friability.

Example 2.

F-MELT® Acetaminophen formulations with additional excipients like corn starch, microcrystalline cellulose (MCC) and change of lubricant from magnesium stearate to sodium stearyl fumarate

Acetaminophen (wt%)	30.0	40.0	40.0	40.0
F-MELT® Type C (wt%)	-	-	-	59.0
F-MELT® Type M (wt%)	49.6	34.6	59.0	-
Other Excipients (wt%)	20.0	25.0	-	-
	Corn Starch	MCC	-	-
Lubricant (wt%)	Mg-St	0.4	0.4	-
	S.S.F.	-	-	1.0
			1.0	1.0
Compression Force (kN)	10.0-11.0	6.8-7.8	8.4-9.2	8.4-9.6
Tablet Hardness (N)	45.6	55.2	63.8	59.4
Oral Disintegration Time (sec.)	14.1	18.3	25.8	27.8

Tableting conditions: ø8mm × 9R, 200 mg/tablet, Rotary:15rpm
MCC: Microcrystalline Cellulose, Mg-St: Magnesium Stearate, S.S.F.: Sodium Stearyl Fumarate

By changing the lubricant, one could achieve higher tablet hardness and a disintegration time of less than 30 seconds with F-MELT®.

4. Ascorbic acid (Vitamin C) formulations with F-MELT® Type C and M

F-MELT® sample formulation with L-Ascorbic acid. Effect of 2 different lubricants (sodium stearyl fumarate and magnesium stearate) on tablet hardness, oral disintegration time and friability.

Ascorbic Acid (wt%)	30.0	30.0	30.0	30.0	30.0
F-MELT® Type C (wt%)	69.1	-	-	64.1	-
F-MELT® Type M (wt%)	-	69.6	69.1	-	64.1
Crospovidone (wt%)	-	-	-	5.0	5.0
Talc (wt%)	0.5	-	0.5	0.5	0.5
S.S.F. (wt%)	0.4	0.4	0.4	-	-
Mg-St	-	-	-	0.4	0.4
Compression Force (kN)	6.0-6.4	5.8-6.2	5.8-6.0	7.0-7.5	8.0-8.6
Tablet Hardness (N)	53.9	55.9	54.0	49.8	54.2
Disintegration Time JP (sec.)	17.7	18.4	16.1	17.9	18.9
Oral Disintegration Time (sec.)	24.9	26.1	24.1	17.7	13.8
Friability (%)	0.29	0.27	0.32	0.22	0.16

Tabletting conditions: ø8mm × 9R, 200 mg/tablet, Rotary:15rpm
MCC: Microcrystalline Cellulose, Mg-St: Magnesium Stearate, S.S.F.: Sodium Stearyl Fumarate

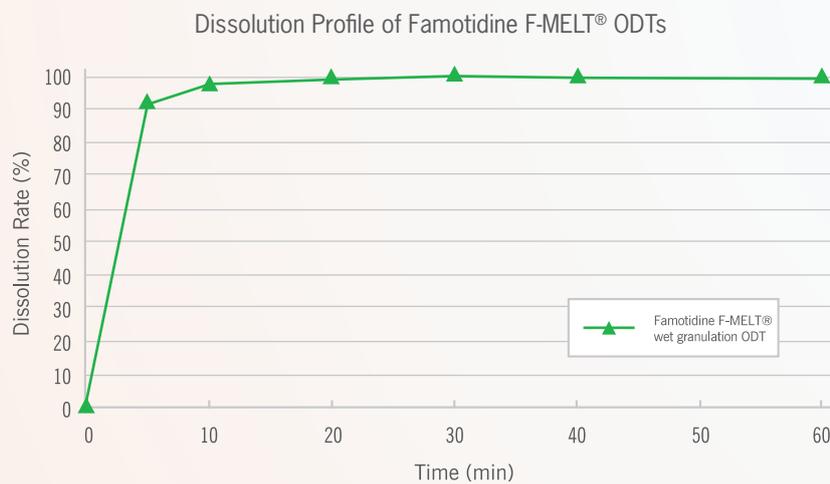
Ascorbic acid, a highly hygroscopic active was successfully formulated into an oral disintegrating tablet with F-MELT®. In order to avoid the sticking/capping, 0.5% of talc was included in the formulation.

II. Formulation Examples - Wet Granulation

1. Famotidine formulations with F-MELT® Type M

Formulation	
Water-granulated Famotidine with F-MELT® Type M (2:5)	70 mg
F-MELT® Type M	127.5 mg
Sucralose	0.8 mg
Acesulfame potassium	0.8 mg
Micronized menthol	0.1 mg
Magnesium stearate	0.8 mg
Total	200 mg
Tablet Characteristics	
Tablet Hardness (N)	47.0
Pharmacopoeia Disintegration Time (s)	13.49
Oral Disintegration Time ODT-101 *(s)	25.19

Tablet condition: ø 8 mm, 200 mg/Tab, Rotary tableting machine
*Equipment to measure ODT (Toyama Sangyo Co., Ltd.)



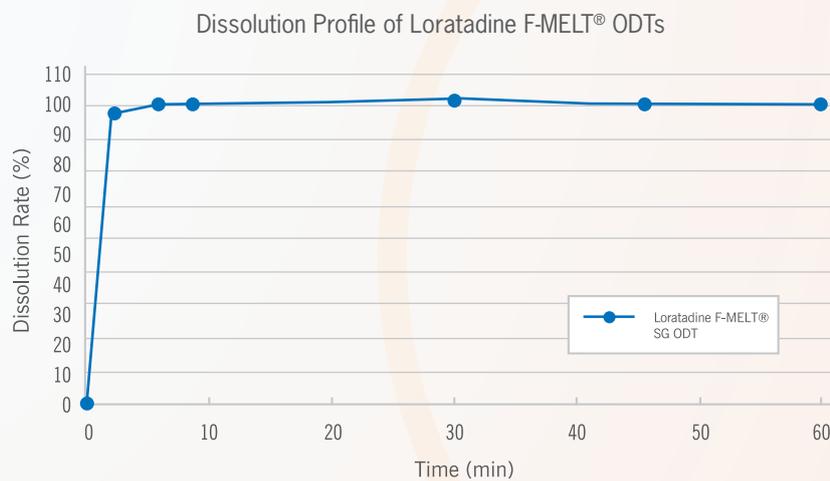
Dissolution was carried out with distilled water 900 ml, 37°C, paddle speed 50 rpm.

Wet granulation of Famotidine with F-MELT® Type M with water improved dissolution profile of Famotidine, a poorly water soluble drug. Dissolution rate of Famotidine F-MELT® ODTs could reach 100% within 30 minutes.

2. Loratidine formulations with F-MELT® Type M

Formulation	
Solvent-granulated Loratidine with F-MELT® Type M (1:5)	60 mg
F-MELT® Type M	139.2 mg
Magnesium stearate	0.8 mg
Total	200 mg
Tablet Characteristics	
Tablet Hardness (N)	47.6
Pharmacopoeia Disintegration Time (s)	11.13
Oral Disintegration Time ODT-101 *(s)	13.38

Tablet condition: ø 8 mm, 200 mg/Tab, Rotary tableting machine
*Equipment to measure ODT (Toyama Sangyo Co., Ltd.)



Dissolution was carried out with JP disintegration test solution #1 (pH 1.2), 900 ml, 37°C, paddle speed 50 rpm.

Wet granulation of Loratidine with F-MELT® Type M with solvent (water:ethanol, 30:70) improved dissolution profile of Loratidine, a poorly water soluble drug. Dissolution rate of Loratidine F-MELT® ODTs could reach 100% in less than 10 minutes.

Nutraceutical application – F-MELT® Type C and F1

Formulation Examples – Direct Compression

1. Vitamin B12 formulation with F-MELT® Type C

Vitamin B12 is accepted as a dietary supplement and is consumed in microgram dosages. Oral disintegrating Vitamin B12 (500 µg) nutraceutical tablets were prepared with F-MELT® Type C.

Vitamin B12 formulation with F-MELT® Type C (V.B12 500 µg/tablet):

Batch Formula

Formulation	Weight(g)
Vitamin B12	1.0
F-MELT® Type C	578.2
Talc	4.0
Strawberry Flavor	12.0
Aspartame	1.8
Glyceryl Behenate	3.0
Batch Total	600



F-MELT® Vitamin B12 Characteristics (Ø10 300 mg flat tablet)

JP Tablet Hardness (N)	50.8
Mean Oral Disintegration Time (sec.) N=5	19.87
Disintegration Time (sec.)	9.9
Friability (%)	0.16

Tableting Condition: Rotary tableting machine (HT-AP18SS) at 15 rpm. Compression force of 4.8 - 5.2 KN



Blending Steps

1. Mill 1.0 g Vitamin B12
2. Add and mix 1 g Talc
3. Add and mix 3 g Talc
4. Add and mix F-MELT® 10-20 g
5. Add and mix the remaining F-MELT® and flavor
6. Add and mix Glyceryl behenate
7. Sieve with 22 mesh

2. CoQ10 formulation with F-MELT® Type C

CoQ10* is a well established dietary supplement. This example shows successful tablet formulations of 350 mg and 1,200 mg oral disintegrating tablets of CoQ10 at 17.5 to 60 mg load. Additional excipients like MCC and CMC and Talc were included to improve tablet properties.

*CoQ10: Molecule Weight: 863, Melting Point: ca48°C, yellowish or orange color crystal powder

Smooth water soluble CoQ10 (5% - 17.5 to 60 mg) OD tablet formulation:

Batch Formula

Formulation	%
CoQ10 Powder	12.5
F-MELT® Type C	61.0
MCC	10.0
CMC-NA	10.0
Talc	2.0
Orange Flavor	2.0
Aspartame	0.5
Sodium stearyl fumarate	2.0

Tabletting Condition: Rotary tabletting machine (HT-AP18SS) at 15 rpm.



Compression Force: 5.8-6.0 kN
Tablet Hardness: 58 N
Oral Disintegration Time : 119 sec

3. Vitamin B12 formulation with F-MELT® F1

Oral disintegrating Vitamin B12 (500 µg) nutraceutical tablets were prepared with F-MELT® F1.

Vitamin B12 tablet: ø 10 mm, 300 mg/tablet (V.B12 500 µg/tablet)

Batch Formula

Formulation	%
Vitamin B12	0.17
F-MELT® F1	96.33
Talc	0.7
Strawberry Flavor	2.0
Aspartame (Sweetener)	0.3
Sucrose Ester	0.5



Compression Force: 3.9-4.0 kN
Tablet Hardness: 59.8 N
Oral Disintegration Time : 30 sec

4. Improvement of commercially available multivitamin-mineral tablet with F-MELT® F1

Sugars and cellulose in original formulation were replaced with F-MELT® F1.

Iron, Copper, VB12 tablet: ø 8 mm, 240 mg per tablet (4 tablets per day)

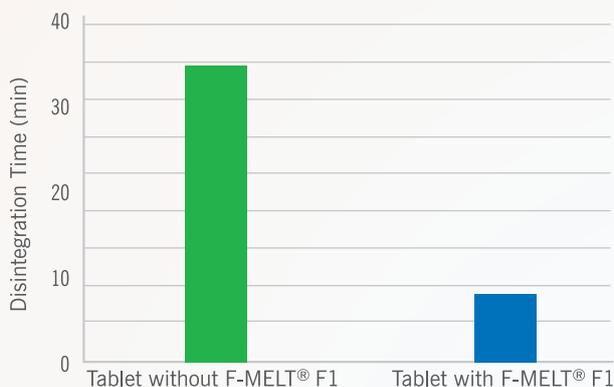
Formulation	%
Ferric Pyrophosphate	7.8
Copper Yeast (1%)	9.4
Pyridoxine hydrochloride	0.2
Vitamin B12 (0.1%)	0.3
Folic Acid	0.02
F-MELT® F1	79.3
Sucrose Ester	3.0

Iron: 6 mg, Copper: 0.9 mg, B6: 1.6 mg, B12: 2.4 µg, Folic acid: 200 µg

Iron, Copper, VB12 tablet properties

	F-MELT® F1	Conventional
Compression Force	8.8-9.4 kN	
Tablet Hardness	137 N	121 N

Drastic improvement in disintegration time with F-MELT® F1



5. Improvement of Zinc commercial tablet with F-MELT® F1

Sugars and cellulose in original formulation were replaced with F-MELT® F1

Zinc, Selenium, Chrome tablet: ø 8 mm, 250 mg per tablet (4 tablets per day)

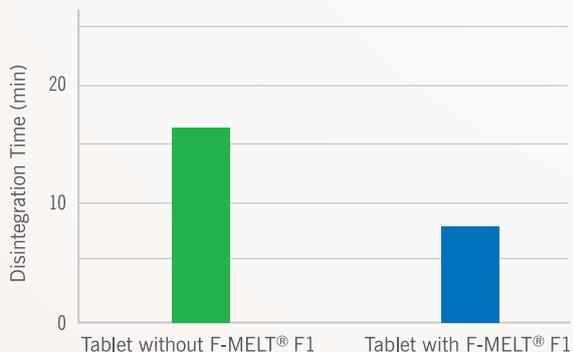
Formulation	%
Zinc Gluconate	11.7
Selenium Yeast (0.2%)	2.5
Chromium Yeast (0.2%)	2.5
F-MELT® F1	82.8
Magnesium stearate	0.5

Zinc: 15mg, Selenium: 50µg, Chrome: 50µg

Zinc, Selenium, Chrome tablet properties

	F-MELT® F1	Conventional
Compression Force	7.4-7.8 kN	
Tablet hardness	71 N	88 N

Considerable improvement in disintegration time with F-MELT® F1



Package size

Commercial size: 20 kg net in aluminium bag in carton box

Sample size: 1 kg net in aluminium bag

All samples are available upon request. Please contact your local distributor or sale person.

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-Medical Ingredients 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® F1

F-MELT® F1 is for nutraceutical/food applications.

TSE/BSE, Non-GMO, Allergen free certificates are available upon request. F-MELT® does not contain any residual organic solvent.

Patent status

Patent: Composition for rapid disintegrating tablet in oral cavity

Content: Principal compositions of F-MELT® (Carbohydrates, disintegrants and inorganic excipients)

Status: Patented in Japan, USA, India, China and Korea. Patent pending in EU.

Details available on request. Please contact your local distributor or sales person.

Further reading

Machimura H. F-MELT® -An ideal excipient for orally-disintegrating tablet formulations. JSPME, 2011, Vol.20(1) p26-32. <In Japanese>

F-MELT®