Moisture Protection and Taste-Masking with Polymethacrylate Coatings

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- **Eudragit® E Polymer Properties**
- **Moisture Protection**
- **Taste Masking**

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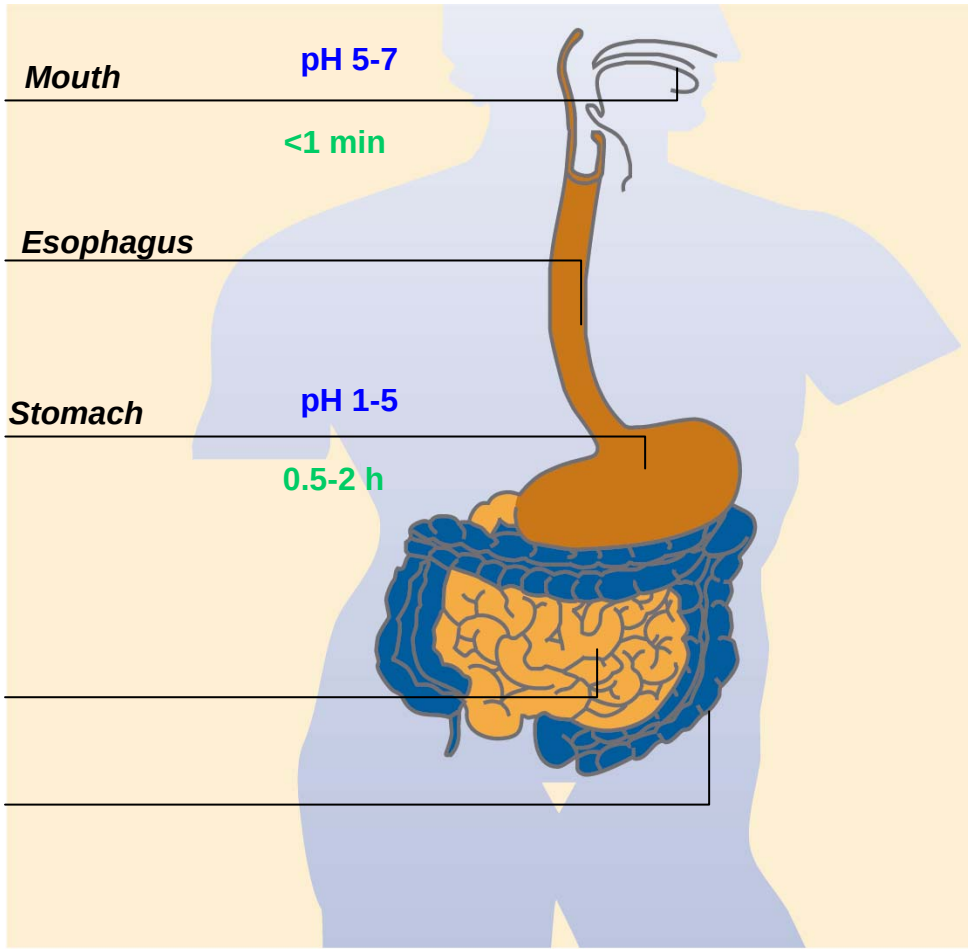
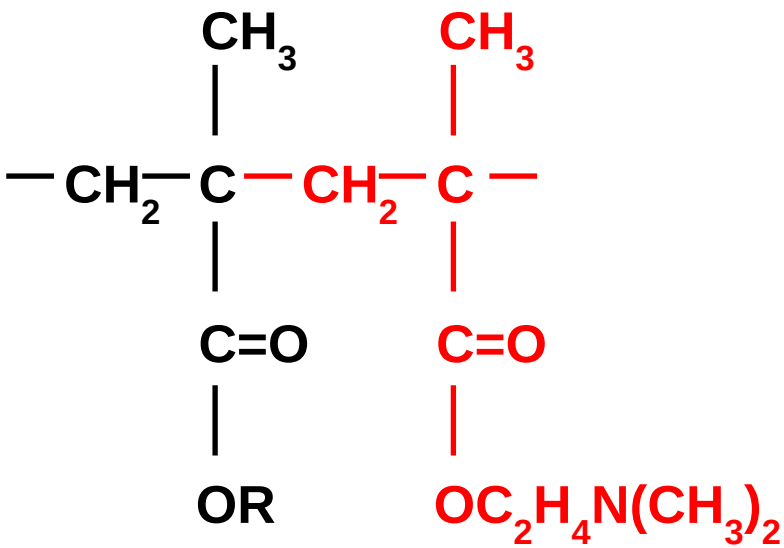
Drug Release in the Upper GI Tract



- pH differences
  - -dissolution of cationic barrier coatings at low pH
- ionic strength and volume
  - - ion exchange for taste masking

EUDRAGIT® E 100 and EUDRAGIT ® E PO



Chemical properties:

- R = methyl, butyl (1:1)
- cationic properties
- swellable and permeable above pH 5, soluble below pH 5

Physical properties:

- Tg (DSC): 50 °C
- Elongation at break* 200 %
- pKa 10.0 (water)
- Particle size EUDRAGIT E PO:
  Spec: >90 % smaller than 315 µm
  V_{50}: 7 - 10 µm, V_{95}: max. 20 µm

* with 10% triacetine

⇨ **Highly flexible and acid soluble!**

Aqueous EUDRAGIT® E PO Formulation

	EUDRAGIT ® E PO	On dry polymer
EUDRAGIT ® E PO	150.8 g	
SLS (Sodium laurylsulphate)	15.1 g	10 %
Stearic acid, powder	22.6 g	15 %
Mg-stearate, or Talc	52.8 g	35 %
Aqua pur.	1258.7 g	
Total	1500.0 g	

Polymer:

10 % (w/w)

Solids:

16 % (w/w)

⇨ **Recommended polymer weight gain 1 – 10 mg/cm²**

EUDRAGIT® E PO Coating Suspension

Na-laurylsulfate

5 min Ultra Turrax

Aq. pur

Stearic acid

15 min Ultra Turrax

Aq. pur
+ SLS

EUDRAGIT® E PO

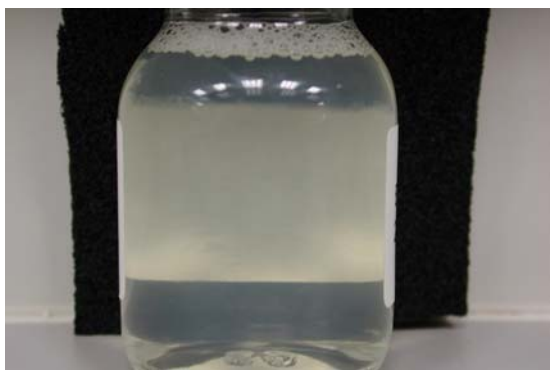
10 - 20 min Ultra Turrax

Aq. pur
+ SLS
+ stearic acid

Glidant,
Pigments (optional)

10 - 20 min Ultra Turrax

EUDRAGIT® E PO
Coating suspension



⇨ 40 - 60 min dispersion time with homogenizers!

EUDRAGIT® E PO – Homogenizing Equipment

Silverson

Ultra Turrax

- Eudragit® E Polymer Properties
- **Moisture Protection**
- Taste Masking

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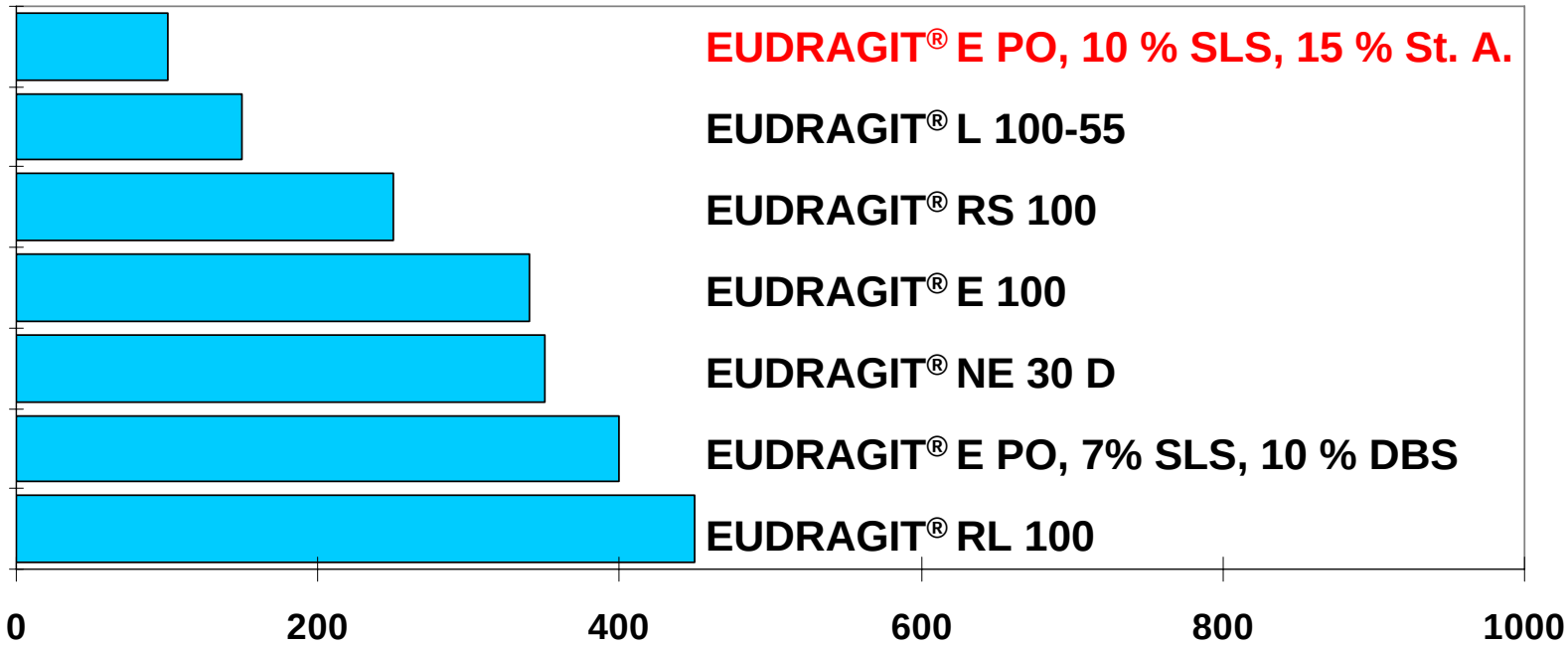
Moisture Protection by Coatings

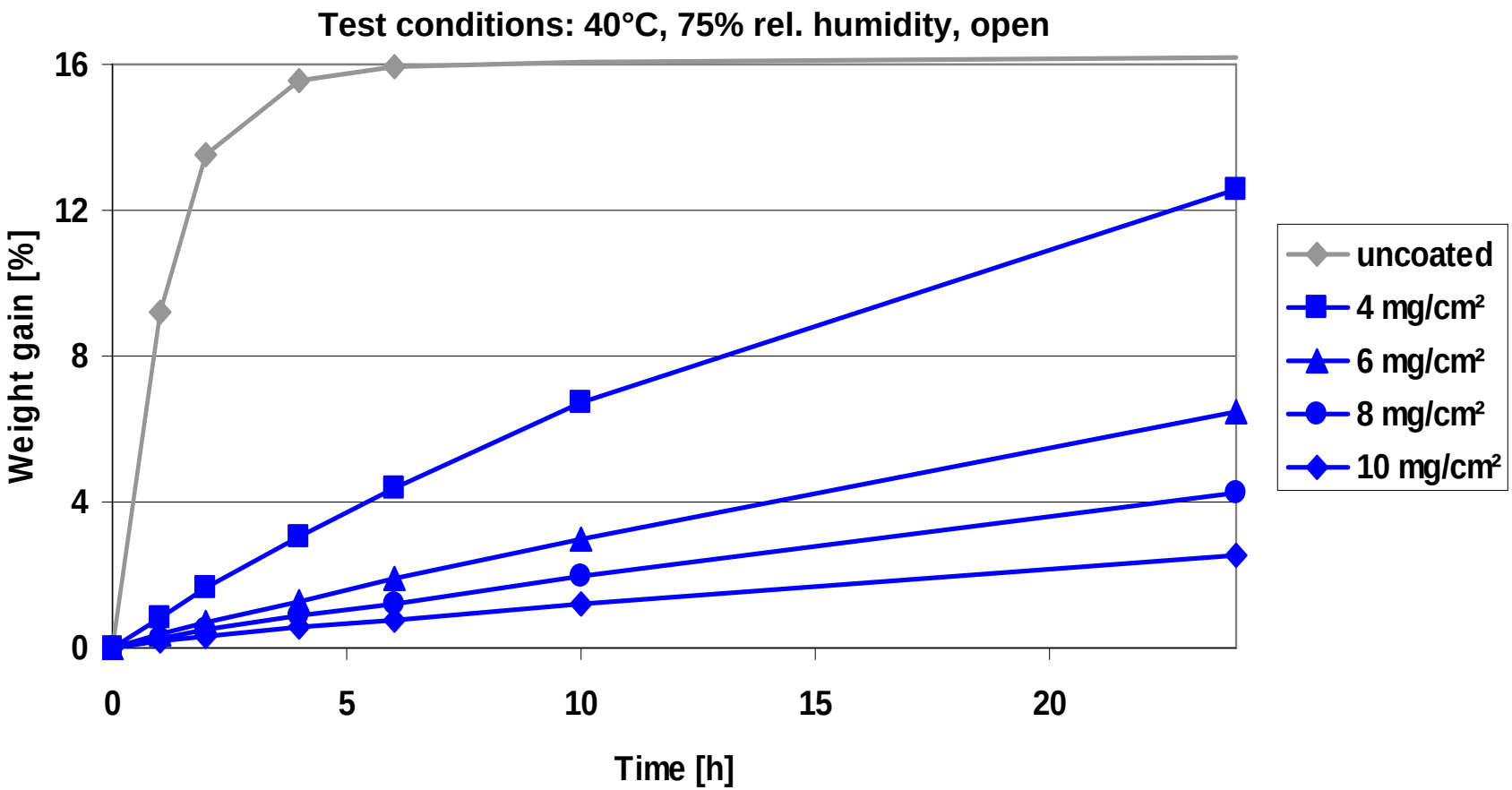


⇨ **EUDRAGIT® E PO provides lowest WVP!**

Materials (I): Tablet Cores

	Placebo (%)	Quinidine sulfate (%)	Silica
Quinidine sulfate	- -	2.0	
Lactose	64.5	61.5	
Avicel® PH 102	30.0	30.0	
Primojel®	5.0	5.0	
Mg-stearate	0.5	0.5	
Diameter (mm)	10	10	11
Weight (mg)	300	300	409,3
Hardness (N)	119	80	151
Disintegration (water, min)	< 2	< 2	n. t.
Disintegration (0.1 N HCl, min)	< 2	< 2	n. t.

Moisture Protection with EUDRAGIT® E PO Various Coating Levels



⇨ **Increasing coating thickness improves protection!**

Materials (II): Coating formulations

Ingredient	EUDRAGIT® E PO
Polymer [g]	285.0
SLS [g]	28.5
Stearic acid [g]	42.8
Mg-stearate / talc[g]	99.8
Water [g]	1982.9
Total	2439.0

Cores:
2750 g placebos and 250 g Silica tablets

Process Parameters Film Coating

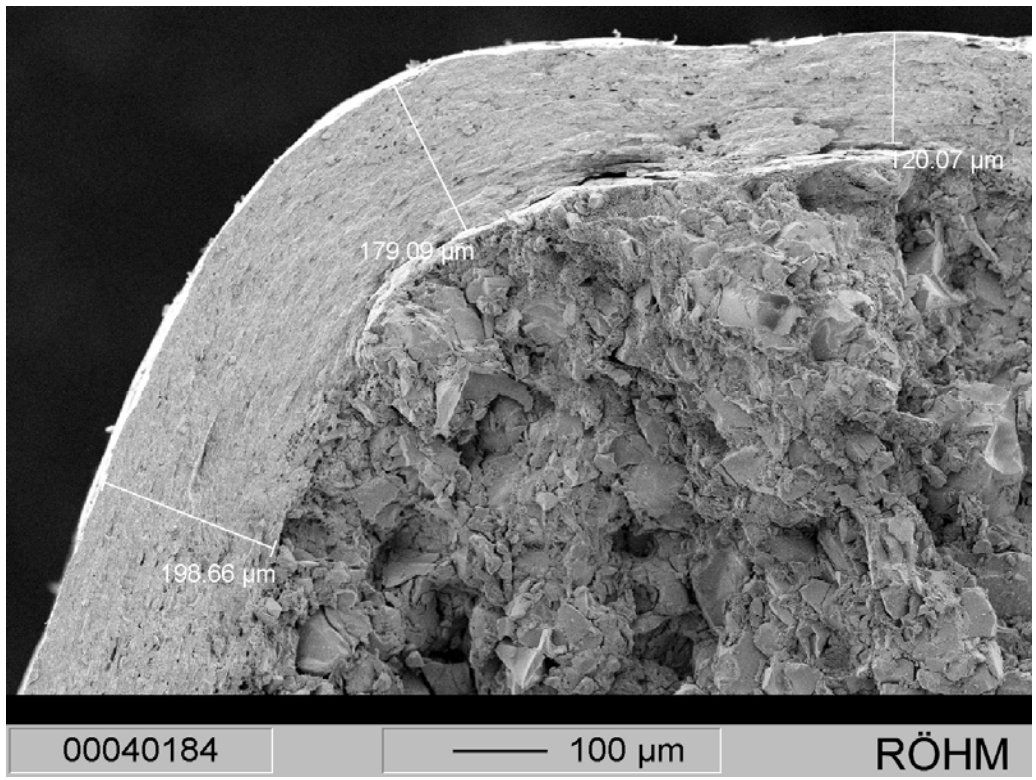
Coating pan : 35 cm diameter

Spray gun: Walther WA 1 NBA

	EUDRAGIT ® E PO
Nozzle diameter [mm]	**1.2**
Spray rate [g/min]	**8.4**
Atomizing air pressure [bar]	**0.8**
Inlet air temp [°C]	**40 – 50**
Bed temp [°C]	**31 - 37**
Coating time [min]	**291**

SEM Pictures of Protective Coatings

10 mg Polymer / cm²



- Eudragit® E Polymer Properties
- Moisture Protection
- **Taste Masking**

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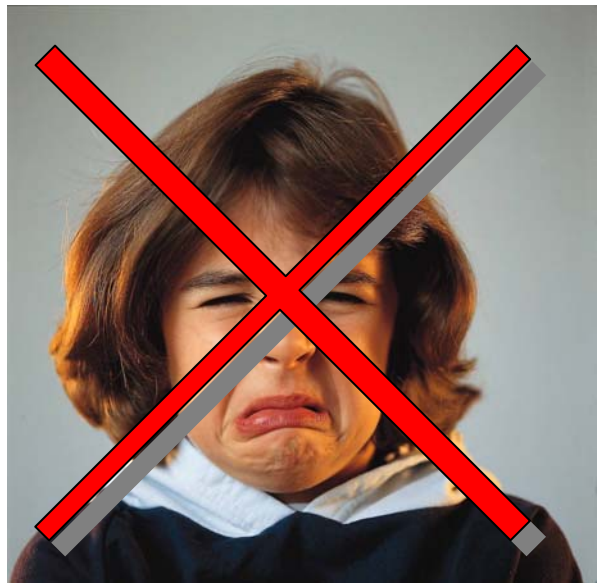
Taste Masking for Improved Compliance



- **Aqueous film coating**
  - tablets,
  - multiparticular systems

- **Fine powders**
  - ionic interactions between polymers and actives
  - alternative production processes

⇨ **Chances for innovative formulations!**

EUDRAGIT® E PO Coating in a Perforated pan

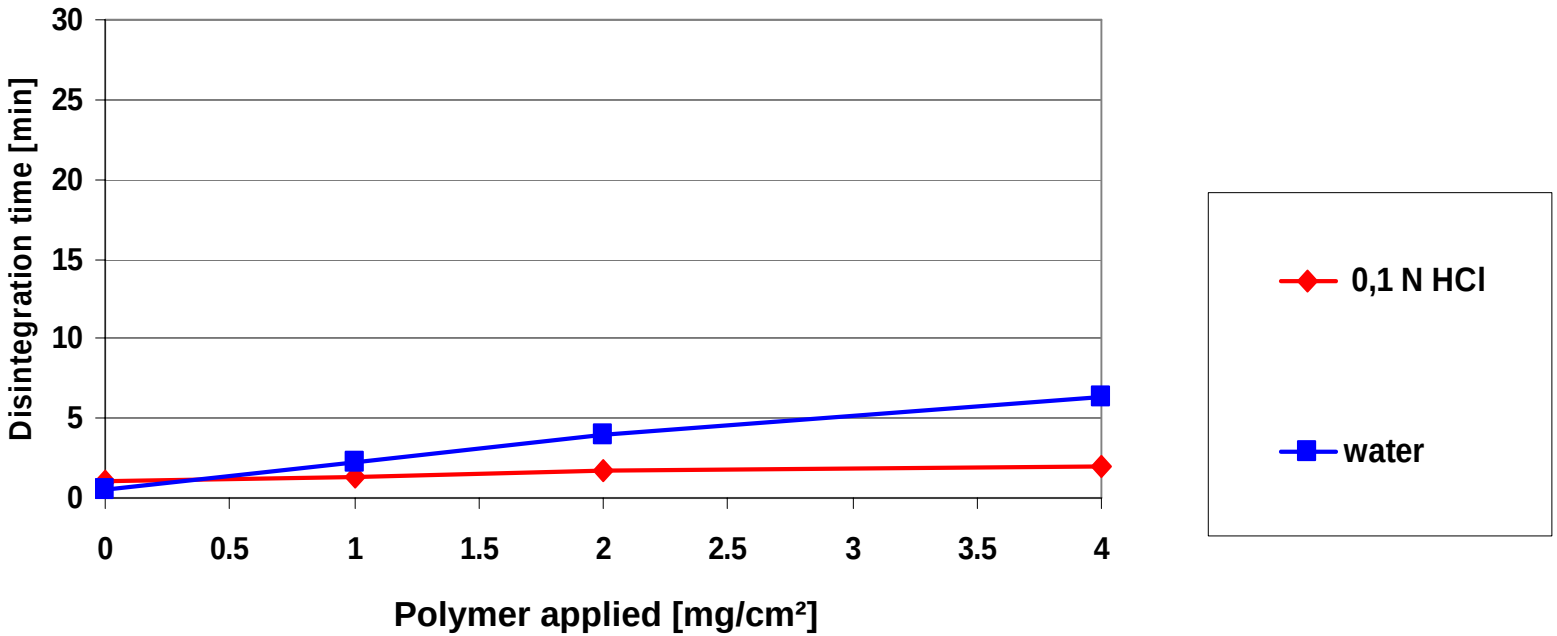
Cores:
Placebo tablets and quinidine sulphate tablets (1%),
10 mm Ø, 4 mm height, 301 mg weight
Batch size: 8 kg

Equipment:
Accela Cota 10

Parameters:

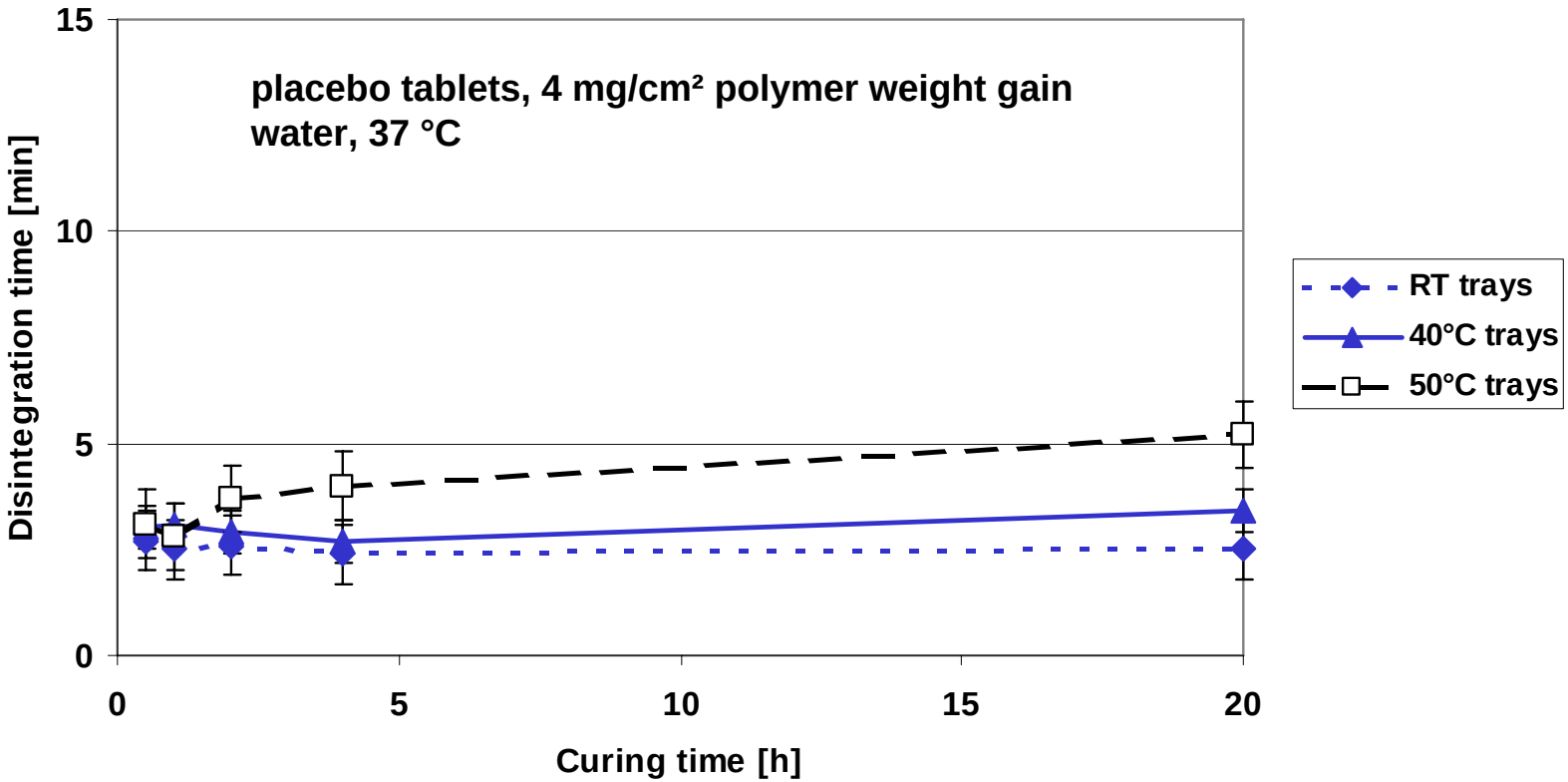
Nozzle bore:	1.0 mm (Watson Marlow)
Spray rate:	3-5 g/min/kg
Atomizing air pressure:	1.5 bar
Inlet air temp	35-50°C
Bed temp	29-31°C
Coating time:	50 min

Characteristics of EUDRAGIT®
EPO Coatings
Example: Quinidine sulfate tablets (stearic acid, SLS)

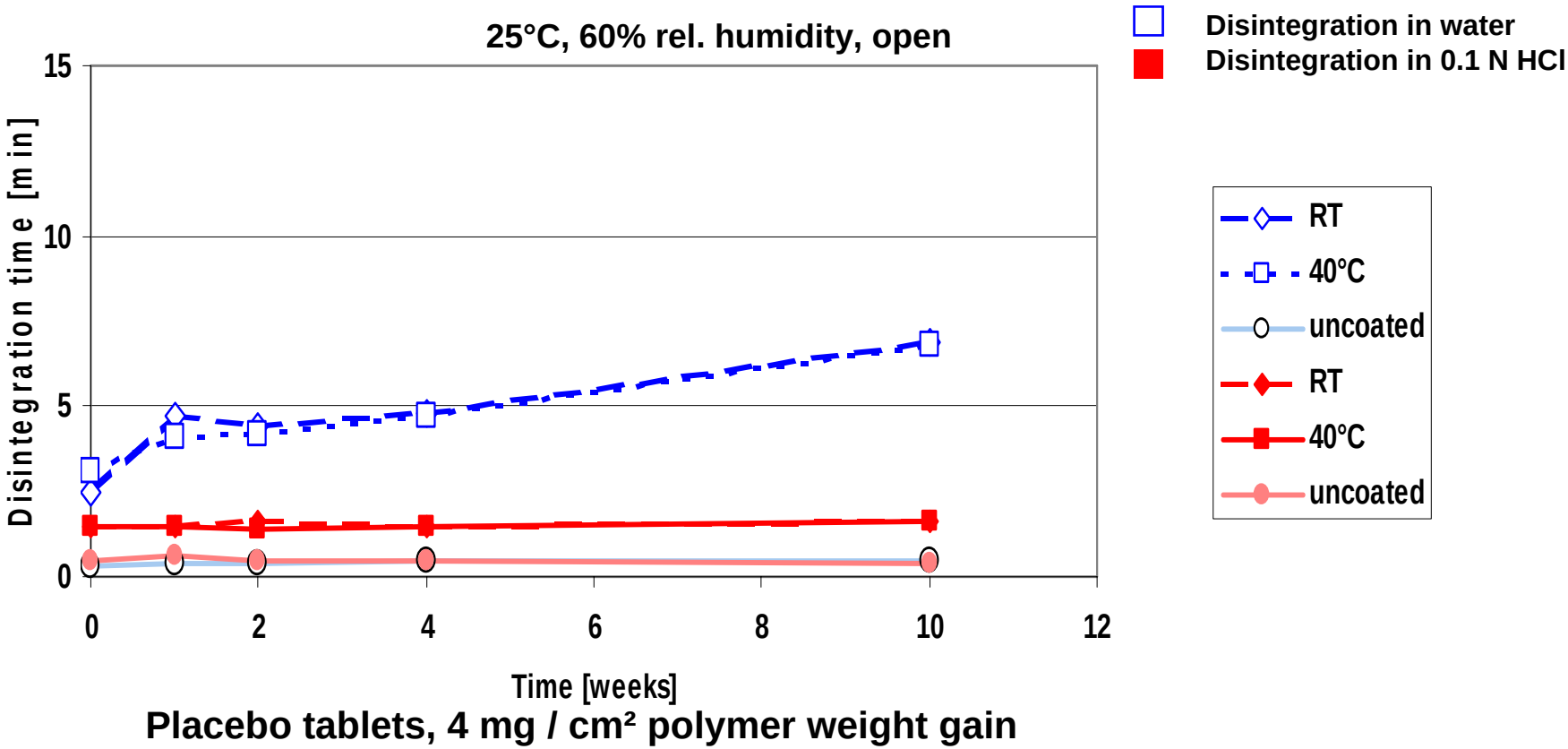


⇨ **Rapid disintegration in artificial gastric fluid!**

EUDRAGIT® E PO – Post Coating Treatment

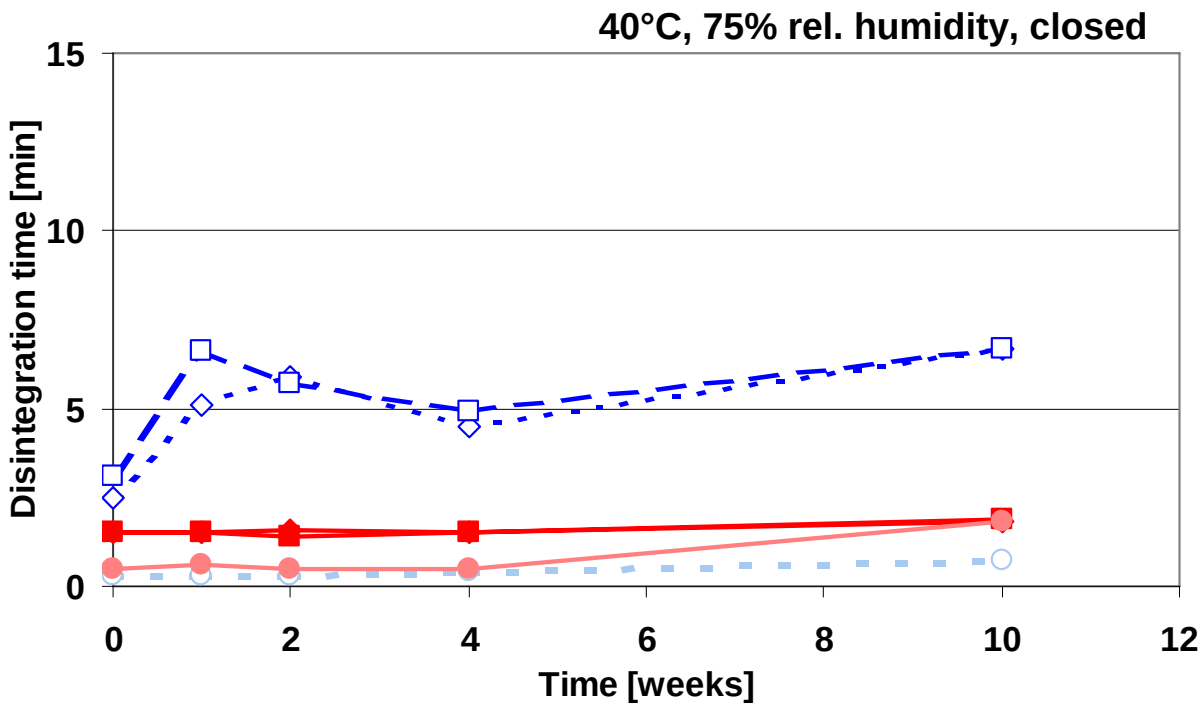


Storage Stability



Placebo tablets, 4 mg / cm² polymer weight gain

Storage Stability

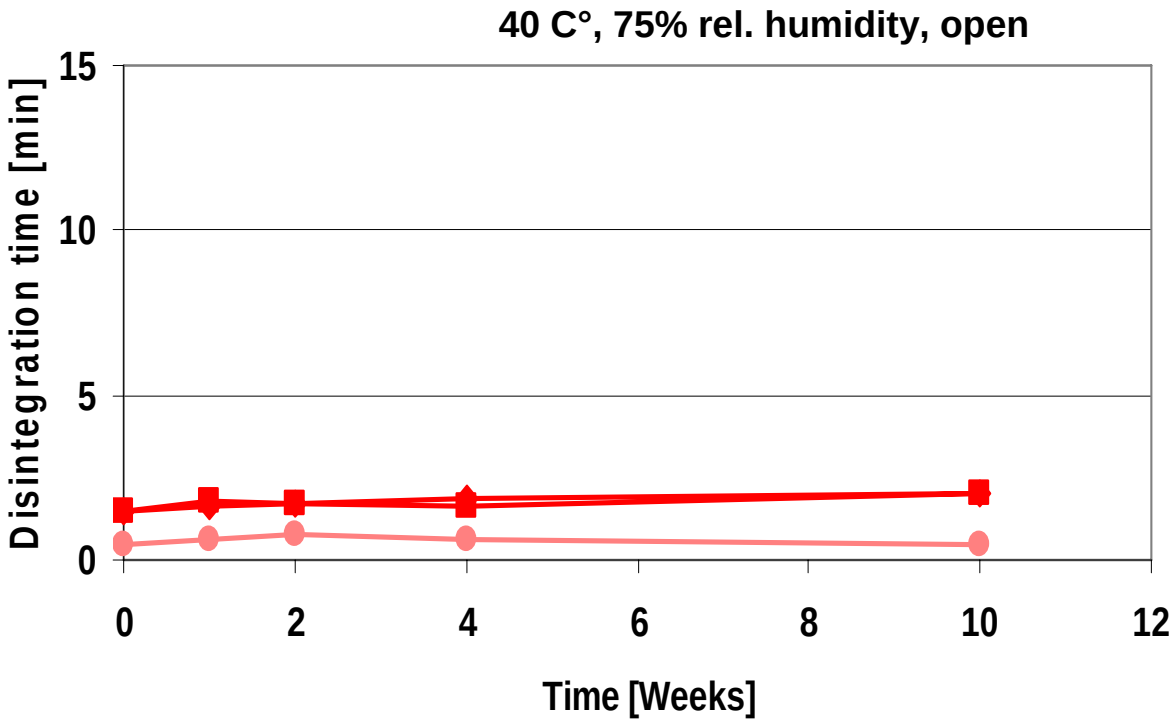


Disintegration in water
Disintegration in 0.1 N HCl

RT
40°C
uncoated
RT
40°C
uncoated

Placebo tablets, 4 mg / cm² polymer weight gain

Storage Stability Under Stress

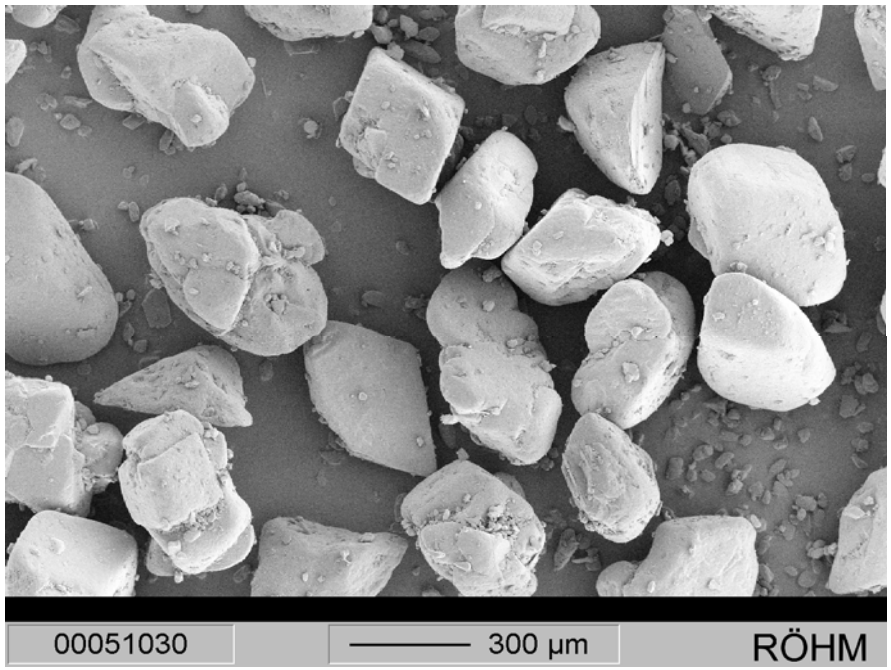


Disintegration in 0.1 n HCl

RT
40°C
uncoated

Placebo tablets, 4 mg / cm² polymer weight gain

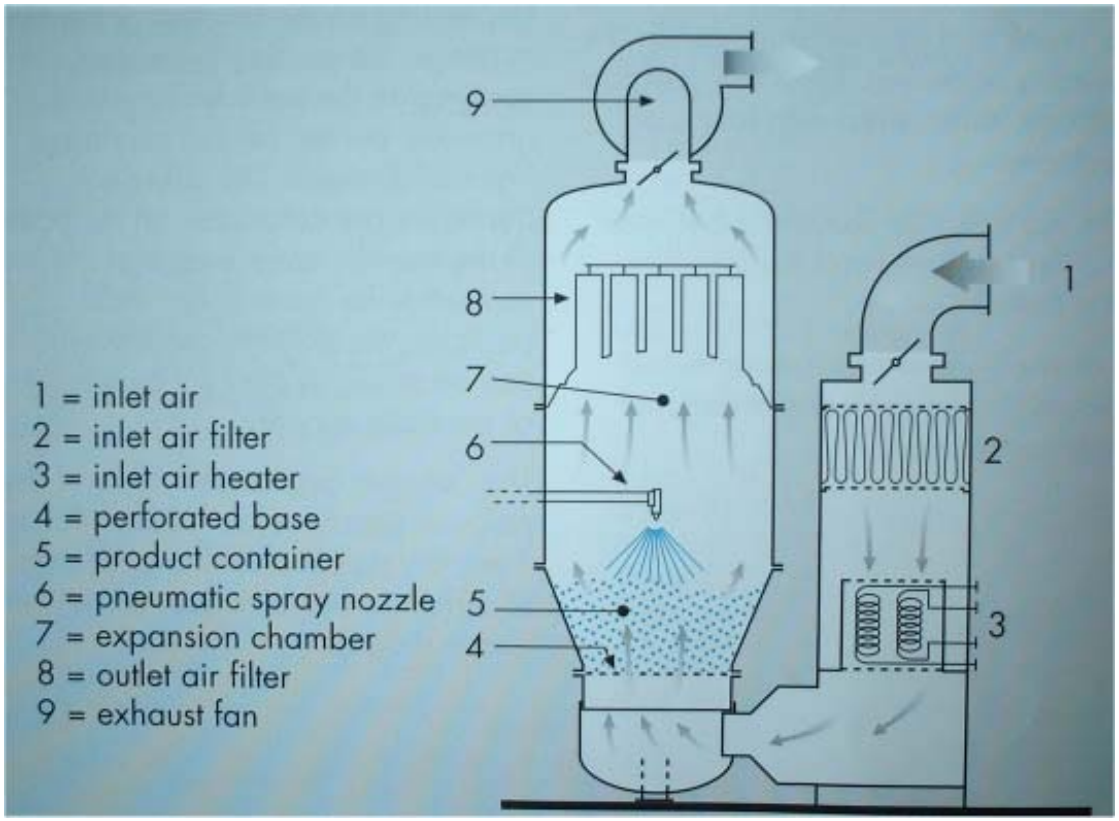
Taste Masking by Particle Coating



Paracetamol Special Granular
Mallinkrodt Inc.
Particle size: 99.5% 150 - 420µm
Surface area (Blaine): 259.4 cm²/g

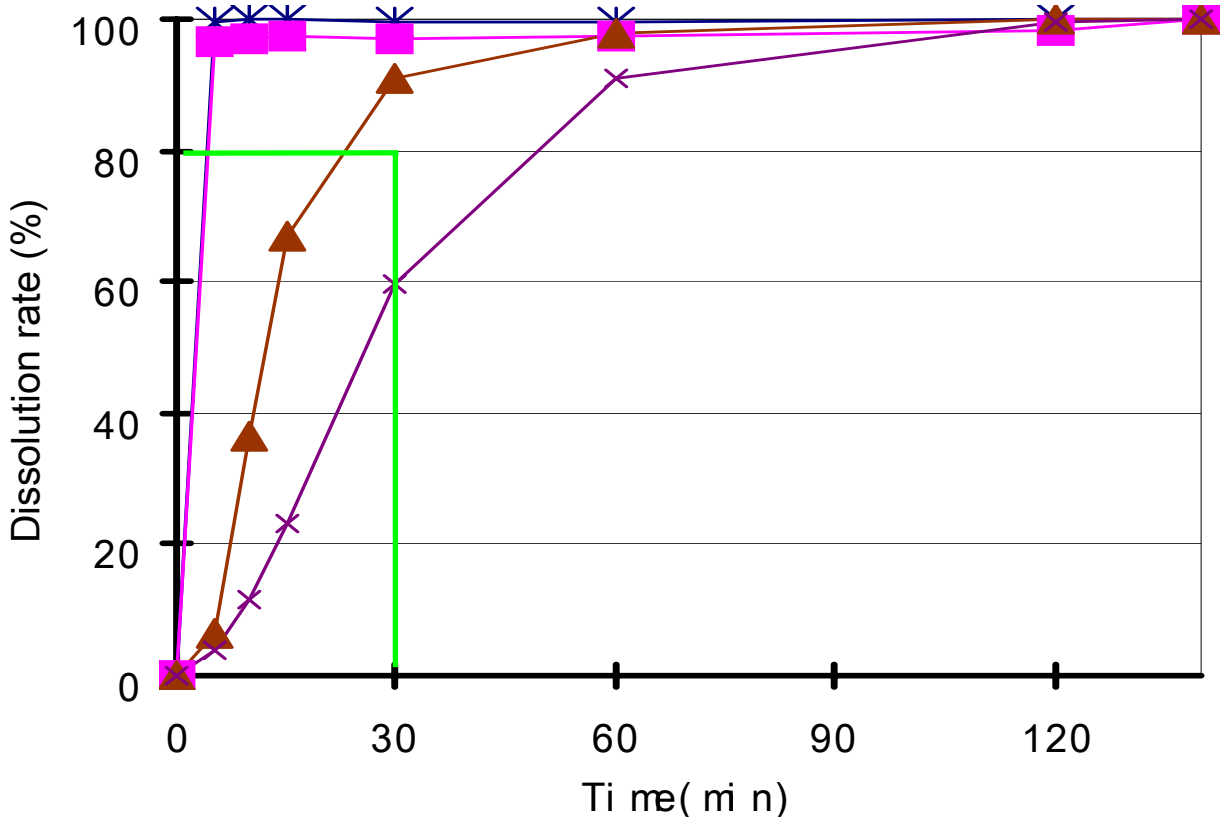
Particle Coating with EUDRAGIT® E PO

Glatt WSG 5 with 2kg insert (top-spray)



Nozzle diameter
1.2 mm
Atomizing pressure
2.0 bar
Distance nozzle - products
15 cm
Inlet air temperature
26 ~ 38 ℃
Outlet air temperature
22 ~ 30 ℃
Air flow rate
1.0 ~ 2.0 m/s

Drug Release from Coated Paracetamol Granules



uncoated
* **pH 1.2, 5.8, 6.8**

30 % polymer weight gain from EUDRAGIT® E PO
- **pH 1.2**
- **pH 5.8**
- **pH 6.8**

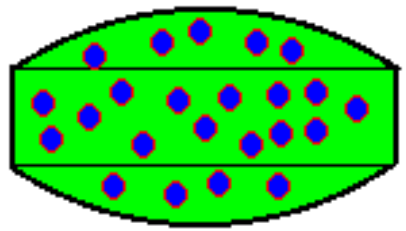
Taste masking (n=9)
15 % polymer:
27 sec (1 – 110)
30 % polymer:
59 sec (10 - 120)
Smooth and mild

⇨ **pH-dependent solubility:**
Release testing in acid media!

Model for Chewable Tablets

Compositions

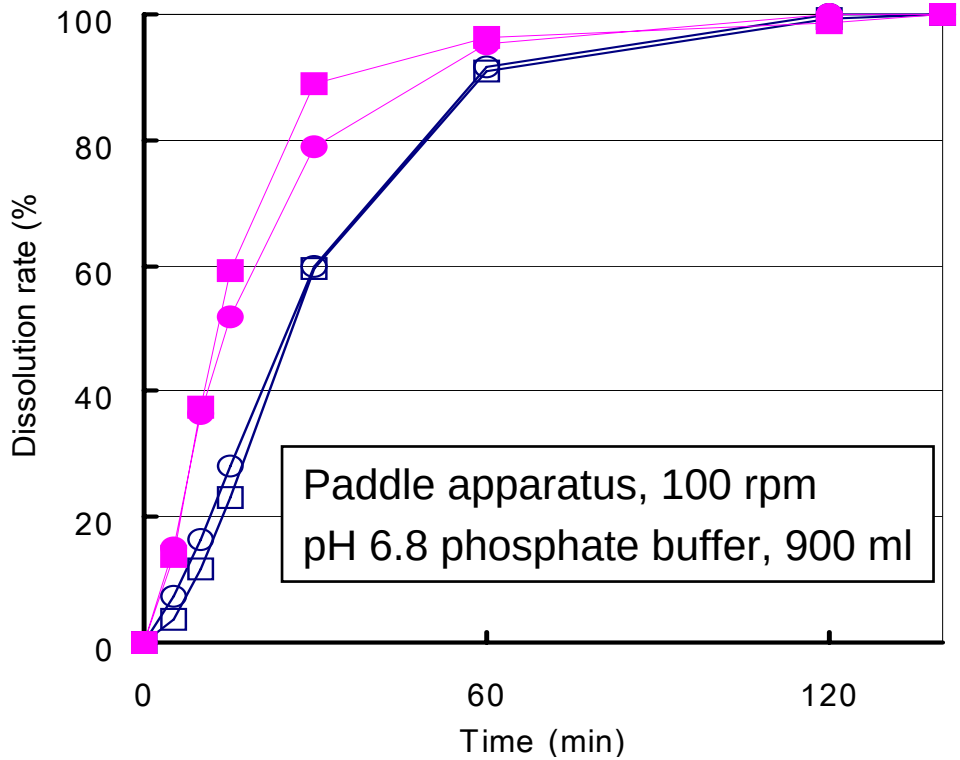
	15 % polymer weight gain [mg]	30 % polymer weight gain [mg]
Paracetamol	300.0	300.0
as coated	371.7	447.8
Microcrystalline cellulose	216.8	261.2
Na-carboxymethyl starch	31.0	37.3
Total	619.5	746.3

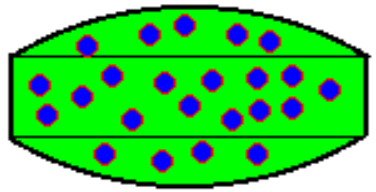


Manufacture & Characteristics

Compression pressure (kN)	2.5	3.0
Tablet hardness (N)	61-68	60-79
Weight (mg)	731-747	615-622
Height (mm)	8.5	7.2
Diameter (mm)	12.0, radius of curvature 9.0	

Dissolution Profiles of Particles and Tablets





15% polymer weight gain
- **particles**
- **tablets**

30% polymer weight gain
- **particles**
- **tablets**

⇨ **Coatings resist compression due to high flexibility!**

EUDRAGIT® E PO – Colored coatings

- **Compatibility with iron oxide pigments**
- **Povidone K 25 and Poloxamer 188 can be used to stabilize spray suspensions containing aluminum lakes**
- **Moisture protective film coatings might require higher weight gains.**

Kucera and Assmus. Presented at the 2007 Meeting of the American Association of Pharmaceutical Scientists, San Antonio, TX

EUDRAGIT® E PO with Aluminum Lakes

- Applications where EUDRAGIT® E PO is combined with a pigment are especially attractive due to the pharmaceutical elegance of the final dosage form.
- Lakes are formed by the precipitation and absorption of a water-soluble dye onto an insoluble substrate, such as aluminum hydroxide.
- When added to polymethacrylate coating systems, it is possible for a lake to cause coagulation due to the action of the water soluble dye as strong electrolyte.

EUDRAGIT® E PO solutions

- EUDRAGIT® E PO solutions were prepared and then mixed with red (E127), blue (E132), or yellow (E104) aluminum lakes in the presence of polymeric additives

- The suspensions were agitated for 10 hours via a magnetic stirplate and then passed through a 0.2 mm sieve to observe the effect of polymeric additives on coagulum content.

Formulation

EUDRAGIT® E PO	**7.37%**
Sodium Lauryl Sulfate	**0.74%**
Stearic Acid	**1.10%**
Talc	**3.70%**
Titanium Dioxide	**0.74%**
Aluminum Lake Pigment	**1.10%**
Stabilizing Excipient	**0.74%**
Water	**84.50%**
----------	**----------**
% Solids:	**15.5%**
Polymer Applied:	**4 mg/cm^2**
Solids Applied:	**8.4 mg/cm^2**

Coating Equipment

Coating Equipment

- Erweka AR400 Coating Pan
- Schlick 970/7-1 S 53 Spray Gun
- Watson-Marlow 505 S Peristaltic Pump

Coating Parameters

Coating Parameters

Inlet Air Temperature (°C):	34 ± 2
Product Temperature (°C):	26 ± 1
Atomizing Air Pressure (bars):	0.8
Pan Rotation Speed (rpm):	50
Coating Time (min):	120 ± 8
Spray Rate (g/min/kg):	3.2 ± 0.2

Placebo Tablets Coated with EUDRAGIT® E PO, 10% Kollidon® K25, and 15% Aluminum Lake

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Placebo Tablets Coated with EUDRAGIT® E PO, 10% Kollidon® K25, and 15% Aluminum Lake

Summary

- **EUDRAGIT® E PO provides an effective moisture barrier coating system**
- **Aqueous EUDRAGIT® E PO dispersions provide efficient taste masking by spray coating on tablets and particles**
- **Coatings are flexible and coated particles may be compressed into rapidly disintegrating tablets**