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Röhm Pharma Polymers

Enteric coatings with EUDRAGIT â L/S from aqueous dispersions.
Active crystals coated with EUDRAGIT® L 30 D-55

Spraying process for the manufacture of taste- and odour-masking, colourless enteric sealing coats with EUDRAGIT® L 30 D-55 on active crystals (acetylsalicylic acid) finished in a fluid bed coater.

Operating method
Ideal structures for such coating processes are evenly shaped, compact crystals or granules. Crystal needles or porous particle agglomerates are less suitable, since they break easily or soak up the dispersion.
The coating suspension is sprayed onto the fluidized particles, which are prewarmed to about 30 °C, by means of an air spray gun (top-spray method). Spray rate, inlet air quantitiy and inlet air temperature are adjusted in such a way that spraying can be performed continuously. During the process, the crystals should be maintained at a temperature of 25 to 30 °C and be able to flow freely.
Agglomeration can be avoided by adding suitable glidants (talc, magnesium stearate, kaolin, Syloid®) to the EUDRAGIT® L 30 D-55 spray suspension.
If agglomeration does occur, spraying must be interrupted until the active particles are dry and once more able to float freely. Subsequently, processing may be continued at a reduced spray rate.
To improve the flow of small particles, lubricants such as Aerosil® 200, talc or magnesium stearate (0.2 to 0.5%) can be added.
The following polymers, dissolved in organic solvents, are recommended for subcoating of extremely water sensitive active ingredients:

EUDRAGIT® E 12,5, EUDRAGIT® E 100 ; EUDRAGIT® RL/RS 12,5 ;
EUDRAGIT® RL/RS 100 ; EUDRAGIT® L/S 12,5 ; EUDRAGIT® L/S 100 ;
EUDRAGIT® L 100-55

Similarly to colloidal systems, aqueous dispersions are adversely affected by various factors. Coagulation may occur in the presence of electrolytes, organic solvents or finely dispersed pigments, due to changes in pH, foam formation, heat or frost, or high shear in high-speed mixers and mills.
Finely dispersed pigments in polymer dispersions may cause speckling. Added emulsifiers (polysorbate, polyethylene glycol, polyvinyl pyrrolidone, Na carboxymethylcellulose, etc.) have a stabilizing effect. When speckling leads to coagulation, these dispersions cannot be redispersed and must be discarded.
Dispersions of EUDRAGIT® 30 D-55 are incompatible with magnesium stearate (thickening or coagulation), but magnesium stearate contained in tablets affects neither the spray suspension nor the film properties.

Typical formulation
The formulation gives the polymer and excipients quantities required for coating 1 kg of medium-sized crystals (Ø 0.3 to 1.2 mm) at a polymer weight of 8%.
Triethyl citrate (plasticizer), talc and antifoam (silicone) emulsion are suspended in water. This suspension is homogenized in suitable equipment (Ultra-Turrax, geared colloid mill, ball mill) and stirred into the EUDRAGIT® L 30 D-55 dispersion just before use. After filtration through a 0.25 mm sieve, it should be gently stirred throughout the spraying operation.

Typical formulation

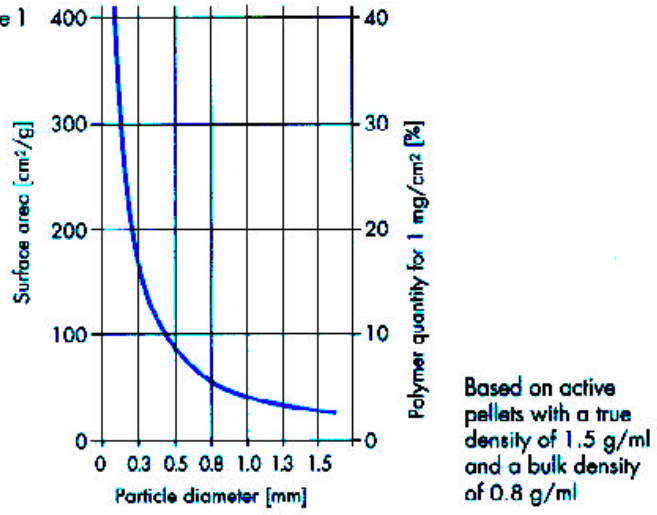
Enteric film coating with EUDRAGIT® L 30 D-55	Parts by weight
EUDRAGIT® L 30 D-55	265 g
Triethyl citrate	8 g
Talc	40 g
Antifoam emulsion	1 g
Water	186 g
	å **500 g**
Solids content of the spray suspension:	25.8%
Content in dry polymer substance:	16.0%

Calculation of surface area

Particles in the range of 0.5 to 1.2 mm usually require a polymer application of about 10 to 20% for sustained release and around 10 to 30% for gastroresistance. The specific surface area of the products increases drastically when the particle size decreases. The polymer requirement can be derived from the specific surface areas calculated as a function of particle size (Fig. 1). For accurate determination, use a Blaine apparatus or a modified Friedrichs manometer.

On this basis it is possible to detect batch-to-batch fluctuations in particle size distribution and to adapt the polymer quantity to the changing product surface area.

Figure 1



Options

Active crystals, pellets or granules can also be coated in a pan, provided it has the necessary air-handling capacity. This applies in particular to coating pans equipped with an immersion tube (Boehringer Mannheim). In this case warm air is introduced beneath the surface of the rotating core bed, giving rise to an air bubble into which the polymer solution is sprayed by means of an air nozzle.

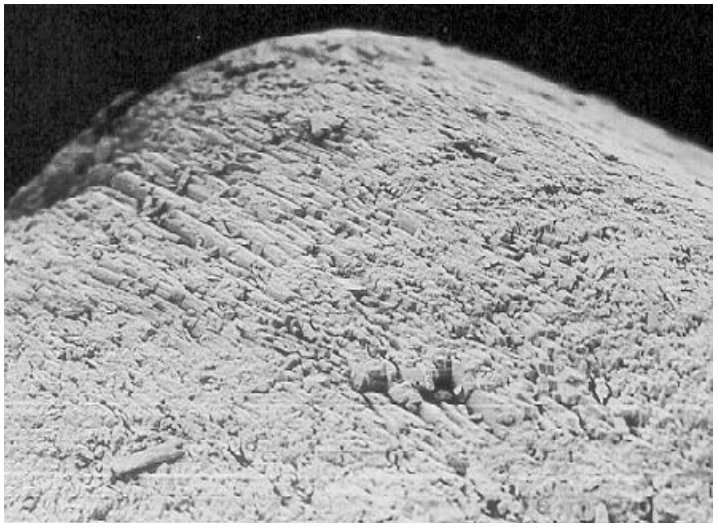
Reducing the thickness of the coating layers with EUDRAGIT® L 30 D-55 often results in coated particles which release the active gradually over the entire length of the intestinal tract. If gastroresistance is specified in addition to delayed release in the intestine, the coating thickness can be increased accordingly. The solid forms EUDRAGIT® L/S 100, which are normally dissolved in organic solvents before use, are also suitable as film formers.

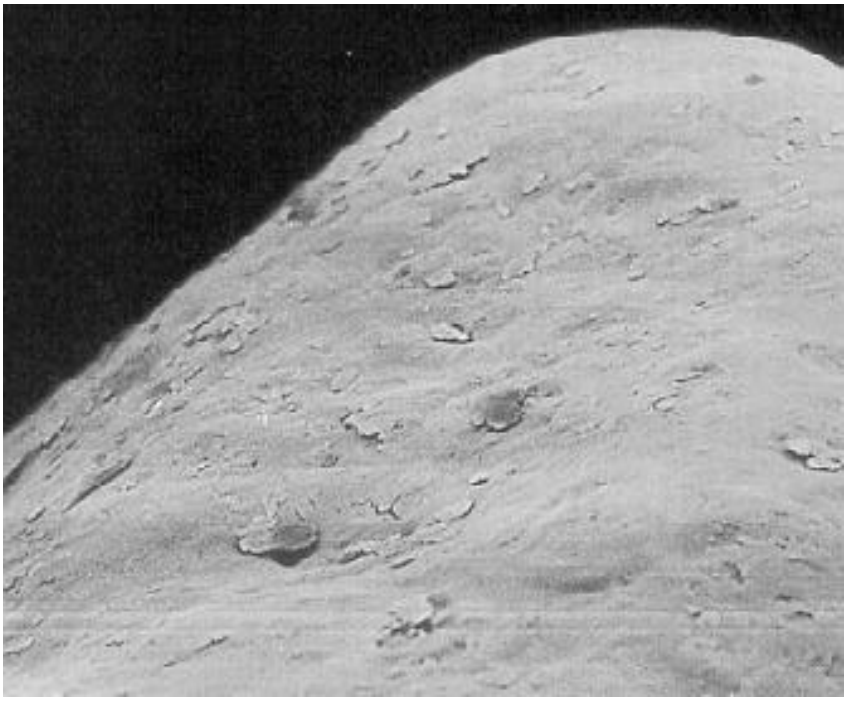
Alternatively, these film formers can be applied as aqueous suspensions obtained by redispersing the polymer powder in water.

Operating data

Example	**EUDRAGIT® L 30 D-55**
Technical data	
Coating unit	Uni-Glatt fluid-bed coater (top spray)
Feed pump	peristaltic pump with silicone tube, internal ∅ 3 mm
Spray system	air spray gun, nozzle ∅ 1.2 mm
Distance nozzle/crystals	100 mm
Coating data	
Crystals	ASS crystals, free-flowing, particle size between 0.3 and 1.2 mm, average 0.58 mm (Gaussian distribution), bulk density 0.781 g/ml, water content 0.3%, salicylic acid content 0.027%
Batch size	1 kg
Spray suspension	500 g, corresponding to 29 g solids or 12.9 wt.-% on crystal quantity 80 g polymer equivalent to 8 wt.-% on crystal quantity

Process data	**Preheating**	**Spraying**	**Drying**
Duration	5 min	38 min	3 min
Air inlet setting	30	40	30
Inlet air quantity	1 m³/min	1.3 m³/min	1 m³/min
Inlet air temperature	42 °C	40 °C	40 °C
Outlet air temperature	32 °C	26 °C	30 °C
Product temperature	30 °C	25 °C	28 °C
Atomizing air pressure	1.8 bar	1.8 bar	1.8 bar
Spray rate	---	13.2 g/min	---
Pump speed	---	12 rpm	---
Other process data			
Spray rate	13.2 g suspension/min/kg product = 3.39 g solids/min/kg product		
Evaporation rate	9.76 g/min/kg product		
Spraying process	continuous		
Total process time	46 min		
Post-drying	2 hours in drying cabinet at 40 °C, alternatively on trays at room temperature overnight		
Results			
Appearance	uniformly coated crystals		
Final specifications	particle size distribution from 0.4 to 1.25 mm, average 0.78 mm (Gaussian distribution), bulk density 0.952 g/ml, water content 0.1%, salicylic acid content 0.02%		
Gastroresistance	acc. to USP paddle method with USP digestive fluids (without added enzymes); after 2 hours transfer to intestinal fluid with gradual adjustment to pH 7.5		
Shelf life	After keeping the coated ASS crystals at room temperature for over 19 months, the salicylic acid content remained at 0.02%.		
Note	The coating example described here was repeated in fluid bed coaters WSG 30 and WSG 60, using 50 and 150 kg ASS crystals, respectively.		
Recommendations	see our Sheets for scale-up instructions in process technology		





The two photographs are scanning electron micrographs of acethylsalicylic acid (ASS) crystals in 500fold magnification before (above) and after (below) application of the polymer.