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Röhm Pharma Polymers

Enteric coatings with EUDRAGIT â L/S from aqueous dispersions.
Tablets coated with redispersed EUDRAGIT® L/S 100

Spraying process for the manufacture of taste- and odour-masking, clear transparent enteric sealing coats with EUDRAGIT® S 100 an tablets in a pan coating unit.

Operating method

The coating suspension is sprayed onto the rotating cores, which are prewarmed to about 30 °C, by means of an air spray gun. Spray rate, inlet air quantity and inlet air temperature are adjusted in such a way that spraying can be performed continuously. During the process, the tablets should be maintained at a temperature of approx. 25 to 35 °C.
Moisture-sensitive tablets are initially sealed at a reduced spray rate. It takes about 30 minutes to apply a thin sealing coat. Thereafter processing may be continued as usual.
Twinning, i.e. sticking together of tablets, can be avoided by adding suitable glidants (talc, glycerol monostearate, kaolin) to the EUDRAGIT® L/S 100 spray suspension.
If twinning does occur, spray application must be interrupted until the tablets are dry and once more able to tumble freely. Subsequently, processing may be continued at a reduced spray rate.
The following polymers, dissolved in organic solvents, are recommended for subcoating of extremely watersensitive 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.

EUDRAGIT® L/S 100 dispersions are incompatible with magnesium stearate (thickening or coagulation), but magnesium stearate contained in tablets affects neither the spray suspension nor the film properties.

Typical formulations

The following formulations give the polymer and excipients quantities required for coating 10 kg of medium-sized tablets (diameter 7 mm, weight 140 mg) at a polymer weight of 8.5 mg/cm^2. The necessary water quantity is filled into a 10 l vessel, and the polymer powder is added in portions with stirring. In doing so, it must be ensured that the powder is rapidly wetted and dispersed without lump formation.

After stirring for 5 minutes, the ammonia solution is added drop- wise at the periphery of the vortex within 5 to 10 minutes, preferably by means of a peristaltic pump, and stirring is continued for another 60 minutes. Finally, the plasticizer triethyl citrate is added in the same way as the alkaline solution, followed by stirring for one hour.

At the end of this period, a fine latex-like dispersion is obtained. This shows in the gradual disappearance of the particles initially present at the periphery of the suspension, giving way to formation of a milky-white, low-viscosity liquid. This latex is then filtered through a 0.25 mm sieve. In the case of pronounced foam formation, 2 to 3 ml antifoam emulsion are added. The talc is homogenized in the remaining water by means of a high-speed mixer (Ultra-Turrax, geared colloid mill) and stirred into the final dispersion. This spray suspension is then also passed though a 0.25 mm sieve and should be stirred through the coating process.

Typical Formulation

I. Enteric coating with EUDRAGIT® S 100

(a) Dispersion	Parts by weight
EUDRAGIT® S 100	1,000 g
Triethyl citrate	500 g
1N NH_3 (1.7% NH_3)	508 g
Water	5,532 g
(b) Excipients	
Talc	330 g
Water	1,130 g
	å **9,000 g**
Solids content:	20.4%
Content in dry polymer substance:	11.1%
Degree of neutralization	15 mole-%

II .Enteric coating with EUDRAGIT® L 100

(a) Dispersion	Parts by weight
EUDRAGIT® L 100	1,000 g
Triethyl citrate	500 g
1N NH_3 (1.7% NH_3)	339 g
Water	5,011 g
(b) Excipients	
Talc	
Water	1,650 g
	å **9,000 g**
Solids content:	
Content in dry polymer substance:	20.3% 11.1%
Degree of neutralization:	6 mole-%

III Enteric coating with EUDRAGIT® L/S 100

(a) Dispersion	Parts by weight
EUDRAGIT® L 100	500 g
1N NH_3 (1.7% NH_3)	170 g
EUDRAGIT® S 100	500 g
1N NH_3 (1.7% NH_3	254 g
Triethyl citrate	500 g
Water	5,616 g
(b) Excipients	Parts by weight
Talc	500 g
Water	960 g
	å **9,000 g**

Solids content:	20.3%
Content in dry polymer substance:	11.1%
Degree of neutralization for	
EUDRAGIT® L 100	6 mole-%
EUDRAGIT® S 100	15 mole-%

This gives a polymer (97.5 g from 877 g spray suspension acc. the formulation with EUDRAGIT® S 100) weight of L = 8.5 mg/cm² by a tablets surface of S = 160.5 mm².

Dispersion of the polymer powder occurs separately in the above described way, adding 50% of plasticizer on polymer. For mixing, the dispersion of EUDRAGIT® S 100 is slowly fed into the EUDRAGIT® L 100 dispersion. If the viscosity of the mixed dispersion increases, more

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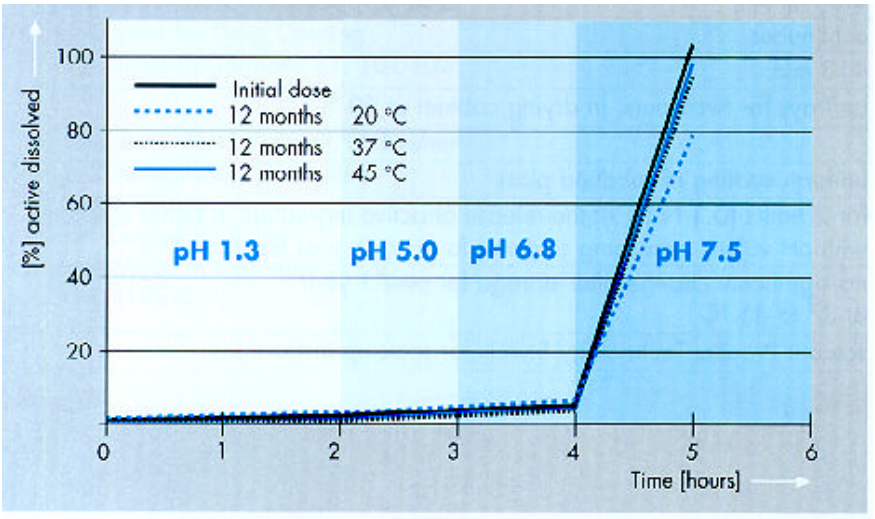
Figure 1. Release of active ingredient



Operating data

Example **EUDRAGIT L/S 100 acc. to formulation I**

Technical data

Coating unit	stainless steel coating pan, 0 250 mm, angle of inclination 35°
Feed pump	peristaltic pump with silicone tube, internal dia. 2 mm
Spray system	Walther Bingo air spray gun, nozzle dia. 10 mm (round spray)
Distance nozzle/tablets	120 mm

Coating data

Tablets	model active: bisacodyl tablets, 7 mm in dia., 3.8 mm in high 140 g in weight; hardness 54 N, active content 5 mg
Batch size	1 kg
Spray suspension	877 g, corresponding to 179.2 g solids or 17.9 wt.-% an tablet quantity 97.5 g polymer equivalent to 9.8 wt.-%. on tablet quantity

Process data	**Preheating**	**Spraying**	**Drying**
Duration	3 min	105 min	5 min
Inlet air quantity	0.83 m^3/min	0.83 m^3/min	0.83 m^3/min
Inlet air temperature	55 °C	55 - 60 °C	55 °C
Tablet temperature	30 °C	30 °C	35 °C
Pan speed	10 rpm	40 rpm	10 rpm
Spray pressure	-	1 bar	-
Spray rate	-	8.4 g/min	-

Other process data

Spray rate	8.4 g suspension/min/kg product 1.71 g solids/min/kg product
Evaporation rate	6.65 g/min/kg product
Polymer quantity	8.5 mg/cm^2
Spraying process	continuous
Total process time	113 min
Post-drying	on trays for two hours, in drying cabinet at 40 °C

Results

Appearance	uniform coating of subddued gloss
Gastroresistance	for 2 hours (0. 1 N HCl); the release of active ingredient in buffer solutions, with pH values increasing stepwise to pH 6.8, was less than 5%
Shelf life	no significant change after storage for over 1 year at 37 to 45 °C
Recommendations	see our Process Technology Sheets for scale-up instructions in process technology