Novel Starch-based Polymer for Aqueous Film Coating

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Presentation Outline

Introduction

- Types of coatings
- Why Film Coating?
- Basic Formulation

Starch in Film Coating

- Structure – Solubility & Retrogradation
- Film forming ability

Innovative Starch-based Coating Polymer

- Ease of dispersion & low viscosity
- Mechanical / thermal properties of films
- Quicker coating at lower temperature
- Excellent stability and appearance
- Regulatory Aspects

Summary

Solid Dosage Form Coatings

Thick Coatings
- Sugar coatings
- Sugar free coatings

Non-Functional Films
(No effect on drug release profiles)
- Aqueous
- Non-aqueous

Functional Films
(Control Drug release profiles)
- Non-aqueous
- Aqueous

Focus on Aqueous Non-functional Film Coating

Why Coat Solid Dosage Forms ?

Improved patient compliance

- ☑ Mask taste and odor
- ☑ Improve aesthetic appeal
- ☑ Facilitate swallowing

Stability

- ☑ Protect from light, moisture, oxidation
- ☑ Improve packaging efficiency
- ☑ Addition of a second API in case of incompatibility

Why Coat Solid Dosage Forms ?

Safety

- ☑ Easy recognition
- ☑ Prevention of cross contamination

Brand identity

- ☑ Imprinting

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Basic Film Coating Formulation

POLYMERS

Cellulosics
HPMC, HPC, HEC, MC

Vinyls
PVP, PVA

Acrylics
Methacrylic acid derivatives

PLASTICIZERS

Polyols
Propylene Glycol, Glycerol, PEG

Organic esters
Citrates, Phthalates

Oils/Glycerides
Castor oil, Glyceryl monostearate

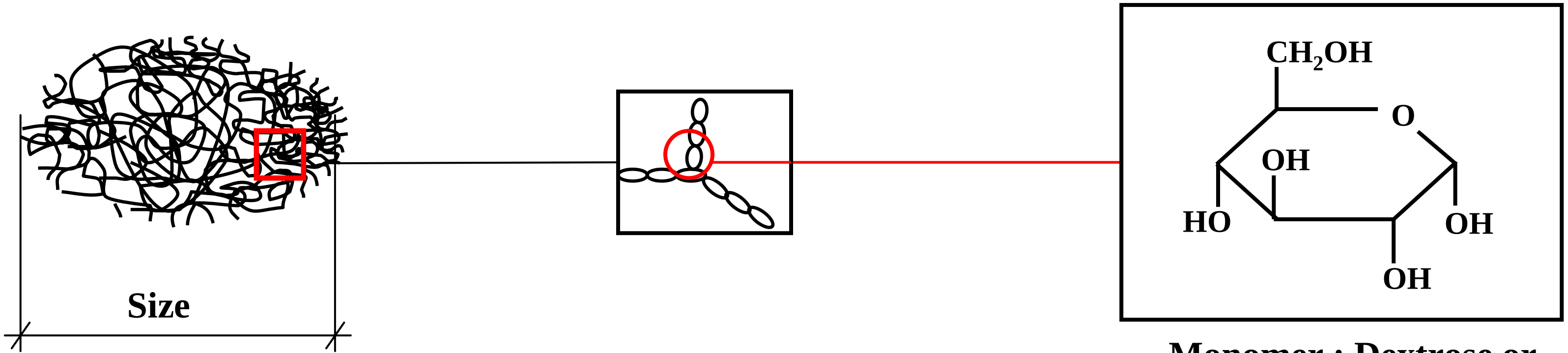
COLORANTS

Dyes
Lakes

OTHER FILLERS

Lactose
Polyols
Stearic acid
Tween
MCC

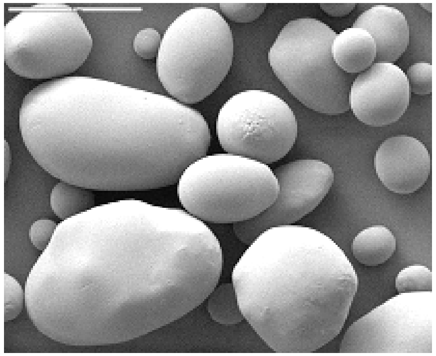
Starch For Film Coating?



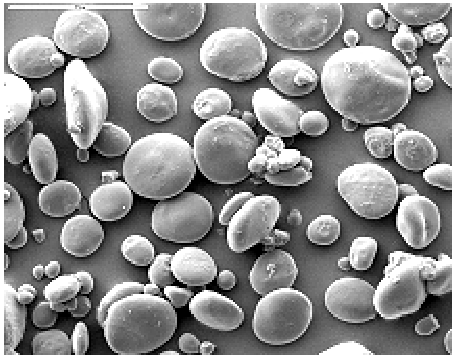
Between 2 and 100 µm

Monomer : Dextrose or α D-Glucose

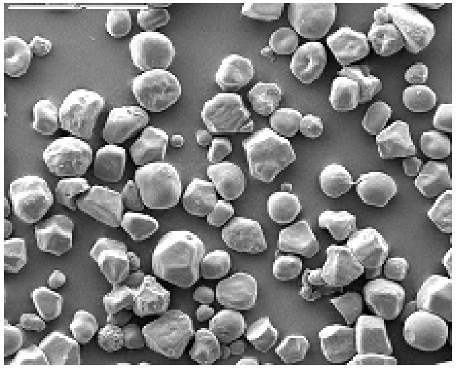
Each strand is a large polymeric molecule containing thousands of monomers



SEM Potato starch granule 10 - 100 µm



SEM Wheat starch granule 2 - 45 µm



SEM Corn starch granule 2 - 32 µm

Starch granules - Ball of string made up of many strands

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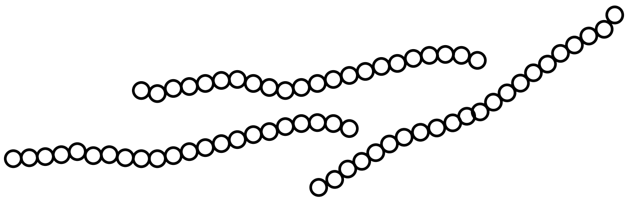
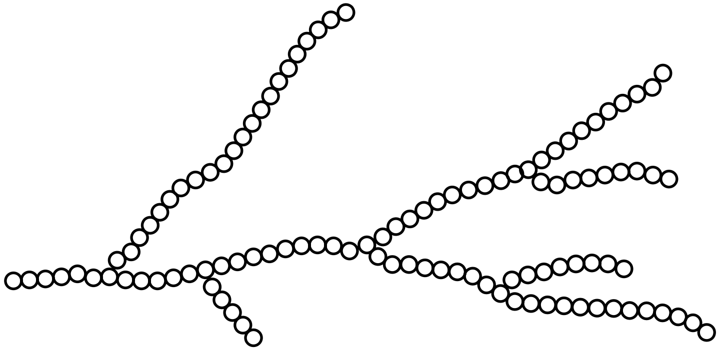
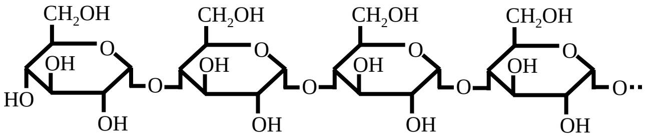
STARCH: Amylose & Amylopectin



Amylose – Slightly Branched

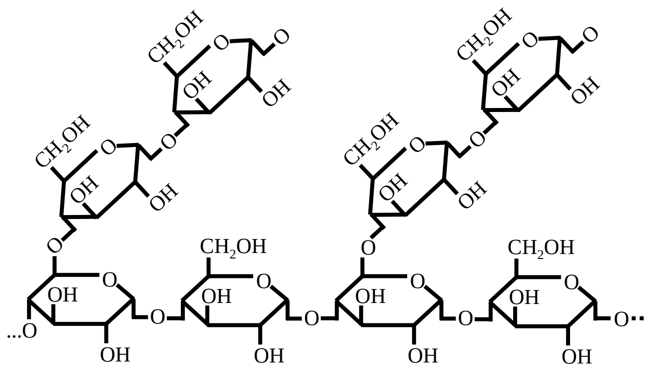


Amylopectin – Highly Branched



α 1–4 **linkage**

α 1–6 linkage

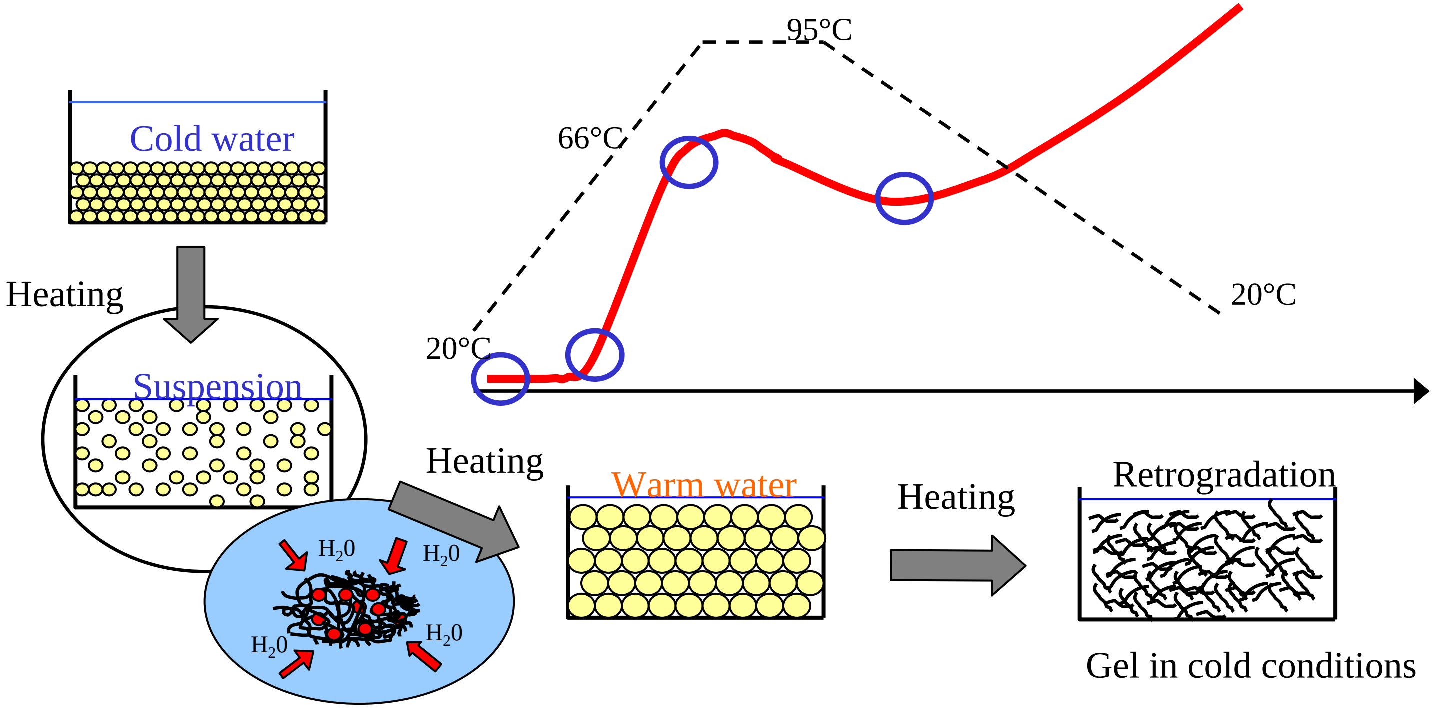


α 1–4 **linkage**

Ratio of amylose to amylopectin varies depending on natural origin of starch

STARCH: Solubility & Retrogradation

Gelatinization: Chemical/mechanical processing to disrupt all or part of the starch granules



Gelatinization

Intermolecular bonds break at high temp

H-bonding sites engage more water

Increased randomness in structure

Retrogradation

Increased H-bonding during cooling

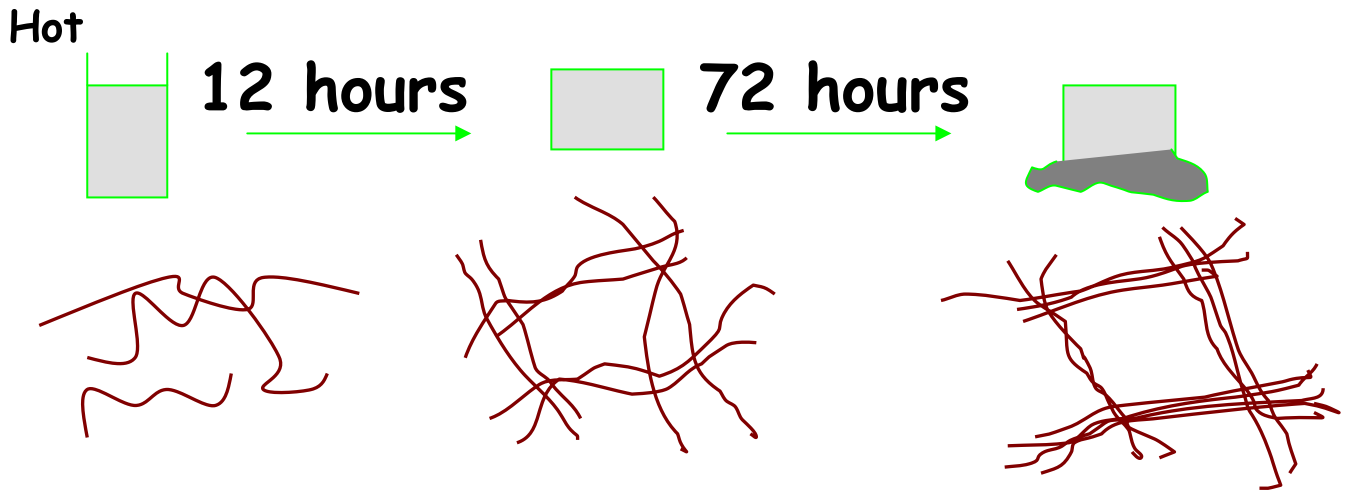
Water forced out of gel and starch insolubilized

Increased retrogradation with High Amylose starches

High Amylopectin reduces retrogradation

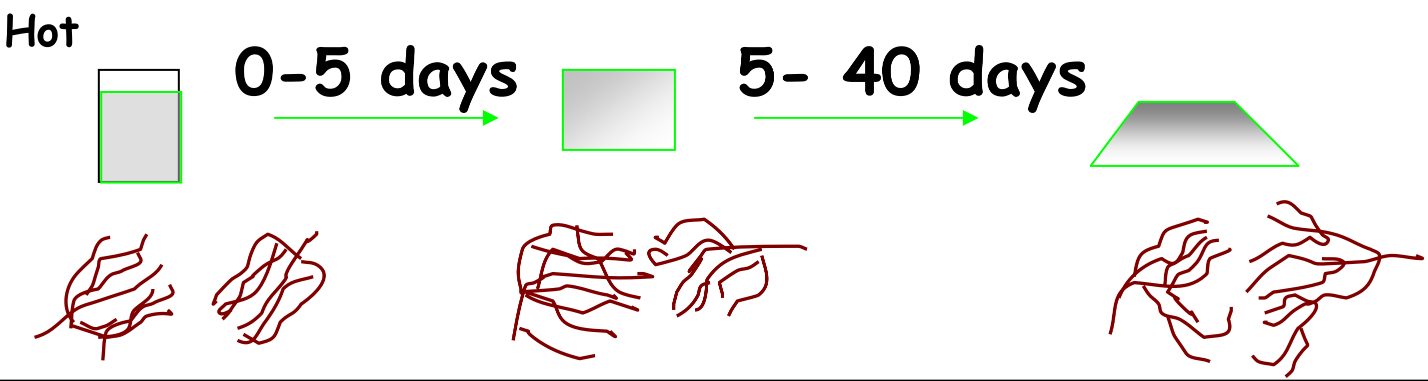
AMYLOSE

Retrogradation results in gel formation due to H-bonding (time and temperature dependent)



AMYLOPECTIN

No retogradation or gelation



STARCH: Film Forming Ability

Amylose & Amylopectin Content Variation

	% Amylose	% Amylopectin
Standard maize	24.0	76.0
Waxy maize	0.8	99.2
High amylose maize	70.0	30.0
Potato	20.0	80.0
Rice	18.5	81.5
Tapioca	16.7	83.3
Peas	40.0	60.0
Wheat	25.0	75.0

AMYLOSE

- Confers film forming properties
- Causes starch retrogradation/gelation
- Amylose rich starches difficult to pregelatinize

AMYLOPECTIN

- Reduces Retrogradation

Optimal Amylose:Amylopectin levels essential for stable film-formation

The Ideal Starch for Film Coating

- –Instant solubility / dispersibility in cold water
- –Absence of Retrogradation
  - – Enabled by chemical modification for stabilization
- –Excellent stability & film forming properties
  - – Source providing the best Amylose/Amylopectin ratio

LYCOAT®

Innovative Aqueous Film Coating Polymer

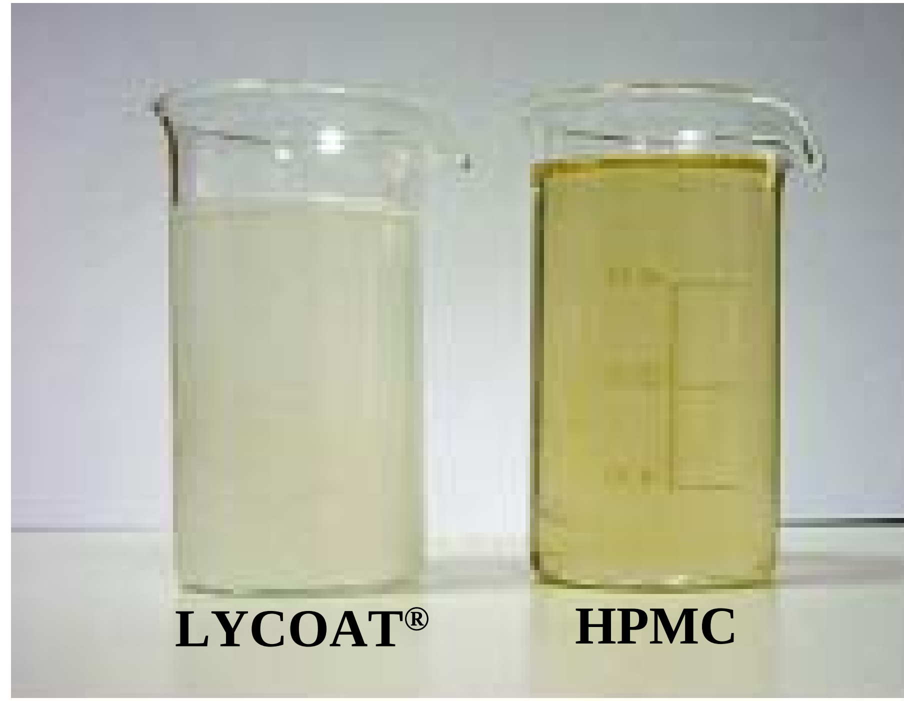
- Instant solubilization/dispersion at room temperature
- Excellent Solution Stability
- Low Viscosity even at High Solids content
- High film adhesion and mechanical resistance
- Quality and regulatory aspects (Pharma, Nutra)

Pregelatinized	Fluidified	Modified	Agglomerated	Pea starch
(water soluble)	(Low soln viscosity)	(hydroxypropyl)	(dispersibility)	(amylose:amylopectin)

➡ LYCOAT® RS 780

LYCOAT® in Film Coating

Dispersion Preparation at its Simplest



- ☑ Instant dispersion in water at RT
- ☑ Suspension is stable up to 48 hrs
- ☑ No Lumping or Foam generation
- ☑ Neutral color and odor
- ☑ NO off-taste or undesirable color

Taste Panel (n=15)	HPMC	LYCOAT®
Odor preference	20%	80%
Taste preference	14%	86%

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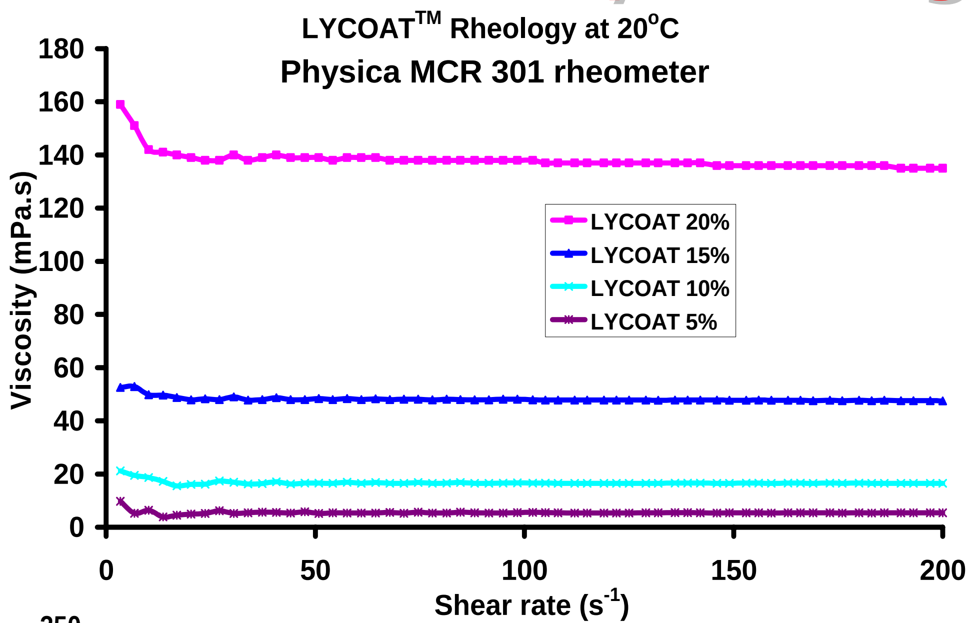
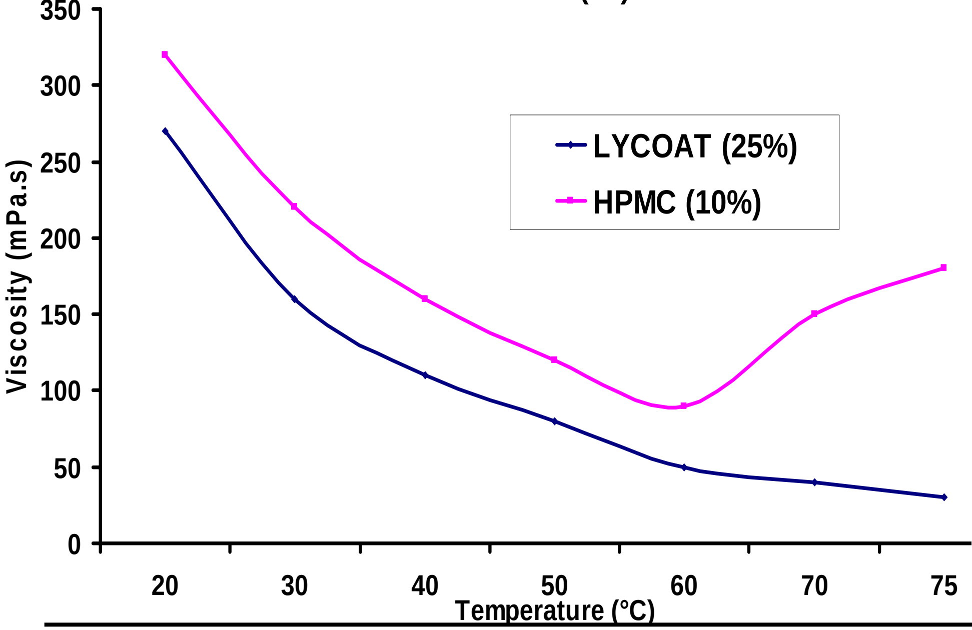
Low Viscosity at High Polymer Content



Higher levels can be used without increasing solution viscosity >500cps

Reduced Coating Time



Significantly lower viscosity vs. HPMC

No gelation above 60°C vs. HPMC

Low viscosity & Newtonian rheology enables spray uniformity

Minimizes "bearding" on spray-nozzles

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Films: Mechanical & Thermal Properties

Films prepared by casting aqueous polymer (LYCOAT® or HPMC) solutions (10% solid content)

4x10cm pieces of film were cut and dried for 24 hours at 50% RH before evaluation

Mechanical Properties by Instron 4502

Film Parameters	HPMC	LYCOAT®
Young's Modulus	4920 ± 700	4040 ± 400
Elongation (mm)	1.50 ± 0.5	2.00 ± 0.8
Breaking Force (N)	76 ± 19	70 ± 17
Thickness (mm)	0.058	0.062

Comparable mechanical properties vs. HPMC

Higher elongation with LYCOAT® allows better flexibility and resistance to deformation and stress

Thermal Properties by DSC

Films Evaluated	DSC Endothermic Transitions			
	Onset (°C)	Peak (°C)	ΔH (J/g)	Tg (°C)
HPMC	43.6	51.8	1.1	91.7
LYCOAT®	39.0	51.7	0.6	69.8

Low Tg of LYCOAT® enables film formation at lower temperatures

Coating Formulations Used

Core Tablet Formulation	
PEARLITOL® 200SD	95.5%
GLYCOLYS®	3.0%
Mg stearate	1.5%
Tablet Shape	Biconvex
Tablet Diameter	10 mm
Tablet weight (uncoated)	330 mg
Tablet Hardness (uncoated)	85N
Tablet loading	5 kg

Ingredients	LYCOAT®	HPMC
Polymer	136.5g	62.6g
GMS	12.5g	-
PEG 400	-	5.5g
Tween 80	1g	-
TiO_2	48g	21g
Lake color	2g	0.9g
Water	800g	910g
Total	1000g	1000g
Solids level	20%	9%
Viscosity	140 mPa.s	150 mPa.s

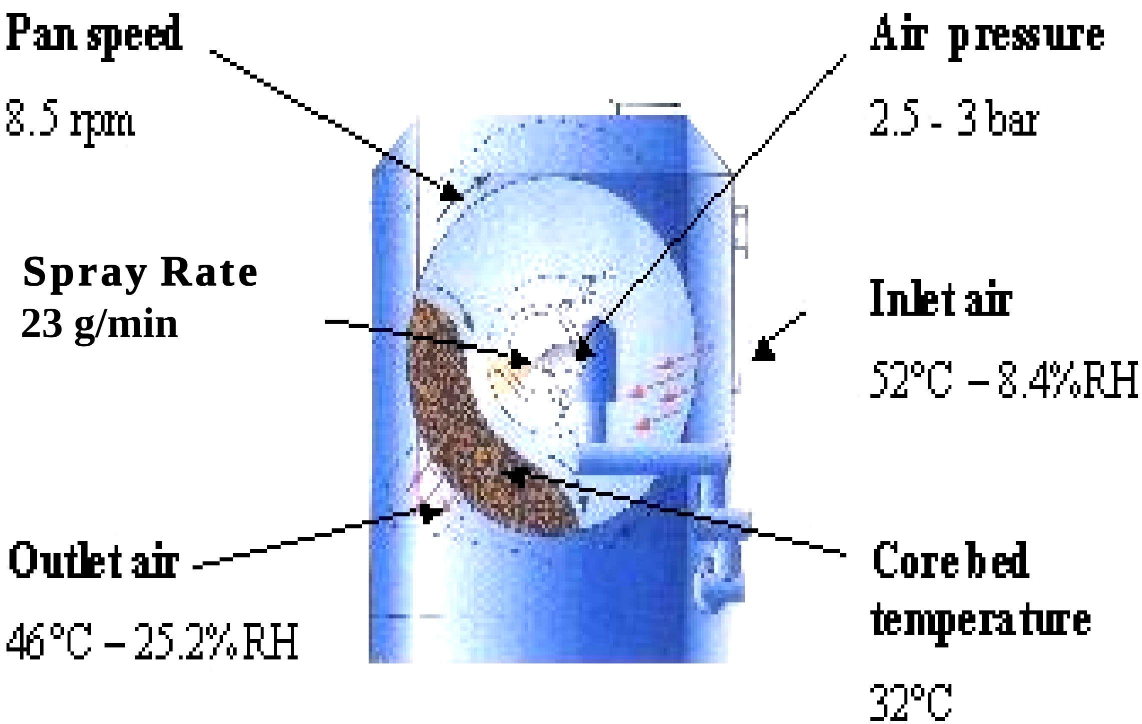
Polymers dissolved in water at room temperature using a magnetic stirrer

GMS emulsified by melting in water and Tween 80 using a magnetic stirrer until it cooled to RT

Pigments / lakes, titanium dioxide dispersed in water using high shear mixer and added to above mix

Coating Parameters Used

FC 19 coating machine (NR Industries), Fully perforated pan, Binks 460 spray gun (040’nozzle diameter)

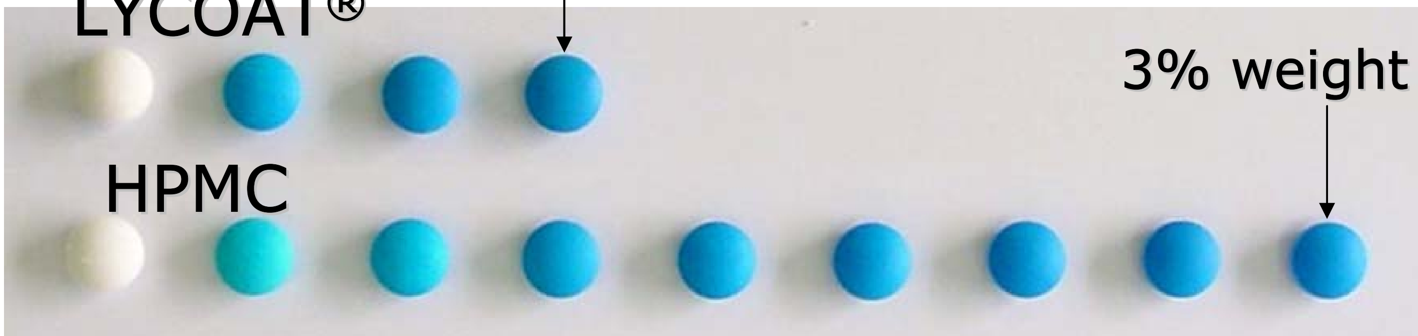


- ☑ Coating at 32ºC bed temp
- ☑ Good for thermolabile API

Film Coating Results	LYCOAT®	HPMC
Total Solution Used	750g	1667g
Mean Coated Tablet weight	340 mg	340 mg
Mean % weight gain	3.03%	3.03%
Total Coating Time	32 min	72 min

- ☑ High polymer % in Low volume
- ☑ 60% reduction in coating time

Coating Completed in 60% Less Time



Reduced coating time at low bed temp enables significant cost savings

If required, LYCOAT® can be used for coating over a wide temp range

LYCOAT® - Reduced Nozzle Bearding

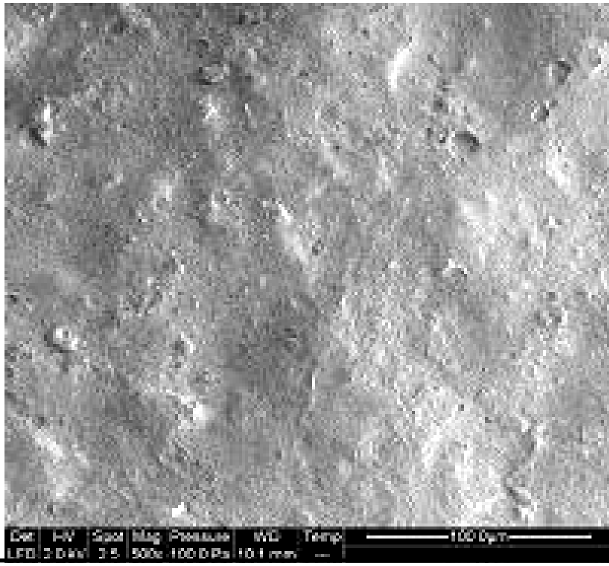
HPMC after 30 min run

LYCOAT® after 30 min run

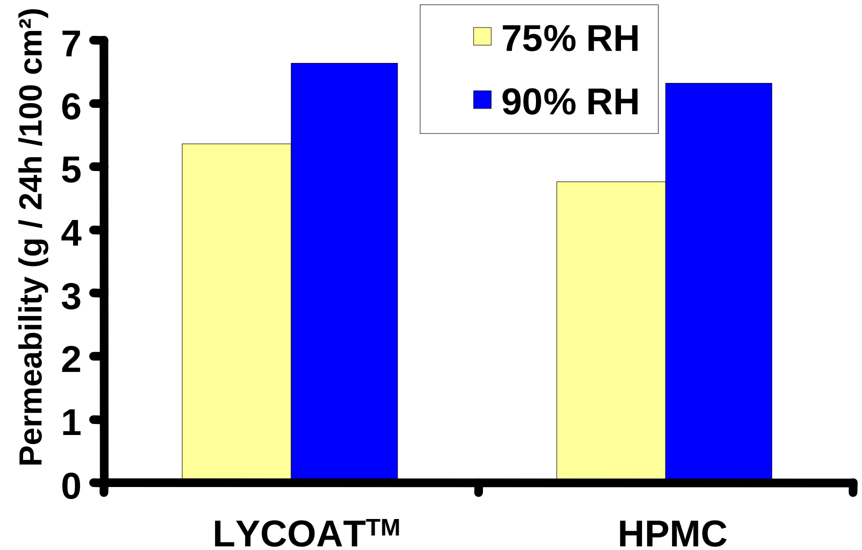
Lower solution viscosity of LYCOAT® reduces nozzle bearding

- Reduction in the coating time
- Reduced cleaning time
- Higher throughput

LYCOAT® - Barrier Properties



ESEM – LYCOAT® Film Surface



Moisture Permeability vs. %RH

Smooth coated tablet surface

No pin-holes or cracks

Enables excellent barrier properties

Equivalent moisture barrier properties

Excellent stability after 3 months at 20°C / 33-85% RH

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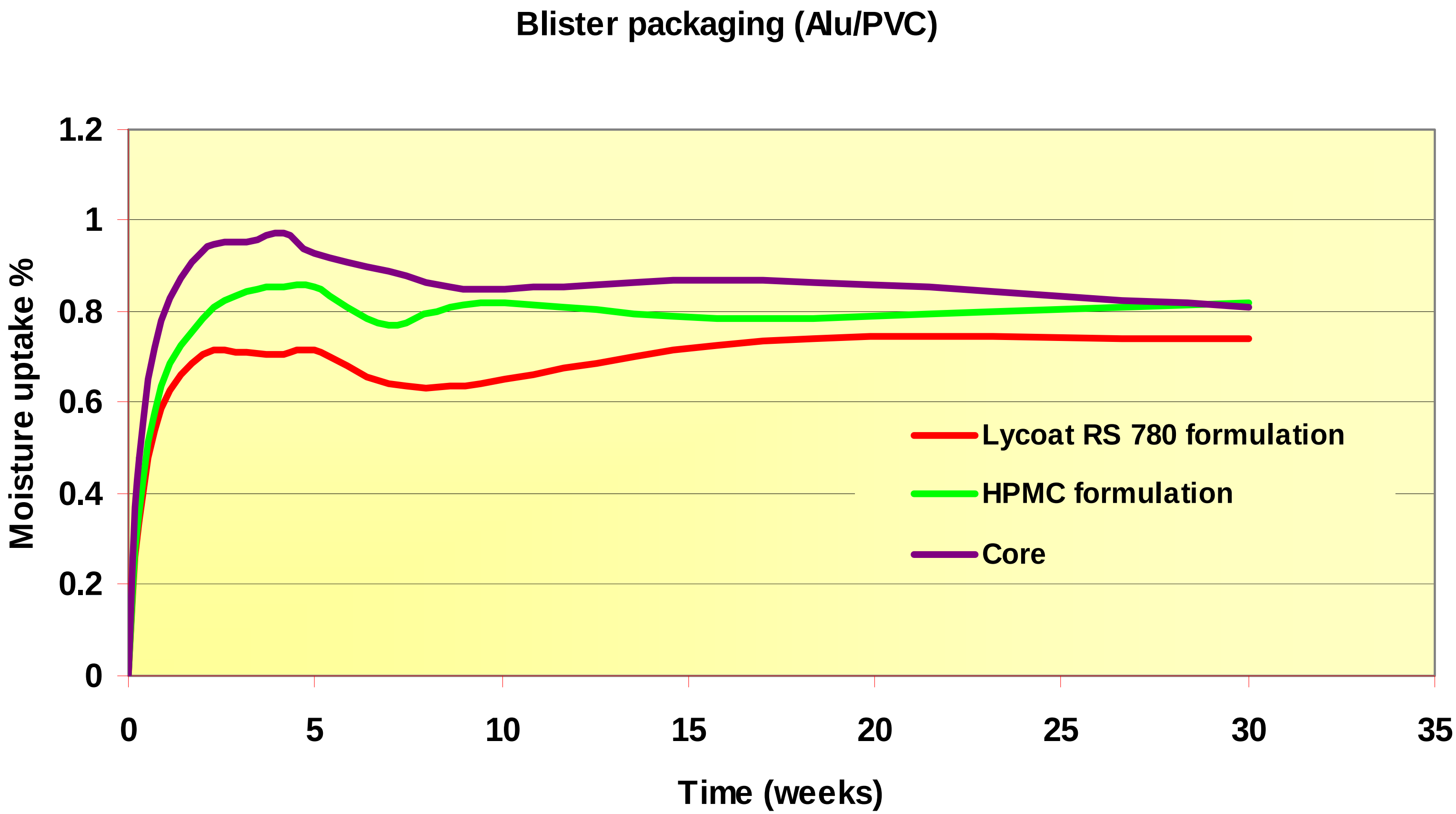
Moisture Stability at 40ºC & 75% RH

Tablets coated with formulated HPMC or LYCOAT®



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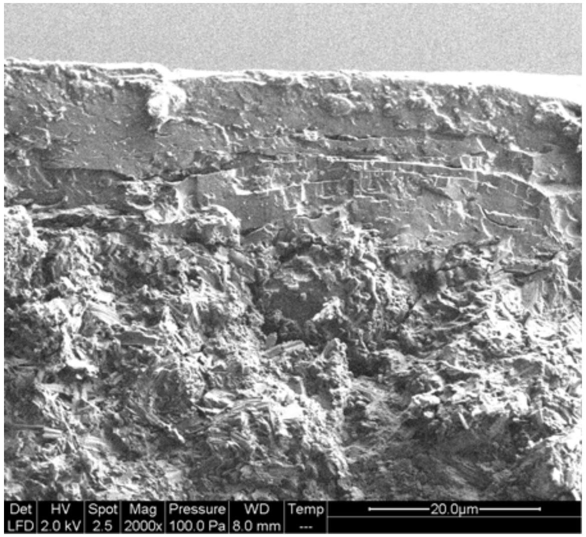
Excellent Film Adhesion

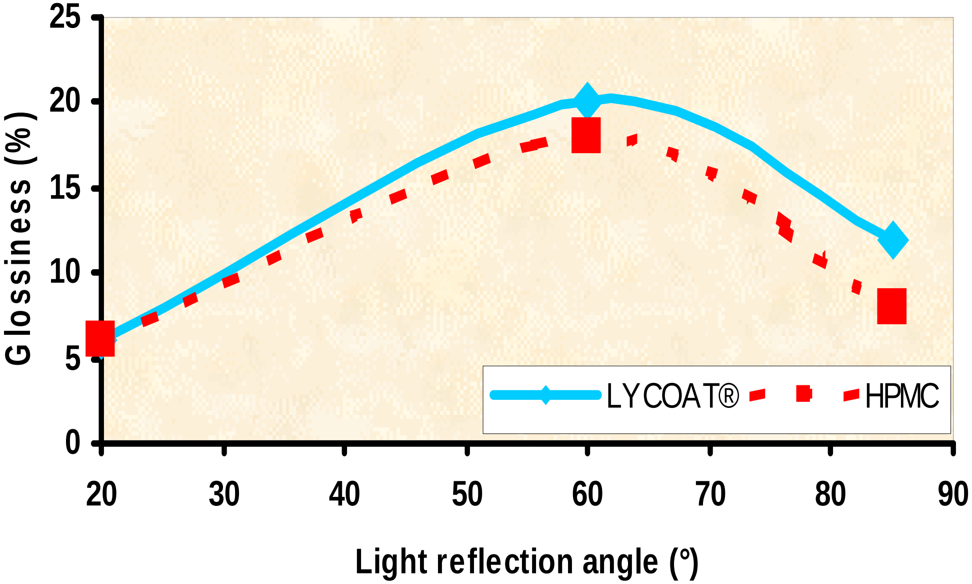


Cross-section of LYCOAT® Coated Tablet

Film Parameters	HPMC	LYCOAT®
Young's Modulus	4920 ± 700	4040 ± 400
Elongation (mm)	1.50 ± 0.5	2.00 ± 0.8
Breaking Force (N)	76 ± 19	70 ± 17
Thickness (mm)	0.058	0.062

Films cannot be peeled off from coated tablets, implying strong adhesion

Evaluation of Tablet Appearance



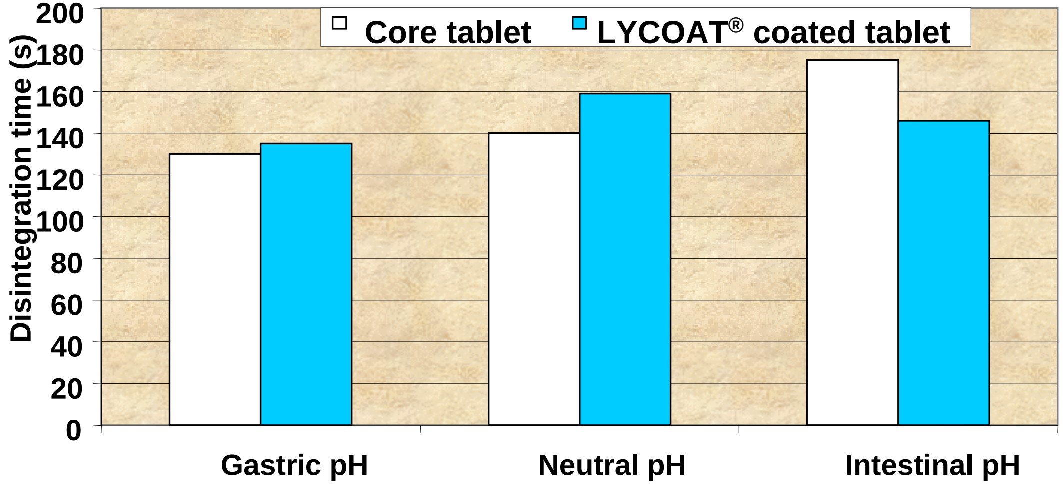
Surface Gloss and Absence of logo-bridging with LYCOAT®

Tablets exhibit an attractive finish with uniform color and smooth surface

LYCOAT® coated tablets appear glossier than HPMC coated tablets

At 3% weight gain, no infilling or bridging of logos was observed

Low Friability & Fast Disintegration



LYCOAT® Does Not Alter
Tablet Disintegration Over Wide pH-Range

Disintegration is NOT affected over a wide pH range (non-functional coating)

No difference in friability of LYCOAT® vs. HPMC coated tablets

Tablet appearance remains unchanged (no chipping)

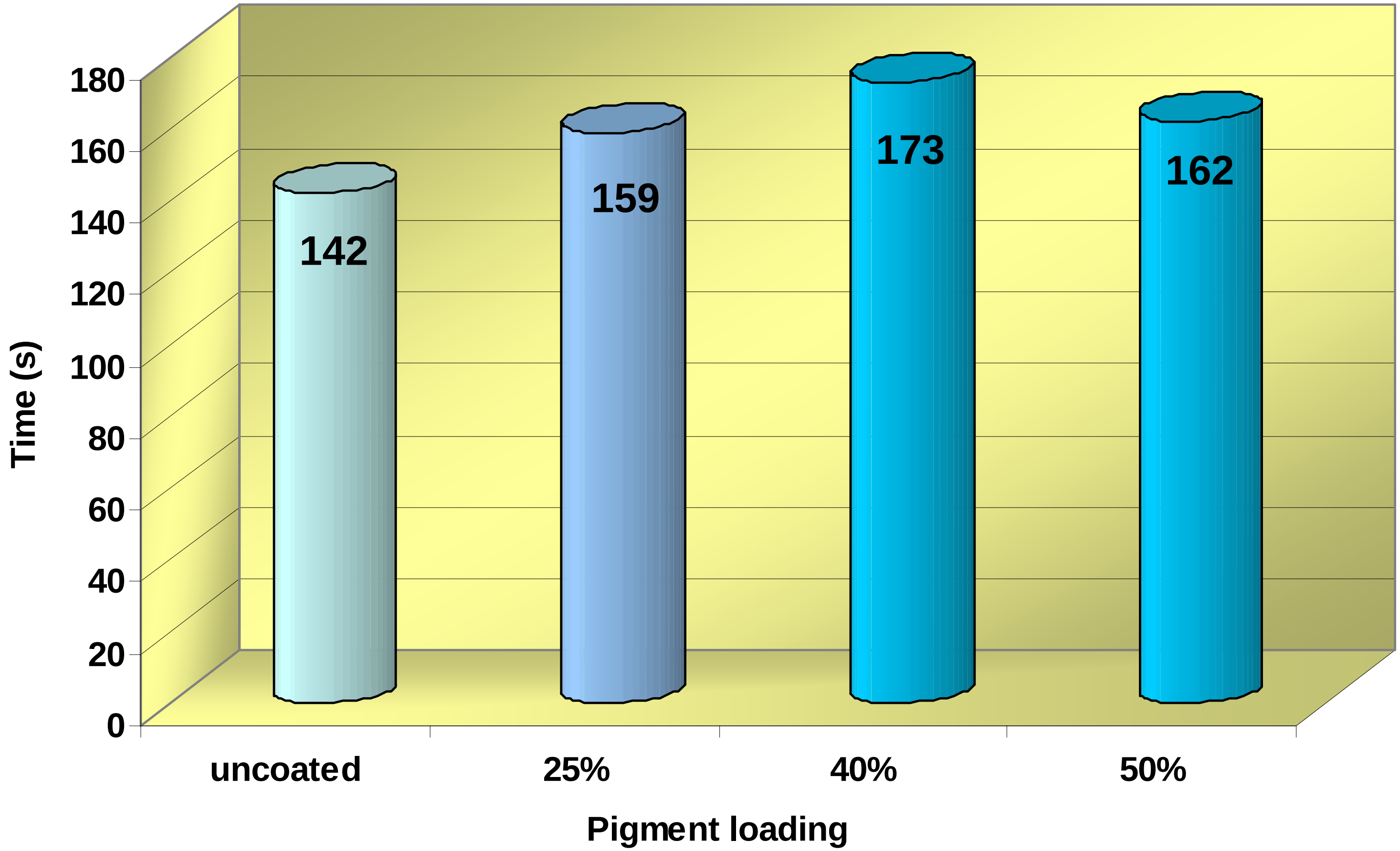
LYCOAT® Coated Tablet Disintegration

Influence of Pigment loading

Coating formulation composition			
	Pigment loading		
	25 %	**40 %**	**50 %**
Lycoat®RS 780	**136.5 g**	**136.5 g**	**136.5 g**
Glyceryl monostearate	**12.5 g**	**12.5 g**	**12.5 g**
Tween 80	**1 g**	**1 g**	**1 g**
Titanium dioxide	**48 g**	**96 g**	**144 g**
Lake	**2 g**	**4 g**	**6 g**
Water	**800 g**	**800 g**	**800 g**
Total	**1000 g**	**1050 g**	**1100 g**

LYCOAT® Coated Tablet Disintegration

Influence of Pigment loading



Hydrophobic pigments have negligible influence on coated tablet disintegration

LYCOAT® offers high flexibility to process as well as formulation parameters

LYCOAT® Regulatory Status

Product	EP	USP	JP
Pea starch	ok[1]	-	-
Modified starch	Draft [2,3]	ok [3]	-
Pregelatinized modified starch	-	ok [3]	-

[1] Already published in Pharmeuropa (January 2007)
Final monograph due in June 2008 (Addendum 6.3 of EP)

[2] Under discussion at the European Pharmacopoeia

[3] LYCOAT® fulfils all the analytical specifications

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LYCOAT® Regulatory Status

- LYCOAT® fulfils the specified tests of modified and pregelatinized starch USP/NF monographs
- LYCOAT® fulfils all the analytical specifications of major food or pharmaceutical modified starch monographs
- LYCOAT® has food regulatory status
  - ✓ E1440 - European directive on food additives
  - ✓ 21 CFR
- In Japan, LYCOAT® is considered as a natural food ingredient
- EP regulatory status of LYCOAT™ is under progress (Chemically modified starches)

Summary - LYCOAT® in film coating

- Novel aqueous starch-based non-functional polymer
- Quickly and easily soluble/dispersible in cold water
- Excellent film stability
- Can be incorporated at high level in solution
  - Allows quicker coating and cost-savings
  - Provides high quality coating (appearance and strength)
- Available in a ready to use form – *ReadiLYCOAT®*

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www.roquettepharma.com

www.readilycoat.com