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TABLET COATING IN AN AQUEOUS SYSTEM

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ABSTRACT

We have studied about the operation technique of film coating with HPMC, Pharmacoat which is our product name, and show here some data in commercial scale using mainly aqueous system which is expected to be carried out in the near future throughout the world.

In case of aqueous system, due to its much bigger heat energy required to evaporate water as soon as it is sprayed on the surface of tablets, it is desirable to use the coating machine with higher drying efficiency, but can use an ordinary pan by careful operation.

Film coating with HPMC makes tablets have stronger surface and more beautiful appearance. Masking of original undesirable taste and color is another purpose of film coating.

In the core tablets were soft and brittle, it is recommendable to take operation like slowing down the begining revolution speed of pan and using well-dispersed spray mist for which air borne spray is easier to control it but in the big and steady commercial operation, airless spray is also applicable.

We will be happy if our data would be of some help to those people intending to do aqueous film coating.

ARTICLE

Film coating is becoming to be popular taking the place of classic sugar coated tablet to get the beautiful appearance, protective coating of fragile tablets and masking of color and bad taste. Hydroxypropylmethylcellulose, especially its lower viscosity types, corresponding to our products Pharmacoat 603, 606 and 615 are playing the important role for this purpose throughout the world.

As a material of film coating, HPMC has the following characteristics.

- Transparent, tough, flexible and non-tacky film can be made from its organic or aqueous solution.
- Stable to a wide range of biochemical and enzyme system.
- More than 30 years history of food and pharmaceutical application of HPMC based on physiological safety.
- Easily printable on it by ordinary printer.
- It can coat on deep engraved tablets even with sharp edge.

At first HPMC was developed on general pharmaceutical application such as emulsifier, protective colloid,

stabilizer, suspending agent or thickener and the application as film coating material has only 10 years history. At that time we introduced Pharmacoat first in the world and fortunately it has gained high reputation.

Film coating technique has been developed by using HPMC in mixed organic solvent base such as methylene-chloride and ethanol.

However some organic solvents have a danger of explosion when mixed with air and other solvents like chlorinated hydrocarbon is not always desirable to use by healthy reason.

Recently environmental regulations about exhausting solvents in every countries are going to be more strict throughout the world.

Some companies are adopting the complete recovery system of solvents, but generally it takes so much money to build up such apparatus and does not pay if it is not fairly big scale plant.

As the result, aqueous system has been rapidly paid attention everywhere, but on the other hand latent heat of evaporating water is about three times bigger than that of general organic solvent for example 539 Kcal/kg of water in comparison with 204 Kcal/kg of ethanol. So drying efficiency in the coating apparatus become the most important aspect in case of aqueous coating.

One way to solve this problem is to use the combined aqueous organic solvent system like ethanol and water as an intermediate step and another is to use more

efficient machine like rotary drum type coater, in which drying air is forced through the tablet bed, or to use the fluidizing column.

However, even in an ordinary pan, if the proper conditions would be chosen up, aqueous coating will be practicable as we write afterwards.

(1) Example in commercial scale operation

. Tablet

Main component:	Hydroxocobalamini Acetas 500 gamma
Size:	6.0 mm diameter, 2.8 mm thickeness
Weight:	85 mg/tab
Disintegration:	10 min 47 sec
Moisture content:	0.25 %
Hardness:	2.0 kg

. Machine

Rotary drum type coater (Hi-coater, Pan diameter 1300 mm, Freund Co., Japan)

Standard charge:	130 - 140 kg
Number of buffles:	4
Drying air speed:	35 m^3/min at outlet
Spray gun:	air borne spray x 2

. Coating solution

Pharmacoat 606	7 kg
Water	63 kg

. Coating conditions

Charge per batch: 140 kg (1,650,000 tablets)

Pan revolution:	10 rpm
Distance of gun:	30 cm to tablet bed
Spraying air pressure:	6 - 7 kg
Spraying air speed:	200 l/min/gun
Drying air temperature:	85 - 88°c
Tablet bed temperature:	43°c
Spraying solution feed:	100 - 110 ml/min x 2
Coating time:	247 min

. Coated tablet

Disintegration time:	12 min 5 sec
Coated quantities:	2.4 mg/tab (3 %)
Thickeness of coating:	0.01 mm
Moisture contents:	0.24 %
Appearance:	fairly good

(2) Aqueous coating on moisture sensitive tablet (Penicillin)

. Tablet

Commercial penicillin tablet
Size: 18 mm x 8 mm, Oblong type
Weight: 1000 mg

. Machine

Rotary drum type coater	(Hi-coater, Pan diameter 1000 mm, Freund Co., Japan)
Standard charge	50 kg
Number of buffles:	4
Spray gun:	air borne spray x 3

. Coating solution

Pharmacoat 606 . . . . . 8 parts

Water . . . . . 92 parts

. Coating conditions

Charge per batch:	50 kg
Pan revolution:	10 rpm
Spraying air speed:	190 l/min/gun
Drying air temperature:	81°c
Tablet bed temperature:	43°c
Spraying solution feed:	50 ml/min x 3
Coating time:	90 min

. Coated tablets

Coated quantities:	24 mg/tab (2.4 %)
Thickeness of coating:	0.04 mm
Moisture contents:	original tablets 0.62 %
	coated tablets 0.65 %

. Analytical method of Penicilline

Penicilline contents of the tablet was determined by iodometrically according to Per Finholts method (Journal of Pharmaceutical Science, Vol 54, No. 3, page 387 March 1965). One penicilline tablet was dissolved in 1 % phosphate buffer with pH 6.0 (2.0 g dibasic potassium phosphate, 8.0 g monobasic potassium phosphate and sufficient distilled water to make 1000 ml) and diluted to 500 ml with the buffer. From the solution, to 2 ml samples, A and B, were pipetted into separate 100 ml universal flasks with glass stoppers. To A, 100 ml of 1 N sodium hydroxide is added. After standing for 20 minutes at room temperature, 5 ml of phthalate buffer solution, pH 4.5, 1.00 ml of 1 N hydrochloric acid, and 10.00 ml of 0.01 N iodine were added. The flask was closed and kept for 20 min.

in darkness at room temperature. Excess of iodine was titrated with 0.01 N sodium thiosulfate using 2 drops of starch mucilage as indicator. (titration a ml). To B, 5 ml of phthalate buffer solution, pH 4.5, and 10.00 ml of 0.01 N iodine were added. The flask was closed and kept for 20 min. in darkness at room temperature, and the mixture was titrated with 0.01 N sodium thiosulfate (titration B ml).

. Results of analysis

	tablet weight	titration (a ml)	titration (b ml)
original tablet	1.0100 g	4.05	9.00
coated tablet	1.0326 g	4.05	9.00

The difference between the two titration (b-a) is considered to represent the amount of iodine equivalent to the penicilline present.

(3) Masking of colored tablets

. Tablet: Placebo (chocolate shade)
Lactose 36, Cornstarch 54, Miccocrystalline cellulose 10
Food dye 0.3 (Amaranth 36 %, Tartrazine 48 %, Indigo carmine 16 %)
Pharmacoat 615 (as binder in wet granulation method)
Pharmacoat is used as 8 % solution in ethanol and water (8 : 2)
Size: 15 mm x 8.5 mm football type
Weight: 450 mg/tab
Disintegration: 7 min 30 sec

Friability: 0.11 %
Hardness: 6.4 kg

. Machine

Rotary drum type coater (Accela Cota 24", Manesty Co., U. K.)
Spray gun: air borne type x 1

. Coating solution

	A	B
Pharmacoat 606	8 parts	8 parts
PEG 6000	2.4	
Titanium oxide	4	4
Water	92	92
	106.4	104

. Coating conditions

Charge per batch: 12 kg
Pan revolution: 15 rpm
Spraying air speed: 180 l/min
Drying air temperature: 60°c
Tablet bed temperature: 42 - 45°c
Spraying solution feed: 40 ml/min
Coating time: A 145 min
B 30 min (discontinued)

. Coated tablet

To mask the dark colored tablets by one process of aqueous film coating, it seemed to be necessary to add so much quantity of Titanium oxide with PEG in coating solution.

Appearance of the tablets thus obtained was satisfactory, but without PEG coating operation

could not help discontinuing because of occuring crack on the film surface.

Coated quantities (A): 17.5 mg/tab (3.9 %)

(4) Aqueous coating by ordinary pan

In the coating operation using ordinary pan, drying air blown on the surface of tablets bed in the surface of tablets bed in the pan is liable to be blown back immediately from the surface without going into tablets bed.

So wetted tablets rolled into the tablet bed are likely to stick each other temporarilly which often cause the trouble of the blistering surface.

Tablets in the pan should be well tumbled by regulating the revolution speed of pan so as not to slip along the inner wall of pan. Setting of several well arranged buffles in the pan have close relation with the beautiful surface of tablets with even color.

It is also effective to regulate the spraying velocity so as not to overwet the surface of tablets and we recommend to use at least two spray guns with smaller nozzle diameter. Finer spraying mist and appropriate spraying on and off intervals are desirable to get the smooth surface.

If the spraying solution will be recycled to the storage tank when stopped, there will be less chance of the damaged tablets by dropping the liquid

when stop and begin to spray through the pressure feeding system during the intermittent spraying operation using ordinary pan.

We recommend to adopt the system which comprise first to push the needle to stop the solution feed in the nozzle, then one to two seconds later to stop the spraying air by the timer.

. Tablet : Placebo

Lactose	150 mg
Micro crystalline cellulose	100
Corn starch	50
Others	30
Tablet weight:	330 mg/tab
Tablet diameter:	9.5 mm
Hardness:	9 - 10 kg
Disintegration:	2 min 35 sec

. Machine

Ordinary pan (Pan diameter 1000 mm)
Standard charge: 50 kg
Number of buffles: 6
Spray guns: air borne spray x 2

. Coating solution

	A organic	B water/ethanol	C aqueous
Pharmacoat 606	8 parts	8	8
Tartrazine Al lake	0.14		
Titanium dioxide	0.35		
Soluble dye		0.04	0.04
Methylene chloride	46		

Ethanol	46		
Water		46	92

. Coating conditions

Charge per batch	50 kg	50	50
Drying air feed	11.7 m^3/min	11.7	11.7
Pan revolution	10 rpm	10	10
Liquid temperature	25°c	40	40
Liquid feed	250 ml/min x 2	90 x 2	50 x 2
Air temperature	60°c	75	75
Spraying cycle	10 sec spray	10	5
	30 sec off	20	7
Tablet temperature	35 - 38°c	40 - 45	45 - 50
Coating time	150 min	310	450
Coating quantities	10 mg/tab	10	10

Every three operations (A, B, C) have been done well without difficulty and coated tablets were satisfactory.

(5) Airless spray in film coating

Most of our studies about aqueous coating have been done by using air borne spray satisfactorily.

We feel airless spray is more sensitive to viscosity change of spraying liquid, although it is more efficient in big scale pan without blowing back like air borne spray.

So we have studied it by using Nordson spray.

. Tablet: Placebo, Lactose and Cornstarch

9 mm in diameter, 260 mg/tab
Hardness: 7 kg

· Machine

Ordinary pan (Pan diameter 930 mm)
Standard charge: 50 kg
Number of buffles: 4
Drying air: 60°c, 5 m^3/min
Spray gun: Nordson type airless spray x 2

. Coating solution

	A	B	C
Pharmacoat 606	8 parts	8	8
Water	46	15	
Ethanol	46	85	46
Methylene chloride			46
Pigment	0.2	0.2	2

. Coating conditions

Charge per batch: 50 kg
Pan revolution: 30 min . . . . 8 rpm
30 min . . . . 15 rpm

	A	B	C
Nozzle diameter	0.33 mm	0.28	0.28
Pressure	50 kg/sq, cm	45	50
Liquid feed	220 ml/min	280	220
Spraying cycle	8 sec spray	10	10
	22 sec spray	20	20
Tablet temperature	40°c	35	33
Coating quantities	2.7 %	2.7	3.5
Coating time	210 min	180	200

In this experiment, we have experienced sometimes the blockage of nozzles, probably due to the

discontinuous spraying. So, tablets obtained were not so beautiful this time, but probably it will be improved in future study.

(6) Aqueous coating in fluidizing system

. Tablets
Placebo mainly composed of lactose-cornstarch 9 mm diameter, 300 mg/tab., 6 - 7 kg hardness

. Machine
Wurster with 12 inches diameter

. Coating solution

Pharmacoat 606	8	parts
Sunset Yellow FCF	0.04	"
Water	92	"

. Coating conditions

Charge per batch:	15 kg
Temperature of air for fluidizing:	70°c
Spraying liquid feed:	70 ml/min
Temperature of coating solution:	20°c
Temperature of exhausting air:	40°c
Spraying air pressure:	4 kg/cm^2
Coating solution consumption:	5.6 kg
Pharmacoat consumption:	450 g (3 %)
Coating time:	65 min

Aqueous coating can be done in a fluidizing system, but the color of the tablets were not so even as those obtained in other systems because the distance between the tablets and the spray nozzle in the column was not constant always.

Blending motion of tablets was seemed to be not so perfect in this system too, although this is the most efficient system in productivity.