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TABLET COATING METHODS FOR VERY SMALL BATCHES AND THEIR SUITABILITY FOR SCALING-UP

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ABSTRACT

Three different laboratory-scale coating devices* were tested for their performance in terms of coating very small batches of solid dosage forms. The need for this study arose from a new film-forming material for colon-targeting which is available only in very small amounts. Particular attention should be paid to the subsequently planned scaling-up procedures. The following properties should be achieved: Homogeneous and smooth surfaces, as well as an overall equal film thickness obtained under controlled spraying rates of the coating solution, and determined flow-rates of the drying air. The obtained results show that all three units are principally suitable. The Hüttlin HKC provides a unique small, variable working segment by subdividing the spherical coating chamber by installing two vertical partition walls. In such reduced coating segments very similar coating conditions, and practically similar material movements were observed, in spite of reducing the batch size as far as possible.

* Glatt Lab-Coater
Uni-Glatt with Wurster equipment
Hüttlin Kugelcoater HKC 5

OBJECTIVES

The methods of film-coating using the processing units of today's practice have been investigated almost completely concerning their applicability, economy and efficiency.

In our case, however, the objective was to find out, which of the current methods is most suitable to coat smallest experimental batches, keeping in mind a close connection to the problems of the practically following scaling-up. In other words, the conditions of these small batches should not be too far from those of the production batches.

The background of this problem was the necessity to evaluate new types of film forming polymers for colon-targeting. These new polymers must be synthesized at high expense, and therefore at the time of development they are only available in very small amounts.

In addition to the pharmaceutical required qualities of the coating layers, the losses during spraying the coating solutions, resp. the utilisation of these spraying solutions were further important topics. In small experimental batches, particularly in small fluidized beds, the beds are sometimes so voluminous, that considerable amounts of the coating solution will be sprayed into void.

Our experiments therefore refer mainly to those specific topics. For more extensive questions or problems in certain cases they may give only guiding hints.

Anybody who ever was confronted with scaling-down and scaling-up in coating, knows the serious problems of the movement of cores and of the change in the friction between the cores. In reducing the batch size to a minimum, the mass forces, and likewise the gravitation forces, are decreased so far, that the cores tend to stick together. On the other hand, if in larger batch sizes the level of the material layers exceeds a certain thickness or height, the friability is unacceptably increased. Therefore the material flow in a coating device must be more gliding, and only to a certain degree whirling or spouting.

Therefore it was the aim to find a very small coating device, in which a smooth homogeneous gliding movement could be adjusted, and in which the conditions and influences can be approximated as close as possible to the production size batches.

REQUIREMENTS AND SELECTION OF THE LABORATORY-SCALE COATING UNITS

Mainly three aspects must be principally considered to obtain homogeneous coated solid dosage forms:

- At any time all cores must be moved to prevent sticking together and they must flow homogeneously. In the following this fact is described as "**material movement**" in the corresponding coating device.
- The cores must be guided into the preferred coating zone, this is called "**guidance of material**".
- The coating layers must dry rather fast, yielding smooth and uniform surfaces ("**Drying**").

The requirements to reach those difficult and problematic aims could not be achieved by means of conventional coating pans. Therefore the following coating units were chosen to approach our objectives, and to try the optimization of coating in smallest experimental batches:

- Perforated, air-ventilated horizontal rotating drums;
  (Glatt Lab-Coater *)
- Air-fluidized or air-suspension coaters;
  (Uni-Glatt with Wurster equipment *)
- Spherical, soft air-fluidized coater.
  (Hüttlin Kugelcoater HKC 5 **)

DESCRIPTION OF THE USED COATING UNITS

Glatt Lab-Coater GC-300

The Lab-Coater, as this unit is called in the following, is a device consisting in a horizontal rotating drum, with a completely perforated wall. The drying air is

* Glatt GmbH, D-79589 Binzen, Germany

** Hüttlin Coating-Technik GmbH, D-79585 Steinen, Germany forced through the perforated wall and through the entire material to be coated. The air therefore not only touches the surface of the material, it flows through almost all of the interspaces between the cores. In this way the surfaces and the drying effect are considerably improved. As the mixing effect in horizontal drums is not optimal, the material movement must be improved by installing suitable buffles, to guarantee coating layers of equal thickness. The drying air is drawn in by a fan from the top through the material, through the perforated wall of the drum, and is finally exhausted. The coating solution is also sprayed onto the cores from above by an air-pressure nozzle, performing an uni-directional flow coating process. The material movement in this coating method is mainly ruled by the drum rotations, and additionally by the buffles, while the air stream can be adjusted independently to its task of drying.

The working load or volume of this unit was 5 litres.

Uni-Glatt with a Wurster Equipment (replaceable inset)

This device, shortly called Wurster Coater, is a vertical cylinder with a perforated bottom. The stream of the drying air is directed upwards from the bottom. Amidst this bottom there is an air pressure nozzle, by which the coating solutions are sprayed upwards. As the wholes around the nozzle in the centre of the perforated bottom are larger, the air flow concentrates more along the axis of the cylinder. This arrangement helps to obtain a material movement, that flows upwards in the centre of the cylinder, expanding as soon as gravity gets predominant, and then flows downwards in the outer zone along the wall of the cylinder. To guarantee a sufficient guidance of the material, amidst the coating cylinder and right above the nozzle, a smaller guiding cylinder is installed.

This coating process is also an uni-directional method, but in this method both the material movement, as well as the drying operation are effected by the air stream. A certain disadvantage of this process is the fact, that the material movement needs more air than the drying process. Therefore the flowing rate of the air stream cannot be adjusted exactly to the drying operation and this is the reason why there is always a tendency of overdrying.

The working capacity of this unit was 2.5 litres.

Spherical Coater (Hüttlin Kugel-Coater HKC-5)

This modern coating device is characterized by a spherical coating container, with a special guided air stream through a ring-slot upwards from the bottom. Because of the geometry of the container and the special air stream, the coater shows a rather soft-gliding, homogeneous rotation movement of the toroidal shaped material bed.

The air enters the coating container at the bottom by the ring-slot around the inlet-air tube, from there it transports and guides the material upwards. The air-pressure nozzles are integrated into the ring-slot. They spray upwards parallel with the air stream, so that also an uni-directional coating process is accomplished. After a sufficient expansion, at the time the gravitation forces get stronger than the forces caused by the air stream, the material is gliding downwards along the rounded walls of the container resp. coating chamber. Subsequently the upward material movement starts again.

The ballistic range of the material movement curve, during the expansion or the transfer of the upward to the downward flow, can be optimized by an suitable shaped umbrella-like deflection (Fig.1). This deflection allows not only a better material movement, it also supports the separation of the outlet-air from the coating material by a cyclone-like effect and herewith considerably relieves the outlet filter system. The main advantage of this construction is the resulting homogeneous, soft-gliding revolving material movements, contrary to the more heterogeneous spouting and whirling fluidized beds.

The average working capacity of this unit was 5 litres.

For performing smallest batches this coating unit can be subdivided by the installation of two vertical partition walls into differently sized segments of the spherical coating container (Fig.2). This leads to material movements, relatively similar to those in non-subdivided or larger spherical coaters. The size of such a working segment is adjustable in a way, that only one of the four nozzles is used. The other nozzles, and the residual coating container volume are set out of operation. In the Hüttlin Kugel-Coater HKC-5 the drying operation is effected mainly by the inlet air, while the material movement is ruled by the co-operation of inlet-air with the geometry of the spherical container and of the deflection.

In Table 1 the fundamental operating forces to perform *material movement*, *guidance of material* and *drying* are summarized.

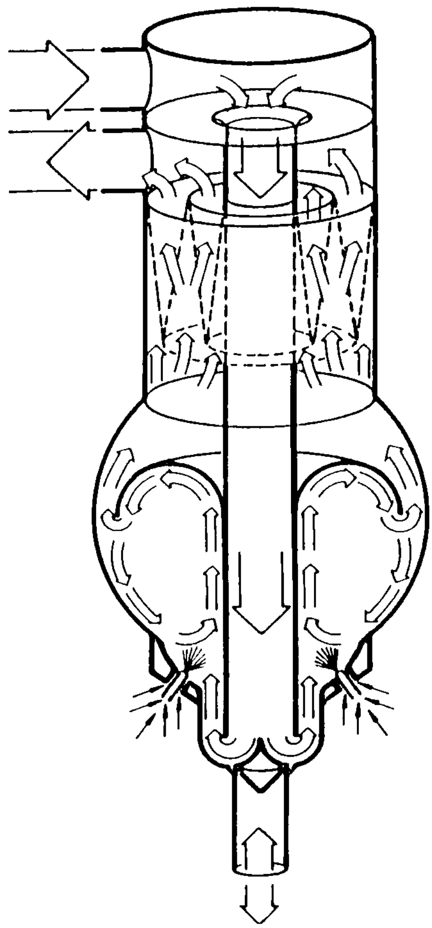

Fig. 1: Hüttlin Kugel-Coater HKC-5 with an umbrella-like deflection.

MATERIALS

The experiments were performed at room temperature. The spraying-rate of the coating solution and the flow-rate of the inlet-air were adjusted to reach minimal mechanical stress on the cores and the shortest possible operating time.

Cores and Coating Solutions

For the experiments, one batch of core material and two different coating solutions were used.

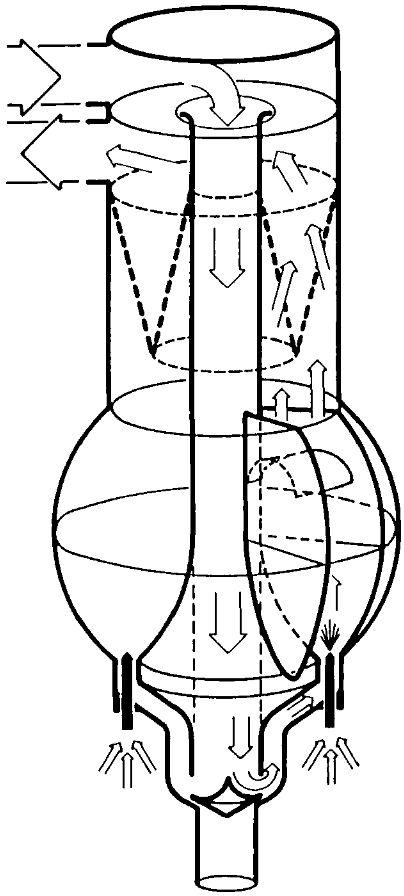

Fig. 2: Hüttlin Kugel-Coater HKC-5 subdivided in a small coating segment by means of two vertical partition walls and an umbrella-like defection.

Cores

The placebo cores used are based on a lactose-starch composition. They are scored, have a diameter of 6 mm, 2 mm of height, 84 mg gross weight and a surface area of 95 mm^2.

Coating Solutions

Solutions of two different film forming materials were tested.

TABLE 1

Methods	Material Movement	Guidance of Material	Drying
Uni-Glatt	Air Stream	Air Stream	Air Stream
Hüttlin HKC-5	Geometry of the Coating Container, Gravity	Air Stream	Air Stream
Lab-Coater	Drum Rotation, Gravity, Buffles	Drum Rotation, Buffles	Air Stream

a) Ethylcellulose N7 (Hercules Inc., Wilmington DE 19894 USA), as a non-ionic diffusion coat.

b) Eudragit L 100-55 (Röhm Pharma GmbH, D-64293 Darmstadt, Germany), as an anionic gastric resistant coat, soluble in the juices of the small intestine.

Ethylcellulose is the less problematic material for our experiments, while Eudragit was expected to be a type of a technological more problematic coating material, because of its adhesiveness.

Coating solution I:	Ethylcellulose	5.00 parts
	Diethylphthalate	0.75 parts
	Methanol	94.25 parts

Drying time:	5 min;		
Aftertreatment:	4 hours at 60°C in a drying chamber.		
Coating solution II:	Eudragit L 100-55	5.00	parts
	Diethylphthalate	0.50	parts
	Talcum	3.00	parts
	Methanol	92.50	parts
Drying time:	5 min;		
Aftertreatment:	24 hours at 40°C in a drying chamber.		

The additions of softeners and antiadhesives were optimized according to our experiences. Both coating solutions were coloured with chlorophyll to facilitate the optical evaluation of the coating layers.

Adjusted Parameters

TABLE 2

Method	Film-forming Material	Batch Size (g)	Spraying Rate (ml/min)	Flow Rate of the Inlet Air (m^3/h)	Drum Rotation (RPM)
Uni-Glatt	EC	150	4.9	210	-
	Eudragit	150	2.7	210	-
Hüttlin HKC-5	EC	100	3.5	60	-
	Eudragit	100	2.5	60	-
Lab-Coater	EC	150	16.0	65	18
	Eudragit	150	16.0	65	18
Larger Batch	EC	800	21.0	110	18

EC = Ethylcellulose (Coating Solution I)

Eudragit = Eudragit L 100-55 (Coating Solution II)

Air pressure at the nozzles = 1 bar

TABLE 3

Methods	Film-forming Material	F/100 (g/100cm^2)	Time of Procedure (min)	Thickness of the Film (µm)	S rel	Colour
Uni-Glatt	EC	11.4	80	30.3	16.8	uniform
	Eudragit	11.4	140	42.4	15.1	uniform
Hüttlin HKC 5	EC	5.7	45	35.5	9.9	uniform
	Eudragit	5.7	55	49.1	8.1	uniform
Lab-Coater	EC	11.4	25	29.4	16.0	uniform
	Eudragit	11.4	25	32.3	13.1	uniform
Larger Batch	EC	5.7	55	21.5	12.0	uniform

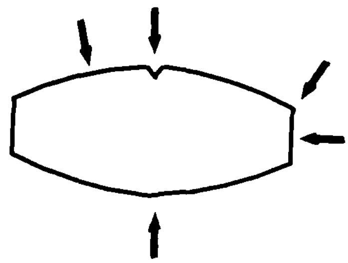

Fig.3: Measure points of the film's thickness

RESULTS

In the following Table 3 all the results of our experiments are summarized. In order to facilitate the comparison of the different batch sizes, the used amounts of film-forming materials were calculated to 100 cm^2 core surface. In this context, it means:

- F/100 = the used amount of film-forming material in grams per 100 cm^2 surface, which is required to guarantee sufficient resistance against gastric juice, resp. to prevent disintegration within the stomach.
- Time of the procedure = coating, drying, and an aftertreatment in min.
- Thickness of the film = the thickness of the film coat after drying and aftertreatment was determined microscopically at a 160-fold magnification*. Fig.3 shows the points measured for each tablet.
- s_{rel} = the relative standard deviation of the film's thickness.

In Table 4 and Fig. 3 calculated values are summarized, which refer to an application of a 50 µm thick dry film-coat per core.

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* Performed at the Fraunhofer-Institut für Physikalische Meßtechnik, D-79110 Freiburg, Germany
Microscope by Zeiss, D-73447 Oberkochen, Germany

TABLE 4

Calculated Comparison
for 50 μm thick dry film coats on 100 cm^2 surface

Methods	Film-forming Material	F/100 *	Time of Procedure*	Amount of Air*
Uni-Glatt	EC	18.8	88	308
	Eudragit	13.4	111	389
Hüttlin HKC-5	EC	8.0	61	61
	Eudragit	5.8	56	56
Lab-Coater	EC	19.4	28	30
	Eudragit	17.6	26	28
Larger Batch	EC	13.3	20	37

- F/100* = the used amount of film-forming material in grams per 100 cm^2 surface, which is required to applicate a 50 μm thick film-coat per core.
- Time of the procedure* = theoretically required time in minutes for coating, drying and an aftertreatment of a 50 μm thick film-coat.
- Amount of drying air* = applied air for the above mentioned use in m^3.

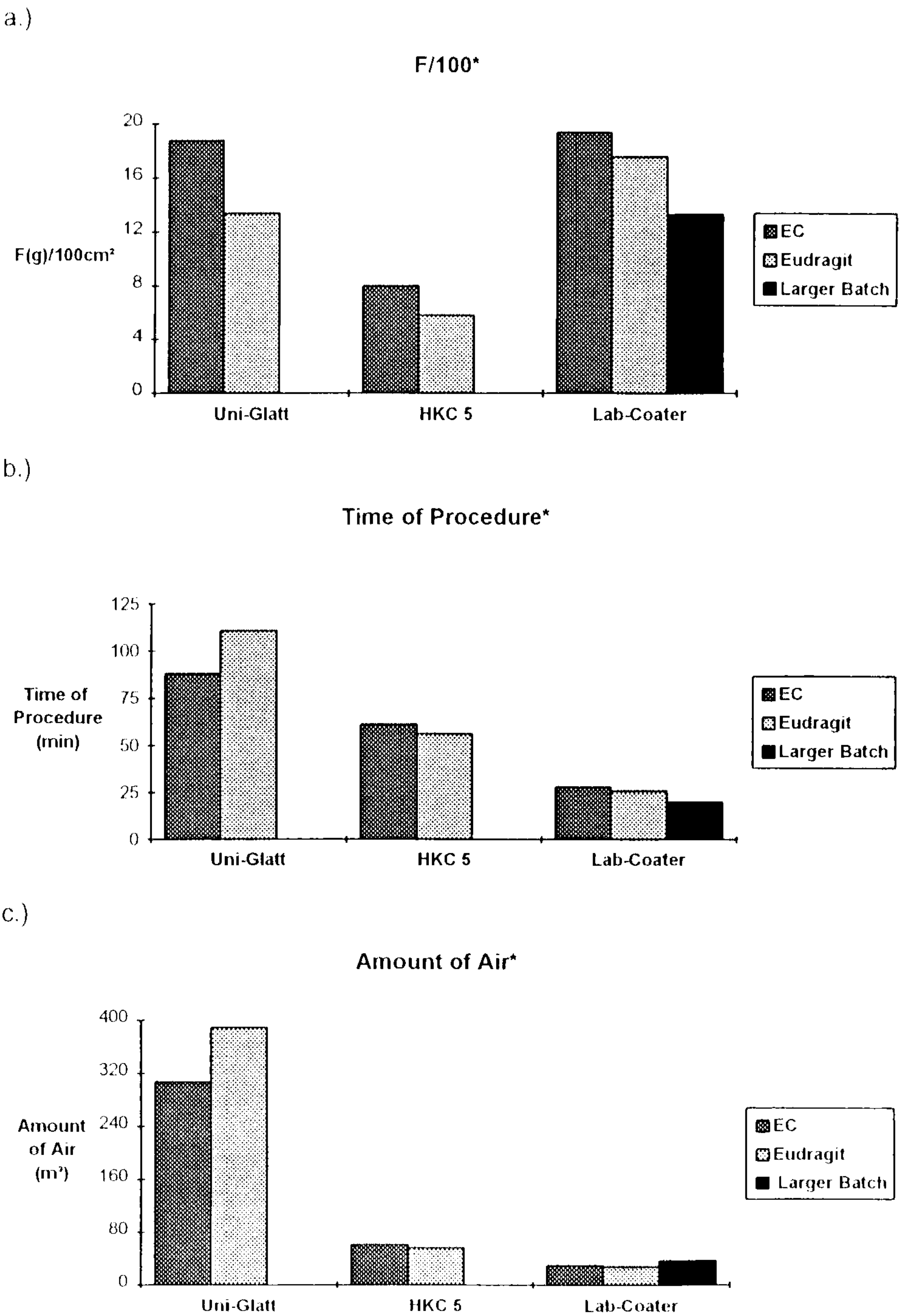

Fig. 4: Column diagrams to explain Table 4

DISCUSSION

Glatt Lab-Coater

The Lab-Coater is distinguished by the lowest consumption of process air and by the shortest time of procedure of the three tested methods. The utilisation of the coating solution however was less satisfactory, particularly with very small batches, resp. not optimally filled drums. Beside of this the coating layers were not equally thick. That means, the layers are thinner at edges or borders, and thicker at curvatures. With larger batches the utilisation of the coating solutions becomes better and more economic.
The device is quite silent, also when the fan is working at highest capacity.

Uni-Glatt Wurster Coater

This device as expected, has the highest consumption of process air because both, the material movement as well as the drying process are operated by the air stream. Comparing the results with those of the Kugel-Coater, it is evident that the majority of the process air is required for operating the material movement. The cores coated by this method were practically satisfactory, except for the batches coated with the coating solution II. Their layers are not even or smooth enough. In the fluidized-bed, apparently by adhering and tearing off, some break marks are formed on the coatings. The utilisation of the coating solutions on the other hand was better than in the Lab-Coater.
This unit was relatively noisy, but this disadvantage could be easily avoided by sound absorption or using an extern fan.

Hüttlin Kugel Coater HKC-5

Compared with the Uni-Glatt Wurster Coater, the consumption of process air in this device is considerably reduced. In addition the spherical coater needs the lowest amount of film-forming materials. The quality of the coated cores corresponds well with our requirements. Although using the coating solution II, it was observed that some surfaces were not smooth enough. Remarkable is the fact, that with this method the curvatures as well as the edges of the cores are coated equally thick. In the segmented unit the discharging is not as simple as in the not segmented ones. The noise-level is very low due to the extern and well sound-isolated fan.

CONCLUSION

All the tested methods are principally suitable to coat solid cores with polymeric films in very small experimental batches. As the summarizing survey (Table 4) clearly demonstrates, the amount of process air depends on the task they have to fulfill. According to the extensive task of moving and drying the material, the Uni-Glatt Wurster Coater has the highest, the Hüttlin Kugel-Coater a smaller, and the Lab-Coater the smallest relative air consumption.

The relative utilisation of the film-forming material was better in the segmented spherical coater, because in this arrangement, the nozzle is almost completely, resp. "interspaceless" covered by the moving bed of coating material. In the coating devices, which need more air, on one hand quite a portion of the coating solution is spray-dried, and on the other hand considerable parts are sprayed into void, particularly if the batches are minimized. Thus the results of improved yields in the Lab-Coater with larger batches are not surprising. Since more of the coating solution is impinging the material, the larger the batches and the smaller the interspaces are.

For our problems and their solution the economical aspects, like time of procedure or required amounts of process air, are of secondary importance. According to our requirements of minimizing experimental batches the spherical coater was most suitable as minimizing was realized under optimal preconditions.