1|2011

INNOVATIV

Start of construction

Reviews Compact Unit

The new advisory board

BÖHLE

Dear Readers,

2010 was a very difficult year for Bohle, as it was for the entire industry. At the beginning of the year we had to institute reduced working hours. We were not sure whether we would be able to maintain current work force or if we would have to make lay-offs. Together with our staff the decision was made to not take the easy road and lay-off employees, but rather to cultivate the experience and dedication of our employees developed over many years. We focused on our innovative potential and the expected economic upswing.

Today we can say we made the right decision. We currently have an order backlog of around eight months and our production will increase by 40% over the previous year. This positive trend is in large part due to our coaters. The properties of the coaters are astounding in many respects: outstanding uniformity, short process times, low spray losses, high spray rates and last but not least a significantly reduced cleaning time.

On behalf of the Bohle team I would like to express my sincere thanks for your support and trust.

You can continue to count on our innovation and reliability in the future!

Best regards from Ennigerloh,
Lorenz Bohle

Bohle expands location for handling machines

Start of construction in Sassenberg

L.B. Bohle creates new capacities for expansion. This year, the company enlarges its production hall and builds an office complex for engineers and technicians in order to make the Sassenberg location a center of excellence for handling machines. For Bohle handling means IBC material handling systems (comprising a large variety of blending-, milling and sieving as well as container lifting equipment).

In April, CEO Lorenz Bohle turned the first sod together with Josef Uphoff, mayor of Sassenberg.

"The previous production area of approx. 1,300 m² will now be expanded by approx. 1,600 m² to more than twice its previous size," said Lorenz Bohle. Additionally, a building of approx. 300 m² for engineers and technicians will be built to provide workspaces for 10 to 12 persons.

Construction works are envisaged to last approx. six months. The entire production of Bohle handling machines will then be located in Sassenberg.

"The investment will ensure enhancement and consolidation of the Sassenberg location. Starting from October 2011, the entire Bohle handling range will be produced in Sassenberg and exported throughout the world," said Lorenz Bohle on the occasion of the construction start.

Caption: Armin Bohle, Head of Technical Operation at L.B. Bohle, Robert Stauvermann, COO at L.B. Bohle, Richard Pawlowski, Architect, Josef Uphoff, Mayor of Sassenberg, Lorenz Bohle and Martin Hagemeier, Contractor (from the left) turned the first sod for the Sassenberg extension in April.

Premiere for the KOCO®

L.B. Bohle at the Interpack

From 12 to 18 May 2011 L.B. Bohle will be presenting a broad range of innovations and developments at the Interpack in Düsseldorf. One of the highlights to be presented on the 230 m² trade fair booth, is the new Bohle Conti Granulator BCG, a synchronous, twin-screw extruder with a downstream dryer. The granulator will be presented along with a tablet press and the semi-continuous KOCO® coater. The Bohle product range on show for the attendees will also include the Film Coater BFC 5, the new Fluid Bed System BFS 3, the Bohle Turbo Sieve BTS, the Containment System BCK 200, the particle analyzer BPA and the control unit KA. Moreover, the attendees will also be informed about the new Compact Unit - a single container granulator and fluid bed system, completed with a sieving step in between.

The L.B. Bohle Maschinen + Verfahren GmbH booth will be located in Hall 3, Booth 3F32.

The new advisory board

Composition, role and vision

Since early March 2011 L.B. Bohle Maschinen und Verfahren GmbH has a new corporate body – the advisory board. It is similar to the supervisory board of a stock corporation: it shall act as a control committee to monitor the business activities of the management and introduce suggestions for the basic strategic orientation.
Lorenz Bohle is the chairman of the new adivsory board. Further members are Dr. Gerd Birrenbach, a pharmacist and former entrepreneur, resident in Switzerland, and Hans Dieter Oesterwinter, lawyer, resident in Beckum.

"I intend to assign the day-to-day business to a new general manager soon and dedicate myself more to the position in the advisory board," stated Lorenz Bohle. I would like to prepare for and implement this transfer while I still feel physically well to prevent an emergency solution becoming necessary in the future. The founder, however, will continue to be involved in the development of innovative solutions for the pharmaceutical industry; he will also be happy to provide advice whenever his experience and competence are needed.

Lorenz Bohle, Dr. Gerd Birrenbach and Hans Dieter Oesterwinter (from the left).

Strong growth stimuli from the USA

L.B. Bohle at the Interphex

The economic upturn in the American pharmaceutical market is clearly noticeable. From 29 to 31 March the Interphex 2011 took place in the Jacob K. Javits Convention Center in New York. Over 650 exhibitors presented their new products and developments for the pharmaceutical industry. The American L.B. Bohle LLC subsidiary from Warminster, Pennsylvania, presented the new BFS 3 Fluid Bed System designed for lab applications at the trade fair. The Bohle team also introduced the innovative BCG granulator and the KOCO® coater, capable of continuous production, to the attendees.
Martin Hack, Vice President and General Manager of L.B. Bohle LLC was pleased with the outcome of the fair: "The Interphex attendees are a clear sign of the upturn in the economy. We had many attendees with active projects and high interest in our products. We look forward to working closely with them in the coming months to develop and provide solutions for their processing needs."

The L.B. Bohle LLC team

Premium quality for customers in the pharmaceutical industry

Interview with Andreas Altmeyer regarding Bohle`s semi-continuous film coater KOCO®

Mr. Altmeyer, Bohle initially focused on continuous processing. Today you are presenting the KOCO® coater as a semi-continuous production machine. Why?

For some years now we have been dealing with the issue of continuous pharmaceutical processing. We have already introduced a number of fully continuous granulation systems. In this segment we currently have our model BCG, a continuous twin-screw extruder with a downstream contact dryer. However, trials have revealed that a semi-continuous system is more adapted for coating applications.

What are the advantages of the semi-continuous coating process?

First and foremost the quality of the coated products. We initially used a coater with a relatively long coating pan however, in continuous production the results did not meet our expectations. We therefore shortened the pan. Furthermore, the coater is filled and discharged automatically. Semi-continuous coating therefore plays an important part for our continuous production line. This is how the excellent coating uniformity observed in batch operation can also be achieved in continuous processing.

Where do you see additional potential?

The extruder granulation allows processing of substances that require high shearing effects for granulation to be granulated which is not always possible in fluid bed granulation or in high-speed blenders.

Which other systems are currently available and what makes your solution unique?

At present, the continuous production revolution has not yet taken hold on the market. Although some of the manufacturers offer various solutions, the great revolution has not taken place yet.

What is the future production design in the pharmaceutical industry and how is Bohle prepared for future challenges?

Due to existing registrations, batch production will certainly remain a priority in the near future. But continuous production will gain market share as a result of the requirements and recommendation of the authorities (FDA). For example, small batches of 100 kg as well as seven-day production will be possible, without the need for time-consuming up-scaling.

The tendency is clearly towards continuous production. This type of production features enormous advantages. What's more, it saves a significant amount of time and money. We will continue to focus in this direction and use our developments to implement new projects in close cooperation with our customers.

Andreas Altmeyer

More solid despite less liquid

Prof. Klaus-Jürgen Steffens of Bonn University has tested the new extruder

Professor, you have already carried out a number of tests with the BCG (Bohle Conti Granulator). Please explain to us the basic operation method of the system.

The core of the system is a newly designed GMP-compliant twin-screw extruder, which is supplied by a continuous mass-controlled powder dosing unit and a continuous liquid dosing unit. The finished granulate falls directly into the continuous rotating vacuum contact dryer, without requiring transport. The dryer operates with an innovative blending and dispersing unit to reliably prevent the wet granulate caking to any surface. The final granulate size is then adjusted using the well known Bohle BTS Turbo Sieve.

Which tests have you carried out with the system so far?

We have carried out tests with substances that are difficult to granulate, such as Paracetamol and Ibuprofen at a high dosage of 75% active concentration.

We have made comparisons with high-shear granulation, tested various binding agents as well as the impact of different screw configurations. Our targets were always the properties of the tablets produced from the granulates, such as strength (format-independent as "tensile strength"), disintegration and substance release.

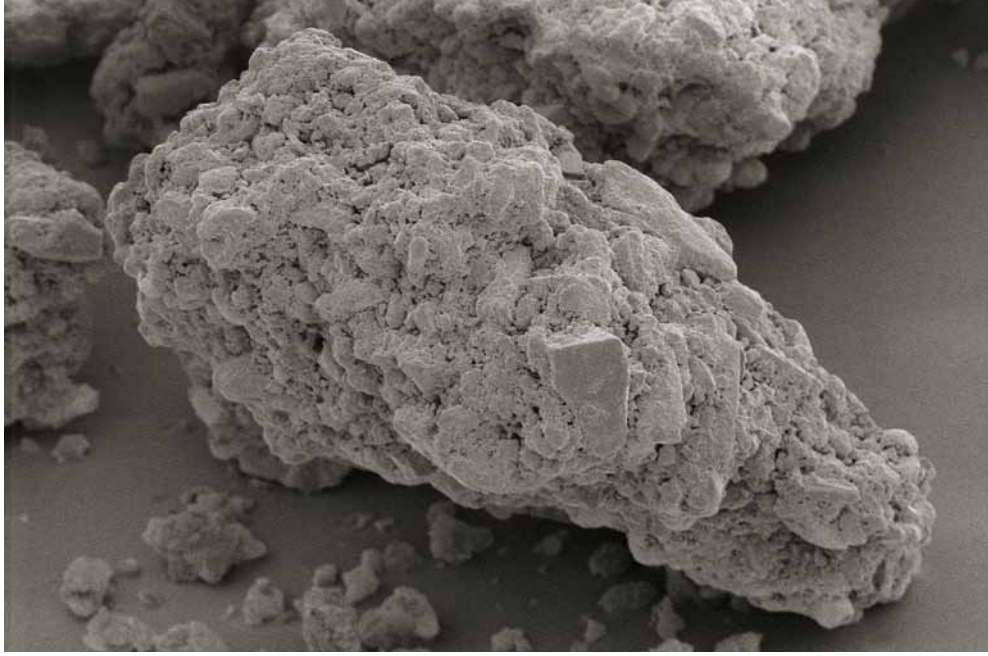
Can you tell us about the initial results?

Out of the many tests, a few results stand out.

With regard to the tablet strength of Ibuprofen tablets (Fig. 1) which were granulated with PVP as the binding agent, two throughput rates in the extruder were compared to high-shear granulation (VMA). The results show the clear superiority of extrusion thanks to a better binding agent distribution.

The same applies to Paracetamol (Fig. 2), where a higher throughput in the extruder resulted in even higher strength values.

We carried out a further test (Fig. 3) on the tablet strength of a Paracetamol formulation granulated with HPMC 4000 as the binding agent instead of PVP. Surprisingly, virtually the same strengths were achieved as with PVP, although in extrusion the binding agent is normally a dry powder



mixture which must first be dissolved in the extruder. We actually expected significant problems with the tablet strength, as HPMC 4000 has a much lower dissolution rate in water than PVP. Specimens A to F were granulated with different screw configurations and different amounts of liquid. Only specimen E showed a significant capping tendency of the tablets. This specimen was produced with the least amount of liquid. Despite having virtually the same strengths, in the range of 2.5 MPa, the tablets from the other specimens revealed varying disintegration times, ranging from 133 sec (specimen F) to 390 sec (specimen A). Scanning electron microscope images (Fig. 4 and 5) showed the typical structure of the granulates which does not differ from that of other granulating processes.

What are the benefits of the Bohle system in your opinion?

Compared to other extruders the BCG extruder is characterized by the typical Bohle GMP design. The monoblock design features no gaps or connections which make it easy to install and clean. The "real" torque measurement – separately on each screw – is particularly noteworthy, allowing outstanding control of the process. This is another step forward in implementing Process Analytical Technology. Last but not least, the new continuous rotating vacuum dryer of the BCG system features significant advantages vs. other systems.

What do you make of other solutions available on the market? For instance, common features / differences compared to Bohle solutions?

So far, a number of tests for continuous wet granulation have been carried out, such as the continuous fluid bed system or the semi-continuous process utilizing very small pulsed batches. They have not taken hold on the market for wet granulates because of their low shearing force and complicated, failure-prone transport systems. Extrusion, however, is a promising solution. During granulation the shearing forces can be significantly better tuned to the product properties than in any other process.

What are the future trends in pharmaceutical production?

The pharmaceutical market will be dominated by dualism. On the one hand, we will have innovative and expensive pharmaceuticals which will be produced in relatively small batches and for which the production costs will be less important. In contrast, we have been observing global cost pressure and a high concentration of manufacturers on the constantly growing generic drug market. This will result in a greater market share for cost-cutting continuous production systems. It is therefore vital that the control and machine technology of the systems are state-of-the-art to ensure elegant and enhanced failure-free production.

Prof. Klaus-Jürgen Steffens of Bonn University

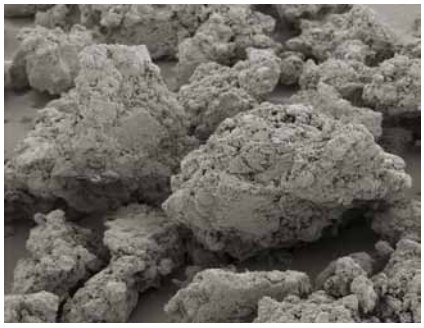
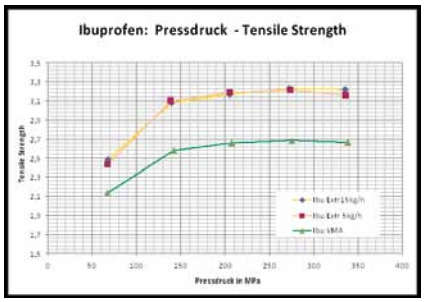
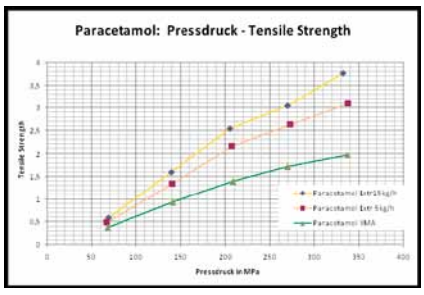
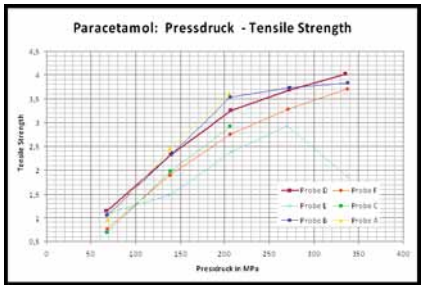


Fig. 4 and 5

Fig. 1, 2 and 3







"Flexibility is decisive"

Interview with Dr. Michael Beyer

Wiewelhove GmbH, a contract manufacturer for the pharmaceutical industry based in Ibbenbüren, has the first Compact Unit in operation. "Innovativ" interviewed Dr. Michael Beyer, Director of Production and Engineering at Wiewelhove, on the application range and benefits of the compact unit.

Dr. Beyer, please explain to us which applications you use the new system for.

Until recently we mainly used tray drying for new projects including drying processes as the existing fluid bed system was operating at near full capacity. However, we wanted to extend our offer for contract manufacturing and increase capacity. In general, we consider drying in a fluid bed system as the better alternative, i.e. the "state-of-the-art" drying process.

That is why we requested quotes for this type of system from different suppliers of pharmaceutical process equipment. From June 2009, we carefully reviewed all offers submitted.

Which features were particularly important to you?

For us as a contract manufacturer, it was decisive that the system features comprehensive functionality and flexibility for different product applications. In addition to fluidized bed drying the system should be able to pelletize products. Moreover, the mechanical engineers had to take the available floor space as well as the limited ceiling height of five meters into account. Technical equipment such as air conditioning, exhaust air filters and fans had to be installed in the technical area above the ceiling. A further decisive criterion was that the process room HVAC unit would not have to be modified for the project. Our goal was to perfectly integrate the new system into the existing environment.

What does this mean in concrete terms?

The granulator and dryer had to be positioned compactly next to each other to ensure short product transport distance.

We also needed the new system to be 12 bar shock pressure resistant.

Did you plan to manufacture a specific product with the new system?
No, there were no particular specifications. For Wiewelhove – as a contract manufacturer – it is of paramount importance that a broad range of products can be manufactured with our systems allowing us to flexibly respond to our customers' requirements.

Please briefly describe the benefits of the new Bohle system.
The name says it all: the outstanding advantage of the compact unit is the very compact, low footprint design. It was easy to integrate into our production premises and there was no need for expensive modifications. The short product transfer distance between the blender and fluid bed system are a great benefit, too. The tangential spray process of the fluid bed system is state-of-the-art and has significant advantages compared to top spraying. Tangential spraying also allows the pelletizing and coating of particles all in the same bowl.

Were there any further benefits?
The cleaning time of the system is a major benefit. Unprofitable down-time has been reduced to a minimum thanks to the one-level design and the system can be back up and running again for production in no time. The mobile and versatile dry sieve (BTS 200) of the system is a further positive aspect.

Are these the arguments that convinced you to opt for the Bohle offer?
Yes, taking all these advantages into account we decided in favour of Bohle. Implementing the project was made much easier thanks to the excellent and extensive communication between our companies.

Finally, can you describe your first experiences with the new system?
We installed the system in our production facilities in 2010. After completing all qualification protocols, extensive tests with the compact unit were carried out. These tests revealed excellent results in the final product quality. Thanks to the good cooperation with Bohle, we were able to quickly implement minor adjustments – these are always necessary and to be expected when commissioning new systems of this size. The logical design of the system made it easy for our staff to understand and learn how to operate it. The system has the same operating concept as the two Bohle film coaters installed at Wiewelhove. The basic features of the system were already known to our operators which made the initial training very easy.

Dr. Michael Beyer

"Cleaning times cut in half"

Interview with Dr. Thomas Koy, Production Manager at Konapharma AG, about the new compact unit

After its founding in 1989, the Pratteln-based Swiss company Konapharma initially focused on preparing dossiers for pharmaceutical customers. Since 1995, the company has also become a contract manufacturer for the pharmaceutical industry.

In 2009, the company relocated to a new, 6000 sqm facility and now employs around 100 staff and has firmly established itself on the market as a manufacturer of solid dosage forms.

"Innovativ" interviewed Dr. Thomas Koy, Production Manager, about his experience with Bohle products.

Dr. Koy, which Bohle systems do you use and how long have you been using them?

Several Bohle systems are in operation in our production hall. It all started in 2003 with the first 600 liter PM container blender, followed in recent years by a number of sieve systems, more blenders, container cleaning systems and lifting columns. Two years ago we put our first granulating line into operation, consisting of the High Shear Granulator GMA 600 and the Fluid Bed System BFS 240.

What are your experiences with these machines and systems?

Well, the results have been very positive. Easy handling of the individual units and the superior quality of the stainless steel finish are major benefits to our staff. Machine cleaning and maintenance are much easier and the time they take is significantly reduced.

You have just decided in favour of a Bohle compact unit. Which features have you specified for the new system?

First and foremost, the small footprint and the easy integration into the production environment. Easy cleaning of the new system was also very important to us.

In your opinion, what were the deciding factors for choosing a Bohle compact unit?

First of all, the optimum product yield that could be achieved with the system. Additionally we were impressed by the extremely sophisticated GMP concept. The compact unit is designed to have no corners, edges, free cables or hoses that might cause problems. This allows easy cleaning and reduces the cleaning time to a minimum. Long cleaning times result in less profit, but these times are reduced to a minimum with the Bohle systems, saving us cash every day.

Which production targets have you set for the new compact unit? Can you assess how much time is saved on cleaning?

The new system was exclusively designed for two new products with similar production processes. The experience we gained from manufacturing one of the products on an existing system greatly helped us optimize the compact system.

At the start of production the new system will operate at near 65% capacity. The capacity will increase within the year and will settle at around 80 to 90%.

Our aim is to reduce the cleaning and turnover time by 50%. We are very confident that we can achieve this goal quickly.

Dr. Thomas Koy

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E-Mail: info@lbbohle.de
Internet: www.lbbohle.de

Layout & Print: www.darpe.de