

1|2013

INNOVATIV



New building plant 3



keystone of this growth is the commercial success of the Bohle Coater – it excelled in particular with highly complex coating tasks.

Our customers told us, for example, that the coaters showed an incredibly optimized performance of uniform application for coatings with active properties. The closest comparable coaters had a deviation of 6%, while the Bohle coater achieved deviations of just 2%. This is a quantum leap in quality.

was able to cover the Handling line of business after expanding its existing production area by an impressive 120%. This additional capacity was completely filled within just one year thanks to the commercial success of the Bohle mixers. It goes to show that Bohle mixers are true market leading products.

Dear readers, I would like to take this opportunity to thank you for recognizing the achievements of the Bohle team and I wish you, also on behalf of the German staff, all the best. May God bless you.

Yours sincerely,

Ihr Lorenz Bohle

Dear readers of Bohle Innovativ,

during this difficult phase of the global economy we – including all our staff – were able to achieve a sales and profit increase of about 30%, which constitutes an overproportional success for the year 2012.

We let the figures speak for themselves! Where does this increase come from? A

If we compare our growth with the pharma industry, we can see the following: worldwide expansion of pharma business came nowhere near the success of the Bohle team! In other words, the growth Bohle experienced is also due to a decrease in sales for our competitors in the coating industry.

Another reason for this increase stems from the end of 2011: Site 2 in Sassenberg



Plant 2 – Development center for engineers and technicians



Plant 3



Production – Plant 1

Growth and investment

A leap in sales in 2012 and new buildings in 2013

With a growth rate of more than 30% and record sales of 47 million in 2012, L.B. Bohle Maschinen + Verfahren GmbH has completed the most successful year of its over thirty-year history. "The ease of handling, process reliability and high quality of our machines are highly appreciated and in demand worldwide", says managing director Lorenz B. Bohle. To meet the demand more quickly, the foundation stone for Plant 3 was laid last autumn. A total of 5 million will be invested solely in the new building in the Ennigerloh Haltenberg-Ost industrial area until its planned completion in September 2013.

Lean production as the key

In the first phase, Plant 3 with an area of 3,700 m² will be built. The production space covers 2,600 m², while the remaining area is divided into 550 m² each of workshop and office space. In the new building, company founder Lorenz B. Bohle is back-

ing "more efficient production through the gradual introduction of lean production." Sixty new jobs are being created at the Ennigerloh site. "The aim of the investment is to further increase the company's sales and to safeguard Ennigerloh as an industrial site in a sustainable way", Lorenz Bohle explained. One basis of the expansion strategy is the success of the coating machines, which will be manufactured at Plant 3 from 2013 onwards.

The company founder also expects the 2012 world premiere of the BRC 100 Dry Granulator at theACHEMA 2012 Congress to provide a further boost. It proved to be a real crowd-puller. This machine closes the last remaining gap in the granulation process. "Up to now, components from third-party suppliers have needed to be integrated in the manufacturing process for the dry granulation procedure", Mr Bohle explained. "Now we can offer the customer a solution from a single source."

The latest investment project also pursues this goal. A new "Global Technology Center" aims to meet the demand for continuous processes. In cooperation with the Universities of Dusseldorf and Graz, and together with control and measurement technology experts from Siemens, a development, test, and presentation unit is being built adjacent to the Service Center by spring 2014.

Lorenz Bohle assumes that growth in 2013 will be more modest than last year. "The goal is to increase sales to approx. 52 million. With this year's growth of around 10%, following on from more than 30% in 2012, we are again exactly on course to fulfil our 'Strategy 2016', which aims for annual growth rates of 20%", the company head added.



Bohle Coating Technology

Pharmaceutical film coating represents nowadays an important process step in the pharmaceutical industry. Derived originally from dragee pan processing, coating technology has developed continuously in the last decades. The majority of coating processes are performed for drug release modification, drug stability improvement against light or moisture and taste masking. Furthermore patient compliance issues play an important role, as swallowability improvement or a simpler identification due to a different colour.

Finally API coating is gaining more and more importance since it enables fixed dose combinations or the combination of incompatible drugs. Also different drug release characteristics can be realized by applying for example sustained release coatings in addition to immediate release coating layers. Such formulations sometimes consist of up to four coating layers, which leads to long processing times. To successfully develop and produce such formulations coating uniformity is a pre-

requisite and a quality attribute, since coated tablets have to pass the test on uniformity of dosage units according to the pharmacopoeias [1, 2]. As a coating process consists of simultaneous spraying, mixing and drying processes, a good coating uniformity can only be achieved with the choice of the proper parameters. To meet these requirements L.B. Bohle developed and improved its coater design in the last years.

The **Bohle Coating Technology** contains three unique design principles which assure a good coating uniformity:

Bohle pan geometry with an L/D ratio >1 offers a large tablet bed surface, which allows the incorporation of a high number of spray guns (Fig.1). Compared to conventional pan geometries that can be found in the market, process time can be saved up to 40% due to larger throughput of coating suspension. Besides the thinner tablet bed induces a minimum shear onto

the tablets, which allows even the coating of very weak tablets.

The unique helical baffles (patented) consist of two layers of baffles (Fig. 2). They are responsible for the continuous and homogeneous axial mixing within the tablet bed. In addition the drum rotation is maintaining the radial mixing. Both movements are a guarantee for a dead zone free tablet bed. Thus a homogeneous mixture in the tablet bed is usually achieved within a few minutes. Due to the constant tablet movement the tablets do not experience any acceleration peaks which could cause tablet damage or even twinning.

The air principle in Bohle Film Coaters utilizes the drying capacity where it is most needed: in the tablet bed (Fig. 3). Thus most effectively the drying capacity of the inlet air is used without heating the rest of the coater inner parts. The inlet air is coming from below the tablet bed and is directly sucked through the rotating tablet

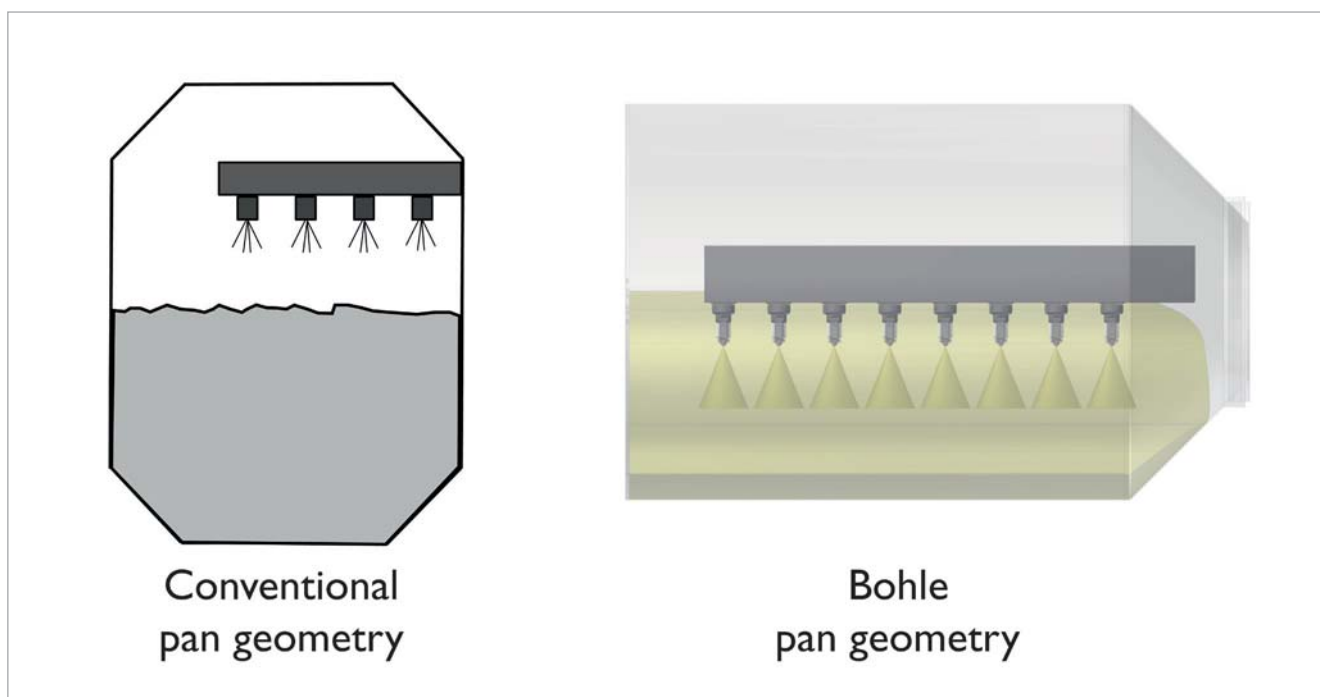


Fig 1: Bohle pan geometry vs. conventional pan geometry

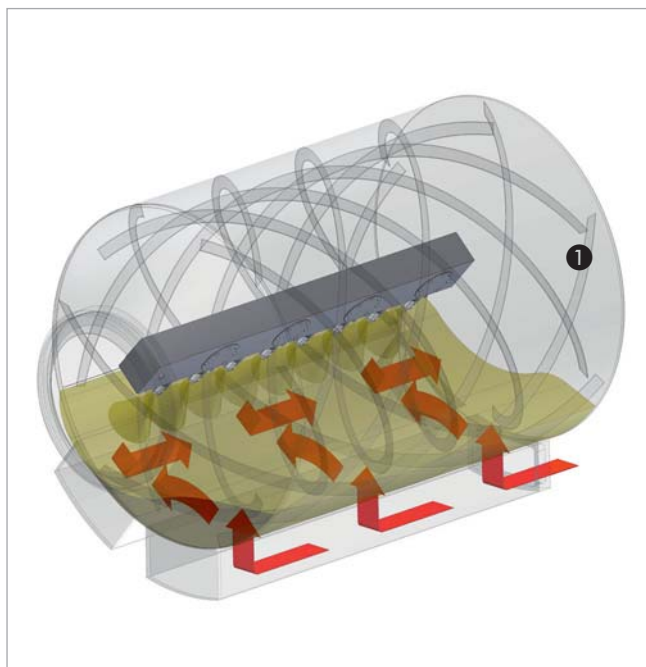


Fig 2: Bohle helical baffle design

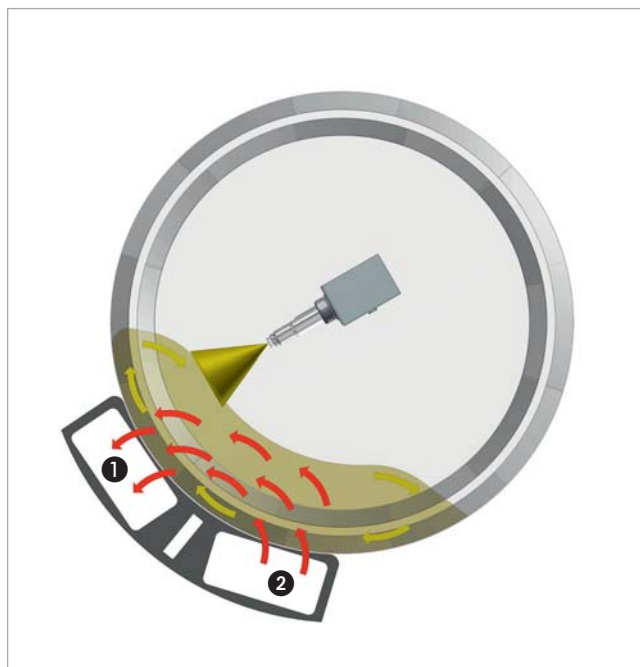


Fig 3: Bohle air flow design

bed into the exhaust air funnel. This setup offers also another advantage: The spray guns are not being heated during coating and remain cool. Therefore spray losses are reduced to a minimum which leads to coating efficiencies of $>95\%$ which is especially beneficial for API coating processes.

Besides these unique features making the Bohle Coating Technology so successful, these coating machines can be equipped with CIP systems. At high pressure values the cleaning takes place with a cleaning lance which effectively cleans the coater after production in an automated mode. The Bohle coating equipment is available from lab scale to large production scale. Furthermore different configuration lines are available meeting different customer needs on all continents. Besides the classical batch mode machine types, semi continuous coaters are also available.

[1] European Pharmacopoeia, Monograph 2.9.40. Uniformity of dosage units, 7th ed., Directorate for the Quality of Medicines of the Council of Europe, Strasbourg, 2011.

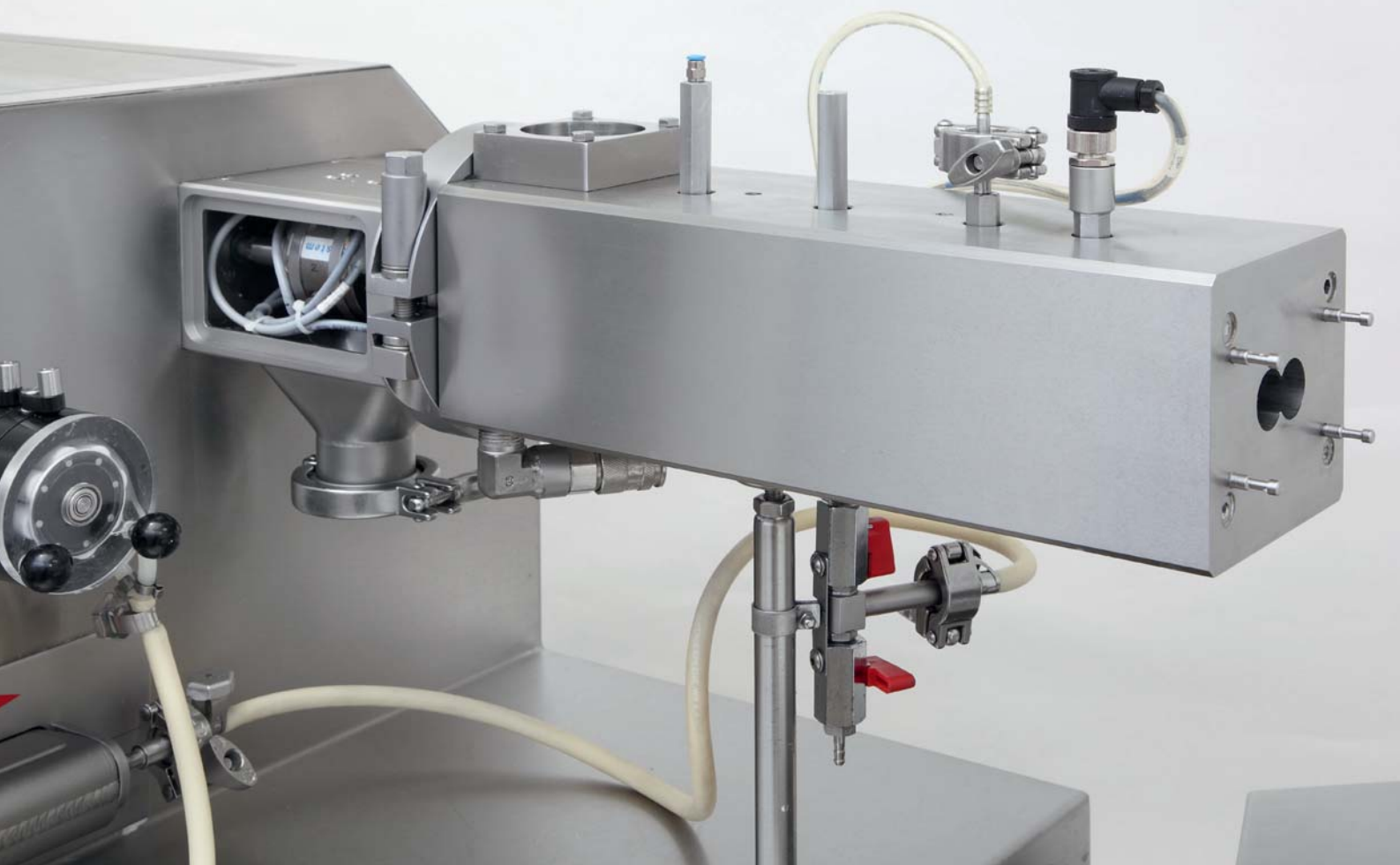
[2] United States Pharmacopoeia, Monograph <905> Uniformity of Dosage Units, 35th ed., U. S. Pharmacopoeia Convention, Rockville, 2011

[3] Optimization of inter-tablet coating uniformity in an active coating process, Just S. et al., Poster presentation AAPS Annual Meeting, Chicago 2012

Dr. Dejan Djuric,
Manager Scientific Operations







Continuous twin screw wet granulation of paracetamol and lactose

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Viktoria Riedel and Prof. Dr. Klaus-Jürgen Steffens

Introduction

Usually, wet granulation is performed with high shear and fluid bed granulators, being batch processes. Twin screw granulators however offer various advantages like e.g. efficiency improvement and reduction of scale-up difficulties. In the first experiments, we will report on the influence of various process and formulation parameters on granule and tablet properties with an instrumented twin screw granulator.

Experimental Methods

Materials: A placebo formulation and a paracetamol formulation were investigated.

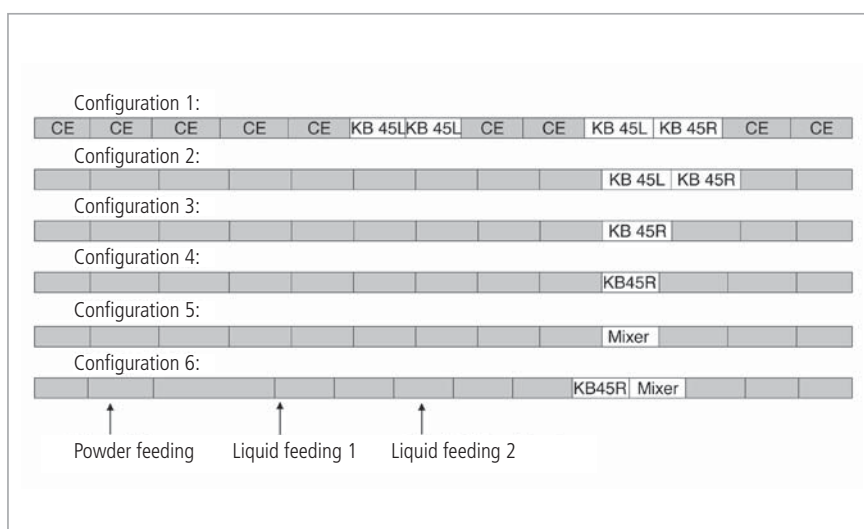


Fig. 1: Overview of screw configurations

Granules were produced with the co-rotating twin screw granulator (BCG 30, L.B. Bohle) and collected after steady-state was achieved and dried at room temperature for 24h using tray drying. After drying, sieving was performed through a 1500 μm Bohle Turbo Sieve (BTS 200, L.B. Bohle).

To determine the impact of the various screw elements, different configurations have been used (refer to Fig. 1). CE stands for conveying element and KB for kneading block, respectively. The variables include the amount of kneading elements, the direction of the kneading elements, as well as the combination of kneading and conveying element.

To investigate the influence of the PVP addition method, granules were prepared both with dissolved and dry binder. The granulation liquid was dosed at the liquid feeding position 2. Feeding pos. 1 has only been used for screw configuration 1.

To determine the particle size distribution of the granules, a vibrating sieve-tower was used. Granule yield is defined as particles between 125 μm and 1250 μm . Tablets, 10 mm flat (305 mg) were produced on a pneumo-hydraulic tablet press (FlexiTab, Roeltgen, Germany). After 24h, tablets were weighed, height, diameter and crushing strength were determined. From these data, tensile strength was calculated.

Results And Discussion

1. Granules

1.1. Influence of screw configuration

With an increasing kneading effect (Fig. 2) lead to larger particle sizes for both formulations, due to a higher degree of densification corresponding to an increase of bonding sites.

1.2. Influence of screw speed

A higher screw speed leads to a higher amount of particles > 1250 μm . This was not due to a change in the kneading efficiency, which within the investigated speed range was thought to be independent of

the speed, but due to a difference in the speed with which the extruded material is crumbling after having left the extruder outlet.

2. Tablets

2.1. Influence of screw configuration

As shown in Fig. 3, only at a low kneading intensity (Config.5) a reduced compactability was found. Screw configurations with a high degree of kneading intensity (with one or two kneading elements) lead to stronger tablets. However this effect could not be enhanced with a higher number of kneading

elements. Apparently, from a given presumably rather low degree of kneading intensity and shearing forces, tableting properties are not improved anymore. These findings could be observed for the placebo- as well as the paracetamol formulation.

Fig. 4 shows that extruded granules resulted in stronger tablets compared to non-extruded powder. Obviously, the shearing forces induced a better binder distribution resulting in larger contact areas between the particles. All this improved the binding properties. The same was found for the formulation, where PVP solution was added.

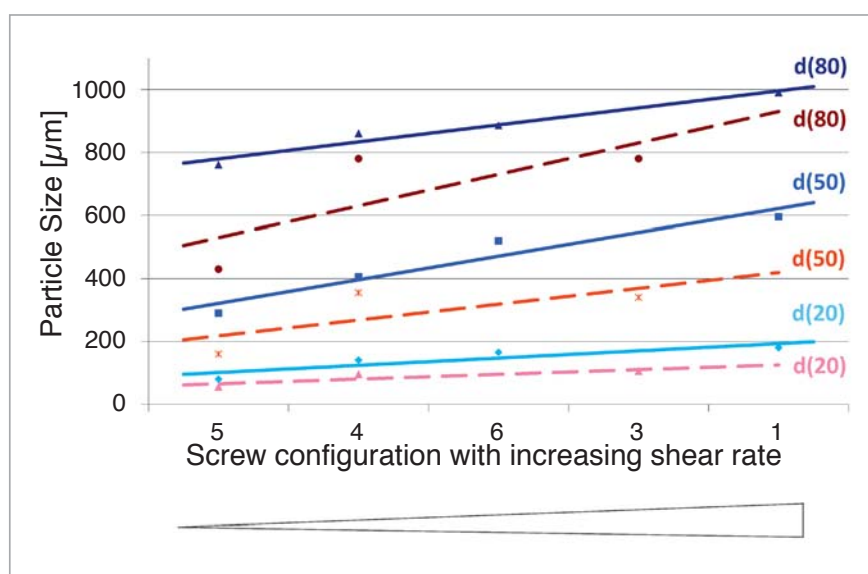


Fig. 2: Continuous lines represent paracetamol granules and dotted lines lactose ones.

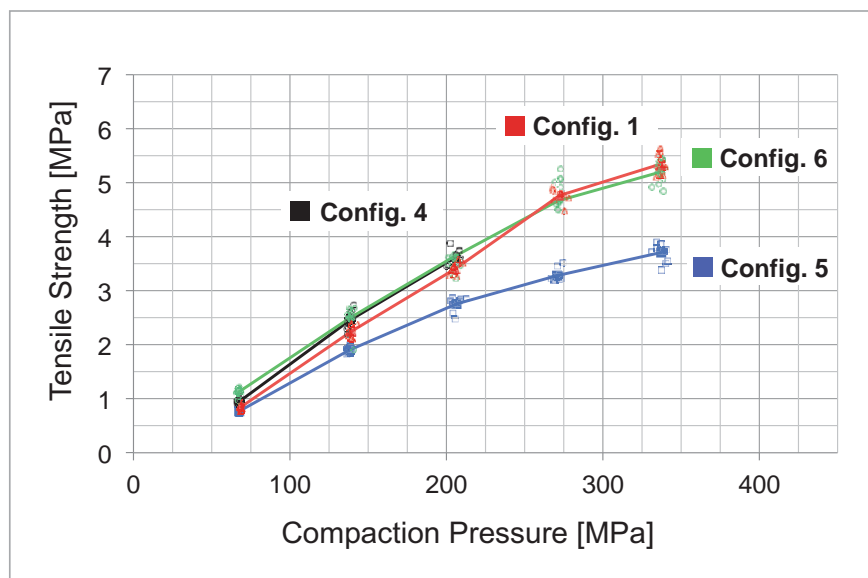


Fig. 3: Influence of different screw configurations on the compactability of paracetamol formulation

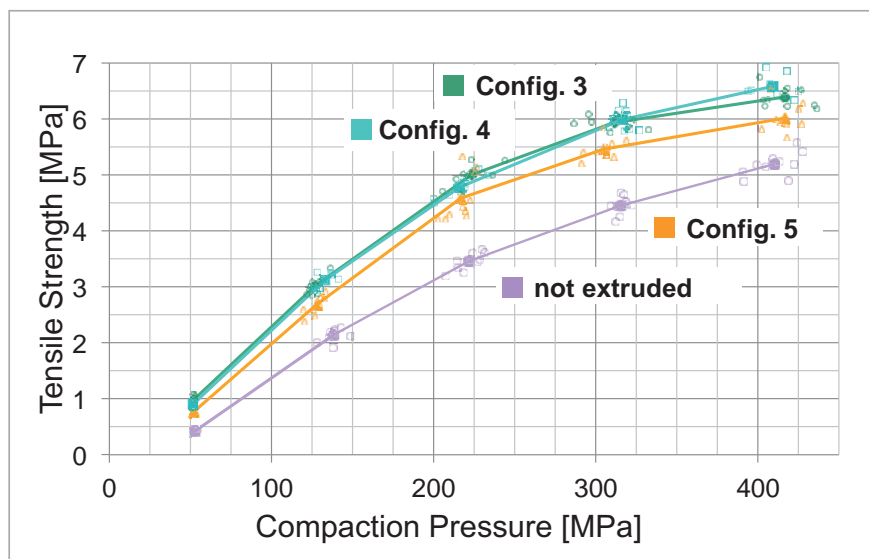


Fig. 4: Influence of different screw configuration on the compactability of placebo formulation

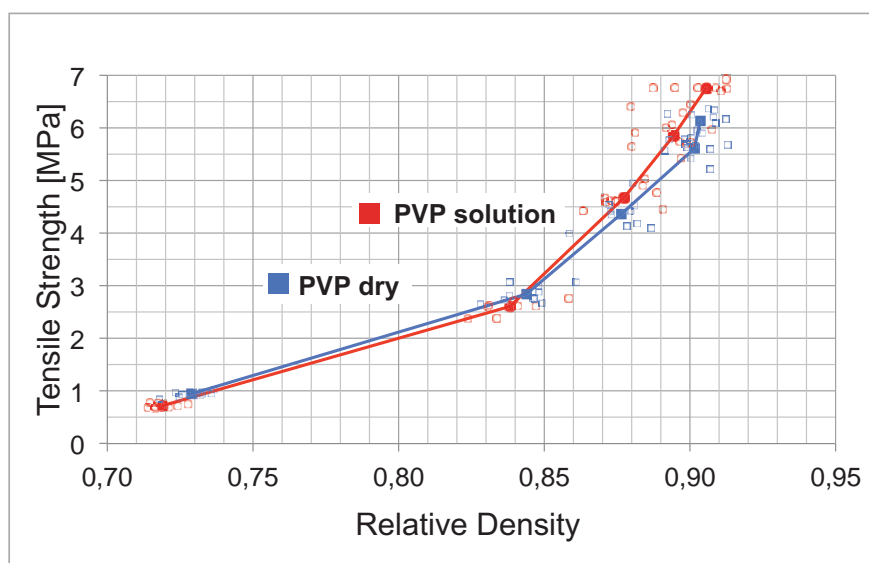


Fig. 5: Influence of PVP addition's method (Configuration 4)

2.1. Influence of liquid feed rate

A trend was observed that a higher water content lead to a higher tensile strength. This was valid for both formulations.

2.2. Influence of administration of PVP

The comparison between PVP added to the powder blend prior to extrusion (blue) or dissolved in the binder solution used for granulation (red) resulted in the same granule and tableting properties. (Fig. 5)

Conclusion

The results show that granulation performed

with a twin screw granulator is a very robust process. Most of the processing parameters had a rather small impact on tablet properties but a remarkable one on granule properties. Thus, the desired flowability for subsequent tableting can easily be achieved. Screw configuration had a pronounced effect on tensile strength. Furthermore, no difference in granule and tablet properties was observed when adding the binder PVP dry in the powder mixture or as a solution. Avoiding the preparation of a binder solution is a remarkable advantage for the production.

Viktoria Riedel



Prof. Dr. Klaus-Jürgen Steffens





L.B. Bohle brings researchers from Siemens and the Universities of Graz and Dusseldorf to Ennigerloh

Construction of the new Global Technology Center

After the most successful year in the company's history, founder Lorenz Bohle is again stepping on the gas in 2013: In Ennigerloh, the new "Global Technology Center" building will start operations in the spring, next to the Service Center.

"Our customers are relying more and more on continuous production processes," Mr Bohle said. "At the new Development, Test, And Presentation Center, we will be pushing this development forward together with the universities of Dusseldorf and Graz as well as with measurement, control, and process technology experts from Siemens." Two million Euros will be invested in the

building with the large glass front alone. "We will be devoting between 6 and 8 million Euro to the cooperation over the next two to three years," the senior director announced. In mid-April, the project was also discussed with potential development pharmaceutical industry partners at the US Interphex event.

The permanent and inter-process measuring, monitoring, and controlling of the production are crucial factors for customers. "Here we will visualize the entire production lines in one plant using material from wet and dry granulation, and we will develop and perform optimized processes

on it", Mr Bohle stated, outlining the goals. The new building, which is also a real eye-catcher, should be completed in the spring of 2014. L. B. Bohle Maschinen + Verfahren GmbH, as investor, will also take charge in the Global Technology Center. "We will bring the specialists to Ennigerloh and provide engineering expertise," Mr Bohle added. The capacities required for the researchers from the universities and the experts from Siemens are being created, and additional experts are employed to reinforce the development team.





From left to right: Armin Bohle, Robert Stauvermann, Christoph Röwekamp (all L.B. Bohle), Gerd Rohrsen (Head of corporate communication Schmitz Cargobull)

"Factory of the Year" visited

Lean Production

Altenberge, Germany. The gradual introduction of lean production at the new Plant 3 is being meticulously prepared by the management team at L. B. Bohle Maschinen + Verfahren GmbH. In the process, Armin Bohle (Technical Director), operations manager Robert Stauvermann, and Christoph Röwekamp (Head of Logistics) have visited three companies from different industries who are already working with production lines. One highlight has been the visit to the main factory of Schmitz Cargobull AG in Altenberge, in North Rhine-Westphalia, Germany. The European market leader in semi-trailer trucks transformed its production processes more than ten years ago.

The corporate strategy is characterized by observing standards from the order process through to the supply of spare parts and custom products, thanks to the use of a modular system and a production process based

on Toyota principles. Previously, the business had been dominated by large stocks, many special requests, and delivery times that were measured in months. Following the changeover, a standard vehicle can now be delivered within just 18 hours. "This means that no vehicle is produced here without an explicit order", explained Ulrich Scheipers, Head of Assembly at the plant. Only precisely those parts that are needed for the current vehicle are delivered to each workplace. "As a result, sources of error are minimized," Mr Scheipers added. In addition to the strictly timed supply, other noticeable features are the cleanliness of the production plant, the ergonomically optimized work processes, and the numerous alcoves where discussions can be held. "Of course, we introduced the Schmitz Cargobull production system gradually and it is constantly being refined by everyone in the team," Mr Scheipers added, explaining the real-life recipe for success.

In recognition, the more than 1,000 employees in Altenberge have also been awarded the prestigious title of "Factory of the Year" by the trade journal "Production."

Just how flexible the production system is became apparent during the crisis and the recovery in growth after 2008. "Before the economic crisis, we had built more than 66,000 vehicles at all locations. Then we plunged to a mere 12,000 within two years, though we are now back to 43,000 units annually," Mr Scheipers reported.

Armin Bohle was very impressed by the consistency with which Schmitz Cargobull is running its lean production system. "While we are certainly no longer right at the beginning, we have already been able to gain a great deal of ideas and inspiration from our experience", Mr Scheipers added gratefully.

International visitors in Ennigerloh

Agent Meeting at L.B. Bohle

A total of 35 agents and distributors of L. B. Bohle Maschinen + Verfahren GmbH responded to the invitation by CEO Lorenz B. Bohle and met on the 12th and 13th March in the service center in the German town of Ennigerloh. During the agent meeting the international guests found out more about the latest developments and took the opportunity to compare notes. In addition to lectures about the new dry granulator BRC 100 and coating technology, strategic questions and the company's expansion plans were also discussed. Agents were updated on the developments for plant 3 that is being built near the head office in Ennigerloh



Attendees of the Agent Meeting, 2013

and that will start production of (mainly) coaters in autumn 2013. After two informative and interesting days, all agents were highly motivated

when leaving the premises and were looking forward to meet again during the next global agent meeting in three years time.

Bücker Exhibition attracts many visitors



From left to right: Walter Tillmann, Bucker-de Silva family of artists, Lorenz Bohle



The arts exhibition of the Bucker family of artists ended mid-January 2013 after attracting a record number of visitors. An essential part formed the pictures and sculptures by Heinrich-Gerhard Bucker who had passed away in 2008. He is one of the most renowned artists in the Warendorf region. Bucker Senior created mainly religious pieces and portrayals of horses. His works are known across Europe and were even exhibited in the Vatican Museums, making him the first living artist to exhibit his works in the Vatican.

In addition to creations by Heinrich-Gerhard Bucker, art lovers could also view artworks, pictures and jewelry by son Matthias Bucker and his daughter Lara in the L. B. Bohle Maschinen + Verfahren GmbH Service Center.

180 years experience

L.B. Bohle honours ten long-standing employees

A small celebration was held in which the German machine manufacturer L.B. Bohle honoured ten long-standing employees. All ten celebrated their ten-year company anniversaries in 2012. Five employees have been working for the company for ten years, while Gerda Trink, Manfred Groth, Andreas Rutsch and Norbert Ohlmeier have been with L.B. Bohle for a full 25 years. And metal engineer Markus

Splietker has been working for the organization for 30 years; he has experienced and helped to shape the company's developments and success first-hand.

On behalf of the company's management, Chief Technical Officer for L. B. Bohle Maschinen + Verfahren GmbH Achim Bohle thanked the jubilarians and expressed that the company was looking

forward to a successful future cooperation to help continue the Bohle success story.

From left to right:

Armin Bohle (Chief Technical Officer), Martin Nienkemper, Norbert Ohlmeier, Daniel Bexte, Andreas Rutsch, Manfred Groth, Michael Kuhnert, Gerda Trink, Susanne Rixrath, Bastian Scheffbusch, Markus Splietker



Walter Tillmann Obituary

No other non-employee had a closer connection with the company: Walter Tillmann passed away on the 23rd January 2013. He had been a steady companion, advocate and supporter of L.B. Bohle Maschinen + Verfahren GmbH. He had served many years as mayor of the German town of Ennigerloh and in the 1980s had offered valuable support to the specialist machine manufacturer during the company's early years.

In the mid 80s the citizens of Ennigerloh met with a significant economic event: the

company Profilia closed down, and numerous local families lost their livelihoods. During this difficult time for Ennigerloh, mayor Tillmann successfully tried to establish young companies. He reached this goal with benevolence and brilliant rhetoric. Under his leadership the town was able to start into a successful future, and life went on, contrary to what many locals had feared.

After his time in office, Walter Tillmann served numerous years as editor for "Innovativ" and as organizer of art exhibitions.

We will remember Walter Tillmann always with great appreciation.



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