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Rotary tablet press

for tablet compression research, formulation development and small-scale production.

The latest addition to the MODUL™ range of tablet presses, based on the well-known patented Exchangeable Compression Module (ECM) concept, is one of the most versatile tablet presses available on the market. It is not only able to compress tablets in the same way as any existing tablet press, but also capable of compressing tablets according to novel compaction principles, resulting in higher tablet quality and/or higher machine output. This article explains the state-of-the-art design principles of the MODUL™ P, which make it one of the most advanced rotary tablet presses – both for research & development and commercial production.

The air compensator: compression to equal thickness or to equal force

Both the pre- and main compression stations of the press are equipped with a so-called air compensator, installed on the upper compression roller. The air compensator consists of a piston that can move vertically in a cylinder filled with compressed air (see Fig 2). The air pressure applied to the air compensator is memorised as a product parameter in the machine's control system and is kept constant by means of a self-regulating electromagnetic valve. The piston is pushed down against a stop with a constant force, F_{max} equalling the air pressure multiplied by the surface of the piston. The upper compression roller is fixed to the piston and can move up and down in a vertical guide bush (see Fig 1).

Compression to equal thickness

If the air pressure in the compensator is such that F_{max} is higher than the actual compression force on the tablet, the system operates in the same way any other tablet press does:

- all tablets are compressed to the same thickness, determined by the distance between the compression rollers – i.e. the "compression height."
- the actual individual compression forces vary with the quantity of powder in the die – i.e. the individual tablet weights.

As all tablets are compressed to identical thickness, this principle is called compression to equal thickness (see Fig 3 A).

Highly effective punch protection

When compressing to equal thickness, the air compensator system acts as a passive punch protection system, providing more effective protection against overload than any other active system. In fact, in case of an overload situation whereby the actual compression force exerted on the punch equals the air pressure force Fmax, the piston will be pushed up and the air volume will act as an air cushion or "compensator." Such a system is passive as no action by a sensor, a PLC or an actuator is required to retract the compression roller. In fact, the compression roller together with the piston is pushed up by the punch to allow the punch to pass underneath the roller. The upward movement of the piston is detected by the machine's control system, which immediately stops the rotation of the die table and displays the overload alarm message.

As the upward movement of the piston is negligible compared with the total air volume in the compensator and the expansion chamber, one can assume that the air pressure – and hence the compression force exerted on the punch – remains constant during the entire time period that the roller moves up and back down. It is as if the air compensator cuts off the peak of the force profile above the set overload limit (see Fig 3B).

Tablet presses without an air compensator will always have to rely on an active system to protect the punches against a possible overload: an overload situation is detected by a pressure sensor or a load cell, after which a valve or actuator is actively controlled via the PLC of the machine or by a hardwired control loop. In both cases, some milliseconds are required; enough time to destroy several punches at high tabletting speeds (see Fig 3C).

Compression to equal force

The air pressure in the compensator and the distance between the upper and lower compression rollers can be set in such a way that the air compensator moves up at each compression. In this case:

- all tablets are compressed at the same peak compression force, determined by the air pressure in the compensator
- the actual individual tablet thicknesses vary with the quantity of powder in the die – i.e. the individual tablet weights. This means that in case of heavier (lighter) tablets, the piston will be pushed up more (less). The maximum distance over which the piston is pushed up is the so-called "displacement" and is measured for every tablet using an accurate LVDT sensor (Linear Variable Displacement Transducer). The displacement is function of the tablet weight.

> "A very important advantage of compression to equal force is that the upward movement of the compression roller results in an important increase of the total compression time – and more particularly the dwell time."

As all tablets are compressed at the same compression force, we call this principle compression to equal force (Fig 4).

Air compensator and extended dwell time

A very important advantage of compression to equal force is that the upward movement of the compression roller results in an important increase of the total compression time – and more particularly the dwell time. The dwell time is defined as the time that the force is above 90% of its peak value. The extra dwell time is the extra dwell "length" divided by the linear velocity of the dies.

The increase in dwell "length" as a result of the upward movement of the compression roller can easily be calculated as a function of the compression roller radius R and the displacement d, using Pythagoras' theorem:

ΔD = 2 * SQRT (RÇ - $(R-d)_c$) = 2 * SQRT(2*R*d).

For a typical situation on a MODUL™ P with R = 80 mm and d = 0.2 mm, this extra dwell length is 11.31 mm. When considering that the flat part of a EURO B punch is 9.53 mm, it is clear that a 0.2 mm displacement allows for a total dwell time that is 219% of the dwell time without compensation (dwell time extension of 119%). An extended dwell time offers significant advantages to achieve optimal compression of a powder into tablets:

- At pre-compression a long dwell time at low to medium pre-compression force is essential for a good de-aeration of the powder bed and a uniform distribution of the granules in the die, prior to the formation of a compact under main compression. If air is squeezed out insufficiently and/or density variations occur within the tablet volume, tablet tensile strength is negatively affected and the risk of tablet capping or laminating increases. Extended dwell time at pre-compression is therefore even more important for larger tablets.
- At main compression, in cases of powders with time-dependent consolidation behaviour, a long dwell time is important to create strong bonds between the particles. Extended dwell time at main compression is therefore more important for formulations with pre-dominantly plastic deformation behaviour, rather than brittle fraction behaviour.

The crucial importance of an extended dwell time is also illustrated by the frequent application in other tablet presses of the following techniques to increase the time that the punch is in contact with the compression roller:

- Reduction of tablet press speed in case of capping or insufficient hardness
- Installation of larger compression rollers to increase the total compression time
- Use of punches with a larger mushroom head.

The use of a moving air compensator at pre- and main compression stations enables the production of high-quality tablets without compromise on the machine speed or the need for special non-standard punches.

It is even possible to actively control the dwell time of the compression profile: when decreasing the distance between the compression rollers, the displacement increases, resulting in an increase in dwell length of 2 * SQRT (R_c - $(R-d)_c$).

FIGURE 1

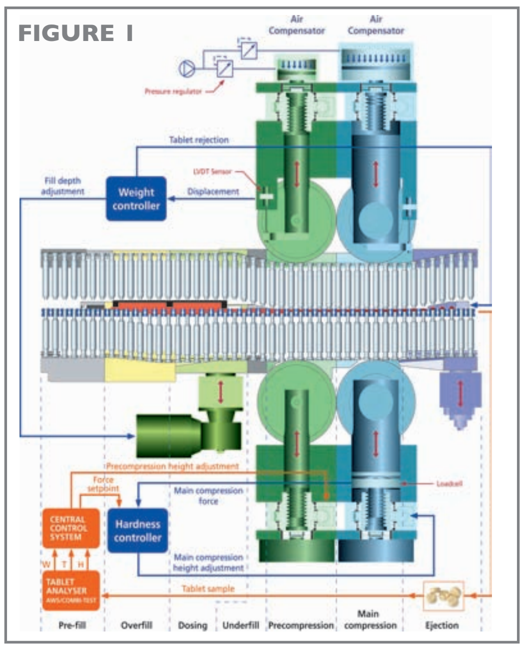


FIGURE 2

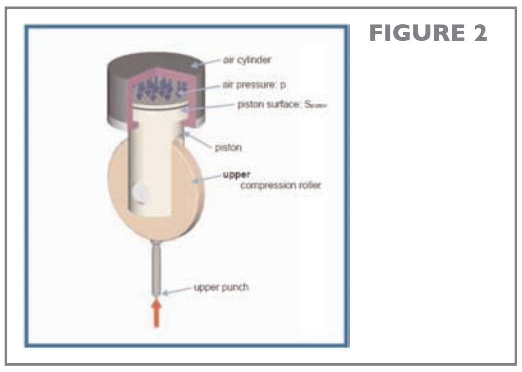


FIGURE 3a

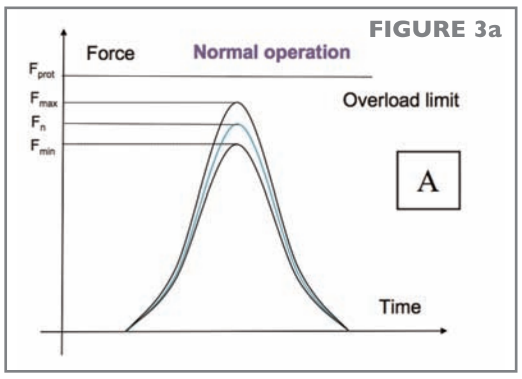


FIGURE 3b

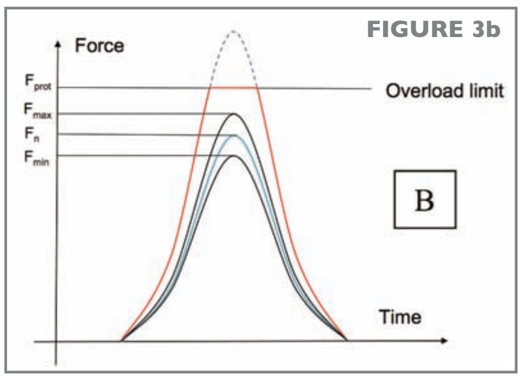


FIGURE 3c

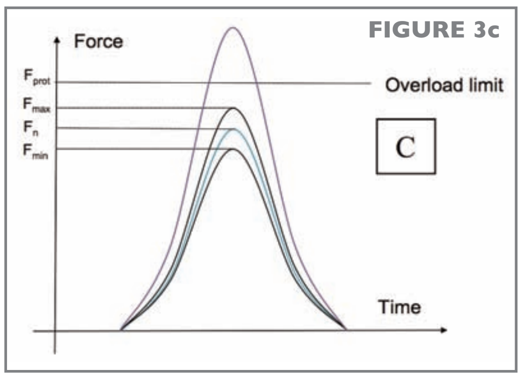


FIGURE 4

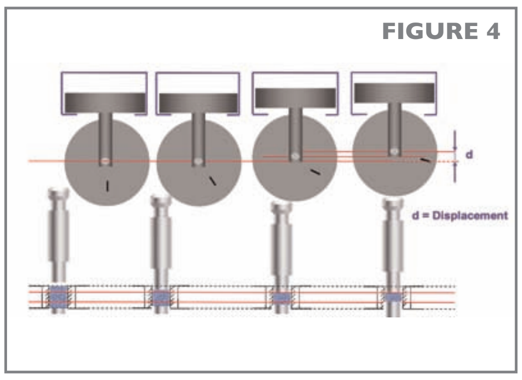
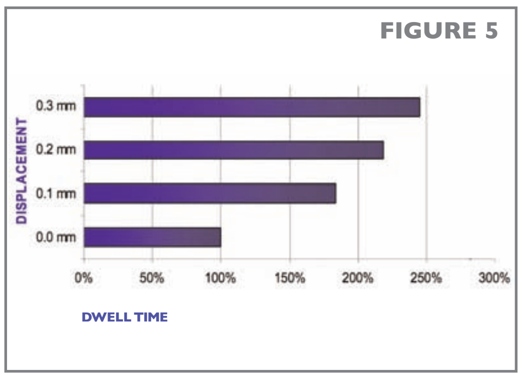


FIGURE 5



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PART TWO

Rotary tablet press

FOR TABLET COMPRESSION RESEARCH, FORMULATION DEVELOPMENT AND SMALL-SCALE PRODUCTION.

Tablet weight control by force measurement at main compression

Most tablet press control systems perform tablet weight control by recording the individual compaction force for each tablet at main compression when compressing to equal thickness. This is the most commonly used method, indicated in Figure 1:

- Individual out-of-tolerance tablets are identified and rejected based on individual compaction force values outside the rejection limits.
- The die's fill depth is adjusted by moving the dosing cam up and down, in order to keep the average compaction force value as close as possible to its set point.

This indirect weight measurement principle based on compaction force under equal thickness has several drawbacks:

1. The rejection limits for the force signal have to be determined empirically for every formulation on every individual machine. There is no method to establish the rejection limits automatically based on the required weight tolerance limits.
2. Machine stiffness varies from one tablet press to another and has a significant influence on the relationship between peak compaction force and tablet weight. As a result, the force set-point and rejection limits need to be established for each tablet press individually.
3. The sensitivity of this tablet weight measurement principle decreases when the diameter of the tablet decreases and/or the compression force decreases. This is the reason why force measurement for tablet weight control is always performed at main compression, where the compression force and sensitivity are highest.
4. During the first hours of production after a cold start-up, the machine and punches expand due to heating up. This causes the compression force to increase, which is immediately compensated by the automatic control system, by means of a gradual reduction of the fill depth. Consequently, the tablet weight gets caught in a downward drift and is only corrected when a tablet sample is taken and measured.
5. After tablet sampling, the force control loop is re-corrected by changing the main compression height, which results in a change in tablet thickness. This can lead to unacceptable variations in tablet thickness. These variations are not detected until the tablets go on the blister line - often after coating, and lead to regular machine stops in the packaging department.

Tablet weight control by displacement measurement at pre-compression

An alternative method for indirect weight measurement is to measure thickness variations under equal force. Experiments have demonstrated that when tablets are compressed to equal force using an air compensator, they are compressed to equal density.

When the density is the same for all tablets at the time of compression, their "in-die thickness" (i.e. the total tablet thickness when the tablet is still in the die and under pressure) is in linear relationship with the weight of the tablets:

W = density x (compression height + 2 x equivalent arrow of punches + displacement)

This in-die thickness can easily be determined as the sum of three components:

1. the compression height = the distance between the compression rollers
2. a constant depending on the shape of the tablet (equivalent arrow of the concavity of the punch tip)
3. the displacement as described above in this article

Therefore, the individual displacement values are in linear relationship with the weight of the individual tablets. In all other respects, the control loop is very similar to a force controlled system (see Fig 2):

- individual displacement values are used to reject out-of-tolerance tablets.
- the average displacement signal is used to correct the fill depth of the dies.

This slightly different principle of measuring thickness under equal force at pre-compression instead of force under equal thickness at main compression has several advantages:

1. Rejection and correction limits can be determined automatically on the basis of the required weight tolerance.
2. Machine stiffness has a negligible influence on the relationship weight/displacement.
3. Sensitivity of the measurement principle increases with decreasing tablet size and compression force; i.e. this system has the best benefits with small tablets and multi-layer tablets, where good bonding between layers has to be achieved.
4. Machine temperature has a negligible influence on the weight control system.
5. After tablet sampling, the displacement control loop is re-corrected by changing the pre-compression height (not the main compression height!), leaving the final tablet thickness unchanged.

Six operation principles for tablet compression and control on the MODUL™ P

Through combinations of the principles described above, the MODUL™ P rotary tablet press has six modes of operation. Modes 1, 2, 5 and 6 are summarised in Table 1. Modes 3 and 4 are explained in more detail below.

Equal Porosity Tabletting

This is the most advanced way of compressing a tablet and controlling the compression process. It ensures that average tablet porosity remains constant and porosity variability is minimal:

- Both the pre-compression and the main compression compensators compress to equal force, providing the most extended total dwell time and therefore the most efficient compaction effort.
- Tablet weight control is performed via displacement measurement at pre-compression.
- Tablets leaving the tablet press are all compressed to the same final compression force and therefore have equal density. Their thickness varies slightly with their weight, but they are all within the specified tolerance limits.
- An additional control loop at the main compression station measures all individual displacement values, calculates the average displacement and automatically changes the main compression height in order to keep the average displacement as close as possible to a desired set-point (Mode 3: Dual Control - Displacement). By keeping the average displacement

constant over time, the dwell time and consequently tablet strength is kept constant over the entire batch.

Compression to constant density is very important from the point of view of drug release profile and bio-availability. When this principle of tablet compression is used, all tablets within a batch will have nearly identical tablet density and thus porosity (i.e. variability will be minimal). As the porosity is strongly correlated to the dissolution time of the tablet, all tablets of this batch will show very similar dissolution times. This will in turn result in significantly less variation in drug release profile and bio-availability.

As an alternative, the control loop on the main compression station can keep the dwell time constant - even at variable machine speed:

- The operator keys in the desired dwell time, expressed in milliseconds.
- The control system converts this required dwell time into a set-point for the displacement, taking into account the actual rotation speed of the die table and the type of tooling used.
- This displacement set-point is then maintained by automatic adjustment of the main compression height.
- When the speed of the machine is changed, the control system automatically calculates the new set-point for the displacement, so that the average dwell time is kept constant.

This operation principle is called “Dual Control - Dwell time” (Mode 4) and offers the highest flexibility with regard to setting the compression profile for any particular powder formulation.

As a matter of fact, the operator enters the desired height of the compression profile (i.e. peak compression force in Newton) and the desired length of the compression profile (in milliseconds). The machine’s control system then automatically adjusts all mechanical settings of the compression cycle and the MODUL™ P starts producing tablets with minimal variability in tablet dissolution time.

The “Dual Control - Dwell Time” makes the compression process the most flexible and robust compression process on the market today.

The equal porosity tabletting principle can, for instance, be very useful when producing oral rapid disintegration tablets. Such tablets often consist of drug-layered micro-granules that are then coated with a taste-masking film. Compression of these granules into solid tablets requires a compression at an accurately controlled and low force to avoid damage to the film coating, but this force has to be applied during an extended period of time in order for the granules to bond together sufficiently. The constant porosity tabletting principle could also prove useful for tabletting granulates or pellets, which are particularly sensitive to compression force and, therefore, now need to be filled into capsules.

Conclusion

The MODUL™ P tablet press is equipped with two air compensators (at the pre- and main compression stations), which can compress to either equal thickness or equal force. The machine also has two different tablet weight control systems. By combining these possibilities, the MODUL™ P can operate according to six different operation principles. One of them is the conventional compression cycle with weight control by force measurement at final compression. This allows MODUL™ P to be used for development and scale-up work for any make or type of tablet press commercially available. The other operational modes offer significant advantages in regard to compression efficiency (extended dwell time, improved bonding, etc.) and control of the compression process, enhancing process robustness. The MODUL™ P can easily be switched from one operational mode to another. This flexibility makes the MODUL™ P a powerful tool for all kinds of research and development work, including trouble-shooting of existing production processes and formulation development for new difficult-to-compress APIs.

For the first part of this article please see European Pharmaceutical Manufacturer Volume 8, Issue 1.

Fig 1: Conventional Force Control. (Mode 5)

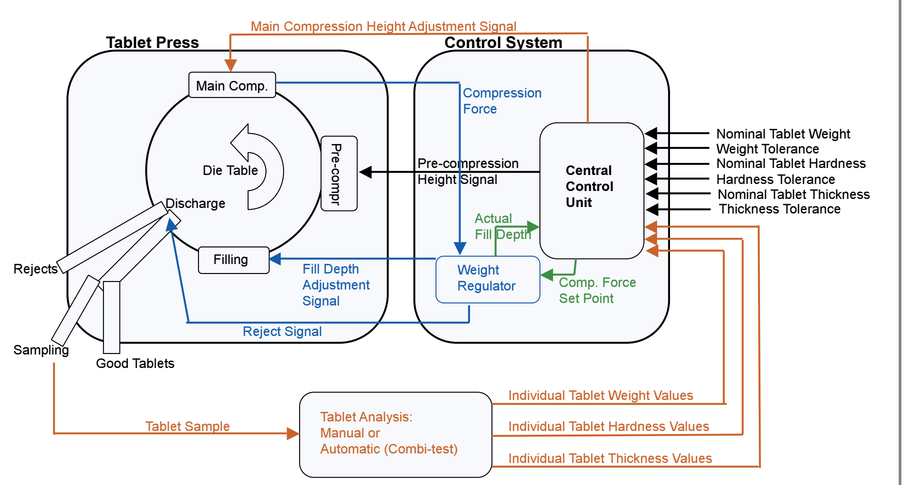

Fig 2: Courtoy Displacement Control. (Mode 1)

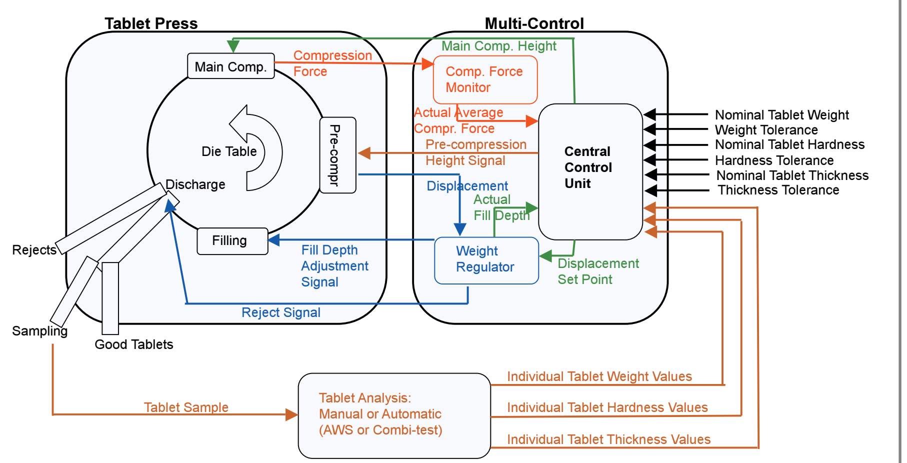

Fig 3: Courtoy Dual Control — Force. (Mode 2)

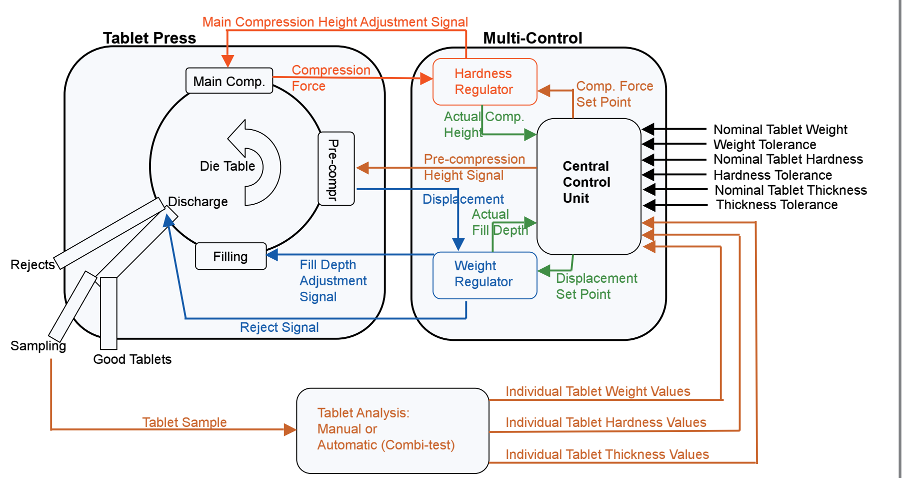

Table 1. Operation modes of the MODUL™ P Rotary Tablet Press

Mode	Type of Compression
1	**Traditional Courtoy Principle: tablet thickness remains constant** Pre-compression station operates to equal force extending dwell time; displacement is measured for tablet weight control and rejection of out-of-tolerance tablets. Re-correction of the weight control loop after taking a sample results in a step-change of the pre-compression height. This leaves tablet thickness unaffected, as opposed to modes 5 and 6. The main compression station compresses all tablets to the same thickness, which remains constant over the entire batch. The main compression compensator operates in equal thickness mode and serves as a punch overload protection system.
2	**Dual Control - Force: average compression force remains constant (See Fig. 3)** As Mode 1, with the activation of an additional control loop on the main compression station. This loop permanently measures the main compression forces, calculates the average and automatically changes the main compression height to keep this average force as close as possible to a desired set point. This additional loop keeps the average main compression force and hence the average tablet hardness constant over time. The tablet weight control loop on pre-compression and the hardness control loop on main compression run both permanently and in parallel, yet they are completely independent from one another - hence the name “Dual Control”.
3	**Dual Control - Displacement: See extended description in text**
4	**Dual Control - Dwell Time: See extended description in text**
5	**Conventional Tablet Compression** As with a majority of rotary tablet presses, tablets are compressed to equal thickness at both pre- and main compression stages. Air compensators protect punches against overload. Tablet weight is controlled by means of compression force measurement at main compression.
6	**Hybrid Mode** As Mode 5, except air compensator on pre-compression works in equal force mode, creating extended dwell time at pre-compression, which helps prevent capping, laminating and insufficient hardness. This mode proves useful when compressing large tablets, e.g. effervescent tablets.