

## From Challenge to Success: Handling Metformin Production

Metformin is the second largest volume of drug processed and as one of the most regularly prescribed oral antidiabetic drugs worldwide it remains a cornerstone in the treatment of type 2 diabetes mellitus. Despite its clinical importance, the large-scale production of metformin tablets poses challenges that must be overcome to ensure consistent product quality and manufacturability.

A key challenge arises in the physicochemical characteristics of metformin hydrochloride. The drug ingredient is hygroscopic and typically shows poor flowability. These characteristics complicate direct compression and increase the risk of issues such as sticking, capping, or weight variation during tablet manufacturing.

Furthermore, the high drug load required in typical metformin formulations - often exceeding 80% of tablet weight - leaves limited room for excipients that could otherwise improve compressibility and lubrication. This combination of factors demands advanced equipment capable of maintaining process stability, minimizing mechanical stress, and ensuring uniformity even under high-speed production conditions.



### Application Case

#### KTP 720X eliminates weight variations in high speed production

The production trial started at a turret speed of 65 RPM, corresponding to an output of approximately 400,000 tablets per hour. Under these conditions, the press demonstrated excellent process stability, achieving an individual tablet weight range of 1150.80 mg to 1180.00 mg, which equates to a narrow variation of  $\pm 0.6\%$  (The tablet target weight was defined as 1,160 mg). Tablet hardness was consistently maintained between 19.50 and 20.50 kP, indicating reliable compressibility and mechanical strength.

To further evaluate the machine's performance, the speed was increased from 65 RPM to 80 RPM, thereby raising the production rate to approximately 488,000 tablets per hour. The press was operated continuously at this higher speed for a duration of 50 minutes, until the blend was completely consumed. Throughout this extended run, weight uniformity remained stable within  $\pm 1\%$ , confirming the robustness of the compression process even under high-throughput conditions.

Subsequent inspection of the compression chamber and drive area revealed no evidence of powder accumulation, highlighting the machine's effective compartment separation and clean design.

As a final step, a product changeover was performed, transitioning from Metformin 1000 mg to 500 mg tablets. The smooth execution of this changeover demonstrated the flexibility of the KTP 720X in accommodating different product strengths with minimal setup time and without compromising performance.

### Tablet Press Set-up



KTP 720X	Mono-layer
Number of press stations	51
Tool type	D
Die type	D
Maximum die filling	20 mm
Maximum tablet diameter	25 mm
Maximum pre-compression force	100 kN
Maximum main-compression force	100 kN
Maximum output Mono-layer	550,800 tablets/hour

## Process Parameters

Parameters	65 rpm (Metformin)	80 rpm (Metformin)
<b>Maschine output</b>	400,000 tablets/hour	488,000 tablets/hour
<b>Die table speed</b>	65 rpm	80 rpm
<b>Main-compression force</b>	19.99 kN	32.50 kN
<b>Main-compression force SD</b>	4.28 %	5.80 %
<b>Pre-compression force</b>	3.50 kN	6.50 kN
<b>Tablet size</b>	19.00 x 10.50 mm	19.00 x 10.50 mm
<b>Ejection force maximum</b>	350 - 450 N	400 - 550 N

## Conclusion

The production trial clearly demonstrated the capability of the KTP 720X to maintain precise weight control even under high-speed conditions. The press was able to achieve weight variations well within  $\pm 1\%$  at outputs approaching 488,000 tablets per hour, despite the inherent limitations of metformin formulations, such as high drug load and poor flowability. This consistent performance confirms the machine's suitability for large-scale manufacturing of demanding formulations, ensuring both product quality and process reliability without compromise at high production speeds.