Unique tablets require unique solutions - read on!

From Powder to Pill: Perfecting Paracetamol Production

Originally known on the market as acetaminophen, paracetamol is a widely used medication primarily for pain relief and fever reduction. First discovered in the late 19th century, it gained popularity in the mid-20th century as a safer alternative to aspirin. Paracetamol is now a staple in medicine cabinets worldwide and is included in the World Health Organization's list of Essential Medicines.

When people think of painkillers, they often consider nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen, which can cause stomach irritation or blood thinning. However, paracetamol stands out due to its gentle effect on the stomach and minimal anti-inflammatory properties. It works primarily in the central nervous system, making it effective for reducing pain and fever without the gastrointestinal side effects common with NSAIDs.

Due to its widespread use, paracetamol is a high-volume product in pharmaceutical manufacturing. However, its production is not without challenges, particularly when it comes to tablet compression. Manufacturers may encounter issues such as sticking, tablet hardness problems and the need to adjust tooling design to optimise it for their product.

Sticking, in particular, remains one of the most persistent problems during paracetamol compression. As with other formulations, sticking is influenced by the interaction between the powder and the punch face during compression. When adhesive forces outweigh the cohesive forces within the tablet, material begins to cling to the tooling surfaces. These forces can be influenced by formulation moisture, electrostatic charge, ambient temperature and many more factors—all of which affect the powder's behaviour under pressure.

Solving sticking effectively starts with understanding its root causes before compression begins. TSAR Predict—I Holland's predictive software—helps manufacturers do just that. TSAR Predict was born after the completion a two-year TSAR (Tabletting Science Anti-Stick Research) project in collaboration with the University of Nottingham's School of Pharmacy and experts from the Laboratory of Biophysics and Surface Analysis in the UK. The aim of the project was to investigate and solve the universal tablet manufacturing problem of sticking. It calculates single particle adhesion to the punch tip face without time consuming and expensive field trials. By simulating how a paracetamol formulation behaves under pressure, TSAR analyses potential sticking risks and recommends the most suitable coatings and tooling. Whether it's punch compatibility, particle size, or flowability, every formulation is unique—and TSAR helps tailor the coating solution to match.

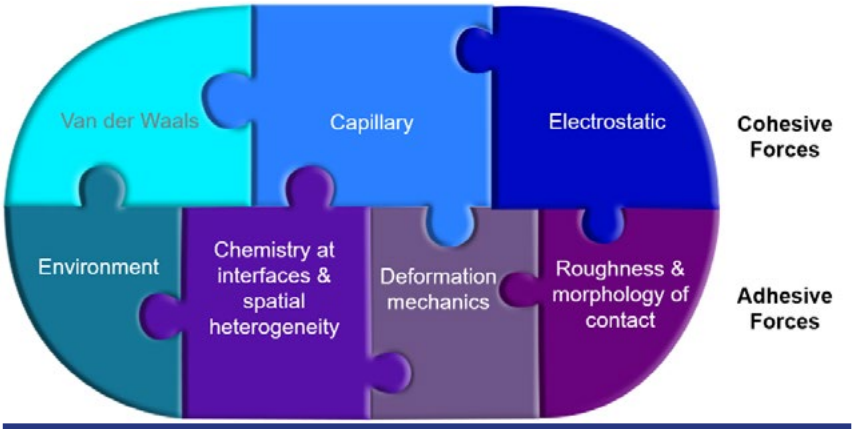
The advantages of using TSAR were exemplified when I Holland helped one of our customers in India who were experiencing a sticking problem. They were manufacturing paracetamol & codeine effervescent tablets and tablet appearance was an important factor for the market they would sell to. During R&D trials, the issue began after just 30 minutes of low-volume production, with the

sticking occurring mostly on the lower punch. A TSAR prediction was run, and CN+ coating was identified as offering the lowest particle adhesion force for their formulation, with a reading of 97.89nN. This pre-emptive approach not only saved time and cost on physical trials but also enabled faster scale-up and reduced downtime.

In some cases, modifying the tooling design itself—by altering the punch tip shape or increasing dwell time with solutions like XDF tooling—can help optimise the compression process for challenging formulations like paracetamol. These strategies can improve tablet hardness, reduce weight variation, and mitigate sticking, all while maintaining production efficiency.

A customer manufacturing paracetamol on a Courtoy press using D type tooling faced a different challenge—excessive fines in the API were escaping through the clearance between the lower punch tip and die bore, leading to contamination and tablet inconsistencies. Initially, the team considered tightening the lower punch tip tolerance, but at an already narrow 0.02mm range, further reduction wasn't practical. Instead, attention turned to the die bore, where tolerance was reduced from +0.00/+0.02mm to +0.00/+0.008mm, effectively narrowing the clearance by at least 0.012mm. Additionally, tip concentricity was tightened to 0.01mm. The outcome? The customer reported that no further issues have been experienced since the update, and they are fully satisfied with the improved tooling and die specifications.

Another common challenge in the production of paracetamol tablets is



Affecting factors for cohesive and adhesive forces

achieving consistent tablet hardness. While it may seem like a straightforward parameter, tablet hardness is a critical quality attribute that directly impacts tablet durability, disintegration time, and overall product performance. Too soft, and the tablet may crumble during packaging or transit. Too hard, and it may fail to dissolve properly, affecting how quickly the medication is absorbed by the body.

Many paracetamol formulations—especially those with fine particle sizes, high-speed presses, or moisture-sensitive excipients—can present additional complications. The active ingredient itself doesn't always compress easily, and this can lead to variability in tablet density and mechanical strength. Several factors can influence hardness:

•Compression force: Too little force can result in weak tablets, while excessive force may cause capping or lamination.

•Dwell time: If the compression time is too short, especially when compressing at faster press speeds, the tablet may not consolidate properly, producing faulty tablets.

•Tooling wear: Worn tooling can affect pressure distribution, leading to uneven hardness across a batch.

•Poor flowability or particle

An example of a particularly bad case of sticking

size inconsistency can affect uniform filling and compaction.

One highly effective strategy is the use of XDF (eXtended Dwell Flat) tooling, which increases the dwell time on standard tablet presses without requiring machine modification. This additional compaction time allows the paracetamol particles more opportunity to bond, leading to stronger, more consistent tablets, even at high press speeds.

In addition to dwell time optimisation, tooling design choices—like multi-tip punches—can also support high-volume production without compromising quality. Designed to produce multiple tablets per punch, multi-tip tooling is a smart solution for increasing output without the need for additional presses or extended cycle times.

But aside from improving efficiency, multi-tip tooling can also have a positive impact on tablet hardness, if implemented correctly. At first glance, one might assume that compressing several tablets at once would reduce the pressure applied to each individual tablet. However, with the right press settings and tooling design, multi-tip punches can deliver tablets that meet the required specification. When designed with precision, multi-tip tooling allows for an even distribution of compression force across all cavities. This uniformity helps maintain consistent tablet density and hardness, batch after batch.

Ultimately, when compressing high-volume drugs like paracetamol, it's not just about making tablets—it's about making them consistently, efficiently, and with minimal disruption. That means understanding the formulation, optimising the tooling, and managing environmental variables to reduce sticking and improve output.

Multi-tips boost tablet output, improving efficiency

Inconsistent hardness leads to inconsistent quality

The ellipictical head allows 50% more dwell time