

Sticking is a commonly reported Ibuprofen issue

## Relieving Your Ibuprofen Headaches

Discovered and developed in 1961 at Boots, UK (in Nottingham!), Ibuprofen is a non-steroidal anti-inflammatory (NSAID) that has taken the world by storm, becoming one of the most prescribed medicines in the UK. Ibuprofen was discovered by Stewart Adams, John Nicholson, and Andrew RM Dunlop after they were researching new treatments for rheumatoid arthritis and other inflammatory conditions. Stewart Adams famously tested the drug on himself to alleviate a hangover, which led to the discovery of its pain-relieving properties.

Ibuprofen works by inhibiting the activity of the enzymes cyclooxygenase-1 (COX-

1) and cyclooxygenase-2 (COX-2), which are involved in the production of prostaglandins, hormone-like substances that play a role in inflammation, pain, and fever. Because of this, Ibuprofen is commonly used to reduce fever and treat pain or inflammation caused by many conditions such as headache, toothache, back pain, arthritis, menstrual cramps, or minor injuries. However, compressing Ibuprofen is not without its challenges, with some reported problems of sticking, press downtime and abrasion, to name a few.

Sticking is the most frequently reported problem with ibuprofen. As many manufacturers will understand all too well,

however, is that sticking can be affected by many factors and what may be a solution in one scenario may not always work for another product. To combat sticking you must first understand the science behind it. When compressing powders into tablets, cohesive and adhesive forces are at work.

Cohesive forces hold a tablet together and are mainly affected by three elements: Van der Waals forces, capillary action, and electrostatic force. Van der Waals forces are attractive forces between molecules. They act over a short range but, in mass, combine to increase the cohesive force within a tablet and can also cause sticking. Capillary action can be linked to tablet formulations with high moisture content and is generated when moisture condenses in the gap between particles or between a particle and a surface. Static electricity is a major cause of sticking and often occurs when tableting dry granules. The resulting force can be relatively strong, with the potential to create both cohesive and adhesive forces.

Adhesive forces cause tablets to stick to the punch faces after compression. Adhesive force is affected by the surrounding environment, and the chemistry between the formulation and the punch. The environment around the tableting process and even around the formulation preparation process are critical. Temperature has a huge influence on some active pharmaceutical ingredients, Ibuprofen, for

example, has a very low melting point. In this case, lowering the temperature in the tableting area can help reduce sticking during compaction. When the adhesive forces between the tablet and the punch are greater than the cohesive forces holding the tablet together, sticking occurs.

In the case of Ibuprofen, I Holland has experience solving tricky cases our customers face. For example, one of our customers was experiencing sticking and picking on their 400mg Ibuprofen product. These common issues were causing press downtime, as tools had to be frequently removed and cleaned. Over 10 months, approximately 9% of production time was reported lost due to tablet press downtime caused by sticking & picking issues. The team wanted to run trials to see if coatings could improve their situation. I Holland was asked to investigate. I Holland supplied 3 sets of coated tooling for trials. 6 stations each of PharmaCote® CT, EC, CN+. We matched a like for like copy of their previous supplier's tablet drawings for consistency. The main aim of the trials was to challenge the press speed where no signs of sticking or picking occurred. It was discovered that PharmaCote® CT performed very well and succeeded the 2-hour target by far, with no sticking issues! Trials were run with a higher hardness range, and PharmaCote® CT was proven successful again for this formulation.

Oftentimes, to remedy sticking, manufacturers will slow down presses, however this can lead to a less efficient manufacturing cycle, with a decreased output. A suggested solution for solving sticking issues, without the need



## Tool coatings can alleviate production issues

for slowing the press, is to use eXtended Dwell Flat (XDF) heads for tooling, designed to increase dwell time by up to 50% on your existing press. Designed to run on standard cams it helps achieve higher press speeds with challenging products and formulations.

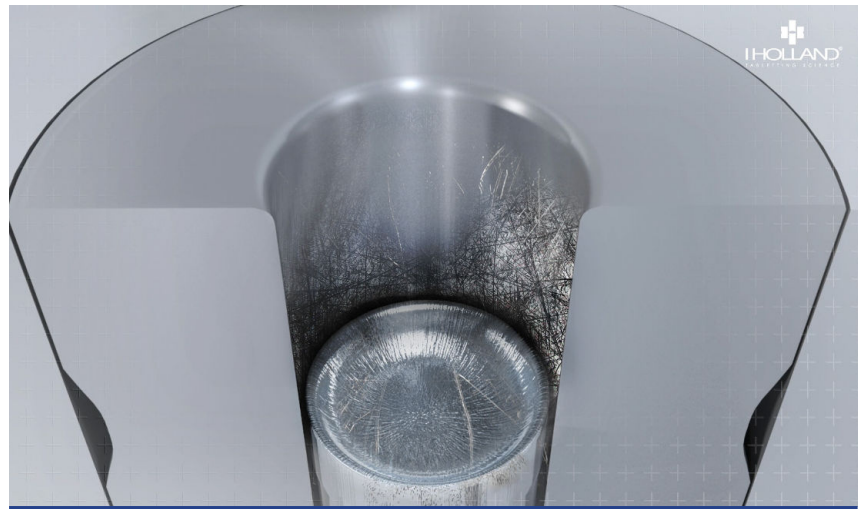
Utilising TSAR Predict prior to manufacturing can also help solve issues of sticking and picking before they occur. Using Ibuprofen as an example, I Holland can run the formulation through the TSAR software, which will then analyse how sticky the product is likely to be during compression, and suggest remedies for this issue, advising on the best tools and coatings for the manufacturing process. Sticking is detrimental to tablet production and costly, as it inevitably results in downtime and reduced productivity. To mass produce quality Ibuprofen tablets, you must first resolve any sticking issues. Because the physical properties of each formulation are unique, there is no one-size-

fits-all, anti-stick solution. Applying a predictive tool such as TSAR that analyses several sticking causes and suggests a suitable punch or die coating solution can save time and money compared to slow and costly on- or off-site compression trials.

With such a world-wide reach, it's important to get it right when compressing Ibuprofen, so that supply can meet demand. Something that must be considered when constantly producing a product to achieve a high-volume output, is the effect it has on the tooling. Simply put, the more you use your tools, the faster they will wear. As with many products, compression of Ibuprofen, can cause tool abrasion. Formulation characteristics like wide variation in particle size, poor compressibility, incompatible ingredients, and moisture sensitivity can lead to abrasion. In turn, this abrasion can lead to weight variation, sticking, and other problems and cause you to scrap punches too soon. Wear also degrades

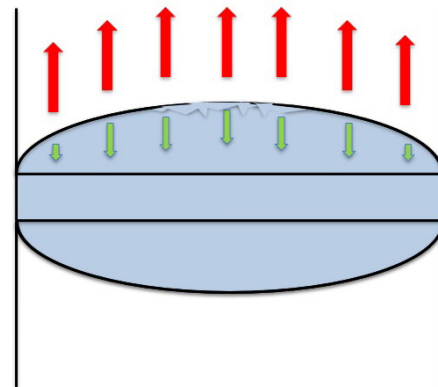
embossing on the punch face, leading to poorly defined if not illegible tablet lettering. To avoid replacing your tooling prematurely and to minimize tablet defects, use punches and dies made from a suitable steel. Also, consider adding a coating to the punch tips, as judicious coating choice can solve issues of both sticking and abrasion with one solution! All good quality coating solutions will increase the life of the tooling as they should have high abrasion resistance due to the coating elemental composition and hardness. Alternatively for abrasion alone, a review of the steel used to manufacture the tooling might be beneficial and this could reduce abrasion by again changing the steel composition and hardness.

Ultimately, issues experienced when compressing Ibuprofen can vary, but with some knowledge on how to deal with these problems, the problems become manageable. Understanding that Ibuprofen has properties that are affected by not only tooling choice, but also environmental factors can put you on track to dealing with them. When it comes to solving these issues, if you are unsure of your next step, contacting your tooling supplier is recommended. Reputable tooling manufacturers like I Holland have a wealth of experience in providing solutions for difficult products. Your supplier should also be able to advise on the correct steel type and coating. Getting it right the first time can save hours of work, eliminate the need for time-consuming trials and save money.

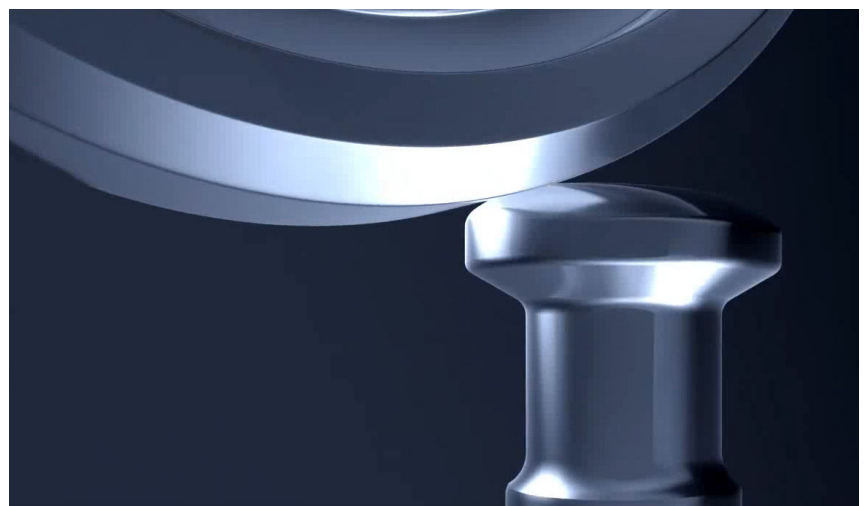


Tool abrasion

ADHESIVE FORCES > COHESIVE FORCES



Sticking is a battle of two forces



XDF heads eliminate the need to slow presses