I HOLLAND®
TABLETTING SCIENCE

A common anti-inflammatory drug

Alleviating Aspirin Issues

Aspirin, also known as Acetylsalicylic acid, is a nonsteroidal anti-inflammatory drug (NSAID) used to reduce pain, fever, inflammation, and as an antithrombotic. Aspirin is also used long-term to help prevent further heart attacks, ischaemic strokes, and blood clots in people at high risk.

In 1853, chemist Charles Frédéric Gerhardt treated sodium salicylate with acetyl chloride to produce acetylsalicylic acid for the first time. However, the real story of aspirins uses start much farther back in time, first in Ancient Sumeria (5500 – 1800 BC) where medicines made from willow and other salicylate-rich plants appeared in clay tablets. Ancient Egyptian texts also record using salicylate to relieve symptoms of pain. Hippocrates the 'Father of Medicine' himself, referred to the use of salicylic tea to reduce fevers around 400 BC.

In modern times, Aspirin is available without medical prescription as a proprietary or generic medication in most countries. It is also one of the most widely used medications globally, with an estimated 40,000 tonnes (50 to 120 billion pills) consumed each year.

With so many manufacturers producing this drug, problems during production are bound to arise, with reported issues of abrasion, sticking and picking, resulting in tablet press downtime.

Demanding processes are applied throughout manufacturing, and despite using hardened and high-quality tempered steel materials, punches and dies used to produce Aspirin can be affected. Abrasion of tooling leads to pitting, erosion, and deformation of the punch tips and die bores, amongst other tooling problems. Over time, the damage from abrasion can result in many downstream defects, including tablet sticking, weight variation, capping, and loss of logo detail. The resulting tablet defects lead to yield loss and product quality issues. If not addressed properly, issues of abrasion will render your tools obsolete, necessitating the purchase of more tooling, which not only slows production, but can also be a costly exercise, especially if new sets are frequently required.

I Holland has experience in helping customers before they reach this stage! For example, one of our customers was seeing severe abrasion on the tooling when compressing Aspirin, so they came to us for solutions on how to extend their tooling's lifespan. Their aim for the project was to have a set of tooling that would last a minimum of 100,000,000 tablets. After inspecting the causes of the abrasion, we offered a coating trial including the RS coating. The RS (Resilient Surface) coating has distinctive silver blue-coloured coating with superb wear-resistant properties and good resistance to corrosion owing to its to very hard surface layer. The customer was to inspect the tooling after every batch.

After running the trial with us, the outcome was fantastic and met their expectation with the RS coating. Even after 24 batches (96 million tablets) were made, thorough inspection showed the tip

face was still in good condition.
This case study highlights the importance of informed selection when ordering tooling from your tooling provider. If you can share your product with your reputable supplier, they can help tailor the tools to your needs, including choosing the correct type of steel and coating for your product. The ideal tool material balances durability and performance properties including anti-stick, abrasion and corrosion resistance. High tensile strength, toughness, hardness, and resistance to chipping and cracking are also important qualities to consider. There is a wide choice of tool steel, some specifically designed to compress abrasive or sticky granules and include high carbon, high chrome, cold work tool steels. For example, our HPG-P (Premium) is suitable for formulations that are particularly abrasive. Very high wear resistance tensile strength and toughness make it resistant to abrasion and fracture, meaning manufacturers experience reduced tabletting problems relating to the tooling.

Perhaps the most common problem manufacturers experience is sticking. Sticking is caused by the battle between cohesive and adhesive forces. 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 the attractive forces between molecules. These relatively small forces, in mass, combine to increase the cohesive force within a tablet but can also act as adhesive force too thus causing sticking. Capillary action can be linked to tablet formulations with high moisture content and is generated when moisture condenses in the gap between particles increasing the cohesive forces or between a

Steels and coatings have varying properties

particle and a surface thus increasing the adhesive forces and then leading to sticking. Static electricity is a major cause of sticking and often occurs when tabletting dry granules.

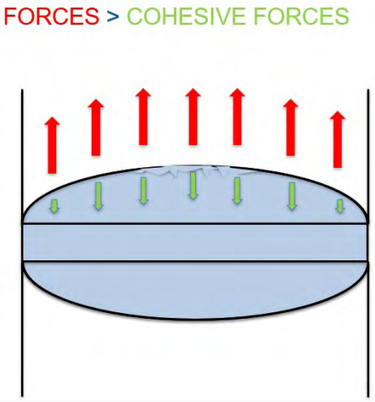
Adhesive forces cause tablets to stick to the punch faces after compression. Adhesive force is affected by the surrounding environment, and the chemistry between the formulation and the punch. The environment around the tableting process and even around the formulation preparation process are critical.
When the adhesive forces between the tablet and the punch are greater than the cohesive forces holding the tablet together, sticking occurs.

In the past, one of our customers was experiencing sticking, following them making changes in their Aspirin formulation. Using our knowledge of tooling we recommended using our CX coating on their tools. With its superior anti-stick properties and good corrosion and wear resistance, we believed it was the right choice to solve their issue. I Holland doesn't solely rely on belief however, so we used our scientific TSAR≈PREDICT model to confirm our choice, which it successfully did, allowing us to move forward with our customer and solve their problem.

TSAR≈PREDICT accurately forecasts the correct anti-stick PharmaCote® coating solution for your formulation. It calculates single particle adhesion to the punch tip face without the need for time consuming and expensive field trials. With a database of thousands of formulations and precedents, the software analyses how predicts the coating with the lowest single particle adhesion to the API and excipients during compression, and predicts remedies for this issue, advising on the best tools and coatings for the manufacturing process. A commonly used solution to sticking is slowing down press speeds, but naturally this only masks the symptoms of sticking rather than dealing with the cause. It also reduces efficiency, leading to some very unhappy managers! Staying informed and using preventive measures like TSAR ensures you don't have to compromise production to deal with problems that could have been solved during the tooling design and manufacture.

Similarly, whilst picking problems can be influenced by sticky products, oftentimes picking can be solved during the design stage of the tablets embossing. Picking is when compressed granule adheres to the detail (embossing/logos) on the punch tip and results in the 'picking out' of parts from the tablet face. This can lead to loss of detail to the embossing, tablet weight variation and can cause problems with downstream processes such as tablet coating.

When producing embossed/ branded tablets, sharp or intricate designs on the tablet can create powder traps. Therefore, it is important to use techniques to prevent this from occurring. To reduce picking the best practice should be to design font styles that have large open counters and no sharp corners, which could act as a trap for granule. Selection of the right font style can also help to avoid coating problems, tooling failures and lack of distinction. Fonts with curved sides can be used to increase spacing between the letters. By using curved characters, the potential for granule traps in tightly spaced embossing can be reduced. It is also essential that the spacing between the embossing is not too small generating further powder traps. As a general guide embossing should sit below the landed edge of the punch tip. If this guide is not followed, then the embossing will be unprotected and prone to damage. Working closely with a tooling manufacturer to



Sticking is a battle of adhesive & cohesive forces

Picking can result in a loss of embossing detail

design out issues like picking is critical to achieving trouble free production. At I Holland we regularly carry our video conferences highlighting to our customers (in real time) the design changes that will help achieve trouble free production.

Ultimately, optimising Aspirin tablet production requires addressing the unique challenges related to its properties. Manufacturers can achieve smooth and efficient manufacturing by combining hardened tool steels, specialised coatings, effective tablet design, and proactive maintenance. It is of course, always important to remember that whilst the problems and methods in this article are all proven methods of solving and minimizing Aspirin production problems, in the world of tabletting there is no one-size-fits-all approach. This highlights the importance of working with a trusted tooling manufacturer and giving them an understanding of your requirements and products during the initial stages. I Holland has almost 80 years of tablet tooling experience, and we're not shy about sharing our knowledge, and it's always better to solve production problems before they arise.