

The Science Behind Sticking & How To Solve It

Sticking is often described as the Achilles' heel of tablet production. It is one of the most common tablet tooling problems and can have a profound effect on production, leading to reduced output and increased costs. This article explains why sticking occurs and proposes several solutions.

Sticking – A Common Problem

During the manufacture of tablets, two of the significant problems that are commonly encountered are sticking and picking. These two issues can often be confused with each other, however put simply, sticking is the build-up of granule on the punch tip face, and picking is when product collects within the design or embossing detail on the punch faces and is 'picked' out of the tablet.

These problems can be caused by several different factors from the physicochemical properties of the formulation to the surface characteristics of the punch face. Issues related to the machinery, for example, the compression force and speed, as well as the environmental conditions like temperature and humidity can also have an affect.

Picking can normally be eradicated by design changes to the geometry of the tablet punch face, for example, changing the font style to one with large open counters and no sharp corners, which could act as a trap for granule. Sticking however can involve many root causes. The battle between the cohesive forces holding the tablet together and the adhesive forces between the ingredients in the formulation and the tablet tooling materials are some examples.

Cohesive vs Adhesive

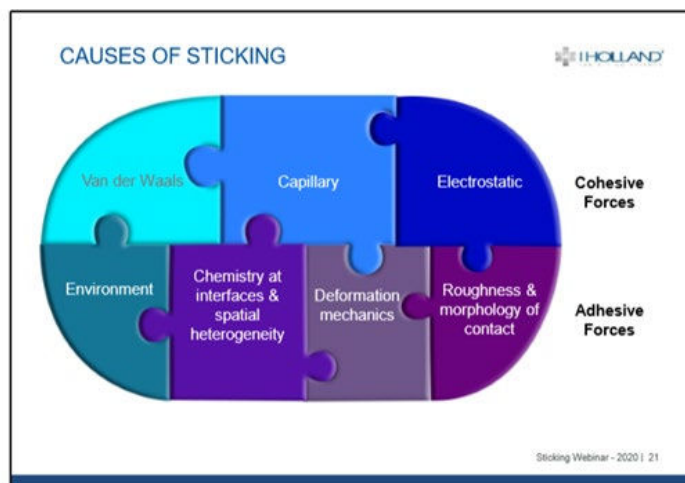
Sticking can occur if the adhesive forces are higher than the cohesive forces. A frequently used method to counter this problem is to boost the cohesive forces by increasing the tablet hardness as much as possible without taking the dissolution rate out of specification. Tablet hardness, however, must be even to prevent sticking.

With a concave tablet profile, the core of a tablet can be lower in hardness thus causing sticking to the centre of the punch face. This occurs because a concave punch tip profile compresses the formulation around the edge of the tablet more than in the centre due to the tablet profile. By adding a flatter profile to the tablet's design and changing the design of the tablet from a deep single radius to a double radius, the soft area in the centre of the tablet with the lowest cohesive force is reduced. This results in a more even tablet hardness, therefore helping to reduce sticking issues by increasing the cohesive forces.

Changing the profile can also be beneficial if the tablet is to be coated. If a single radius design is used, core erosion may take place. This is when the tablet comes into contact with the coating pan and other tablets causing wear. This vulnerability caused by mechanical stress during coating can be reduced by avoiding deep concaves. Additionally, the double radius profile will help the tablet to tumble in the coating pan more effectively, thus allowing an even coating thickness.

The Science behind Sticking

Because sticking is such a universal problem in the manufacture of tablets, tablet tooling experts have long studied how to prevent it through anti-stick solutions. In 2012 a two year project was undertaken by a leading global tablet tooling manufacturer to gain a detailed insight into the problem. The TSAR (Tabletting Science Anti-Stick Research) project investigated the root causes of sticking and looked at the solutions to solve it through a predictive mathematical model.



Sticking can be broken down into cohesive and adhesive forces

It was found that there are several influences that cause sticking from molecular attraction to capillary action. These can be broken down into cohesive and adhesive forces. Cohesive being the forces holding the tablet together and adhesive forces causing the tablet to stick to the punch faces.

Cohesive Forces

There are three elements within the cohesive force; **Van der Waals**, **capillary** and **electrostatic**.

Van der Waals force is the general term used to define the attraction of intermolecular forces between molecules. They act over a short range and are therefore affected by the surface roughness and the effective contact area. These forces are very small but in mass combine to increase the cohesive forces within the tablet and can also cause sticking.

Capillary action is another cohesive force, this can be linked to high moisture content. Capillary forces are generated when moisture condenses into the gap between a particle and surface causing a liquid bridge. The strength of these forces can depend upon the relative humidity, gap geometry and surface chemical condition. These capillary bridges increase the cohesive forces help bind the tablet together but can also have a detrimental effect by increasing the adhesion forces between the granule and the punch tip faces which can lead to sticking.

It is not only the formulation that can be problematic, moisture can also enter the production process through the environment in which the tablet is compressed. Excess humidity in the compression room or areas where the formulation is stored prior to compaction can also have a significant effect on making the formulation adhere to the punch tips.

If the granule is dry, often static electricity is formed, also a major cause of sticking. **Electrostatic forces** can also arise when tribo-charging (a transfer of electrical charges) occurs between contacting materials. The resulting force can be relatively strong and long ranged, and can create both cohesive and adhesive forces.

Manufacturing equipment can also have an influence. Tablet presses are usually connected to earth through means of an earthing cable. This is connected to the press and other components such as the hopper. Having conductive or non-conductive tool coatings or treatments can also influence these forces.

Adhesive Forces

The **environment** around the tabletting process and even formulation preparation processing are critical. The temperature has a huge influence on some Active Pharmaceutical Ingredients (API), for example Ibuprofen which has a very low melting point; it is therefore critical to keep this under control. Lowering the compression room temperature while compacting can help to reduce sticking.

As has already been highlighted, humidity, or moisture, in and around the tabletting machine and formulation processing equipment can also cause 'environmental' sticking problems by introducing capillary bridges between the granule and the tablet tooling faces.

During the TSAR project, and as a common test to measure the influence of capillary forces, a sessile droplet test was used to measure the interaction of each individual surface offered. This research technique should always be used when developing an anti-stick coatings or surfaces for tablet tooling as it establishes the level of hydrophilicity or hydrophobicity.

Hydrophobic surfaces will have a contact angle of more than 90 degrees, with hydrophilic surfaces achieving an angle of less than 90 degrees. During the research, the droplet contact angle is tested against different tool coatings all with varying contact angles.

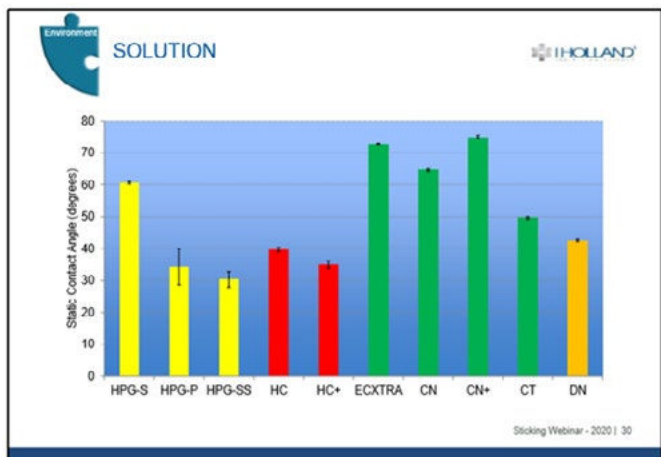


Image A - Water contact angle testing

Image A shows the water contact angle testing on a number of different coatings. The yellow columns represent different steels. These have various water contact angles because they all have different compositions and also polish differently.

The red columns are more traditional hard chromium based coatings which have been used in tabletting for many years. They are however becoming less common today due to the waste product being carcinogenic. Also, when hard chromium is applied to tooling a percentage of hydrogen penetrates the steel which can decrease the working load by 20%. This hydrogen embrittlement will make the steel brittle and prone to unpredictable fracture, therefore resulting in the need to decrease the punches maximum possible press force.

More advanced coatings have been developed in recent years that do not suffer from hydrogen-embrittlement and therefore are rapidly being used to replace the low tech Hard Chromium type coatings, these are shown in the green columns.

A case study was undertaken by tablet tooling expert, I Holland which tested a specific API. Image B shows the different adhesion forces

against the various tool coating solutions when measured using Atomic Force Microscopy. PharmaCote CN for example has a very low force and this stays low even when the relative humidity increases within the test environment. The adhesion forces in CN are low to begin with, this is because the elemental composition of the coating is not attracting the formulation. It stays low because the coating is moderately hydrophobic, or less hydrophilic than some other coatings.

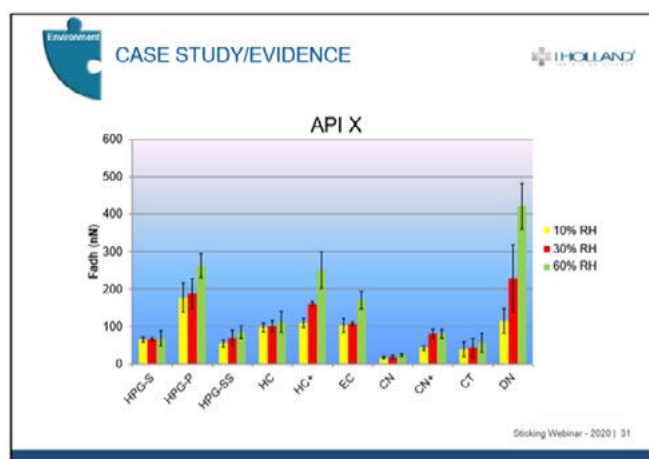


Image B - Case study results of adhesion forces against tool coating solutions

The diamond-like carbon type coating 'DN' represented on the graph shows that as the relative humidity (RH) increases from 10% up to 60%, the adhesion force increases quite dramatically. This proves that the coating would not be suitable for this particular API.

Chemistry at the Interface

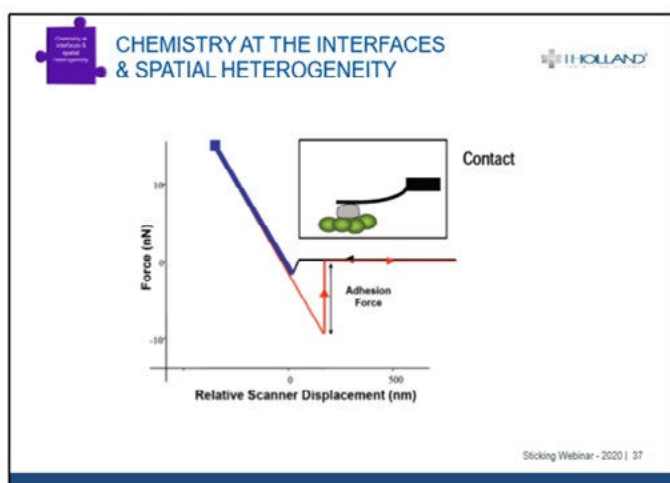
Adhesion forces between particles in a formulation and the surface of a punch are, as we know, the sum of a variety of forces, including van der Waals, capillary and electrostatic forces, all of which are influenced by the surface topography. There are several different instruments used to understand the **chemistry** at the interfaces and **spatial heterogeneity** of the formulation.

Scanning electron microscopy allows for very high magnification of up to 3000 times. This is used by sectioning the coating to look at its structure. Another piece of equipment used to study the chemistry is X-ray photoelectron spectroscopy. This examines the chemical

composition and the structure of either the steel or the coating.

Time of flight secondary ion mass spectrometry can be utilized to identify why particular formulations would only stick on certain areas of a punch tip. The equipment can be used to etch away the formulation that is stuck on one single area of the punch tip whilst identifying the elements within the formulation. This is continued by removing very small layers of the coating and the steel underneath. This examines any interaction in a localised area of the punch tip.

The final piece of equipment that is commonly used during the development of anti-stick coatings is the Atomic Force Microscopy (AFM). This provides nanoscale imaging of surfaces and has been used to provide direct assessment of particle-particle and particle-surface interactions in pharmaceutical research related to a range of issues, including initial work related to tablet punch adhesion (Waknis et al.; Wang et al., 2003).



Case study results from AFM experiment on water contact angles

AFM works by moving the probe functionalised with a single particle of either the API or excipient to the surface of a variety of punch tips and anti-stick solutions. The probe with particle would then be removed and the force needed to detach the particle from the surface of the punch tip would be measured.

Image B illustrates the result of the AFM experiment from the case study and shows the water contact angles, and how the different elemental compositions change the level of adhesion of the API to the surface. This experiment can also be done to measure the forces of an API or an excipient.

If the API is the root cause of the sticking, particularly if it is concentrated in one area of the punch tip, then this can overcome the elemental changes put in place by the selection of a specific coating chemistry.

Deformation Mechanics

The deformation mechanics, or physical properties of the granule being compressed can be either elastic or plastic in nature and this too can lead to sticking. Where the behaviour of a particle under compression can either stay deformed or 'spring back' to its original shape, the dwell time of the machine can be critical. In the case of formulations with more time dependant 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 predominantly elastic deformation behaviour, rather than brittle fracture behaviour. In a situation whereby a greater dwell period may be required, extended dwell flat tooling (XDF) will enable a suitable compression dwell time for a formulation without the disadvantage of slowing the press.

Tablet Tooling Surface

The **morphology** (surface roughness), or the outward appearance of the contact, can affect tablet production. The surface of the tablet tooling is critical to stop sticking. It is still a common misconception with many tooling suppliers that polishing the punch tip faces to a mirror finish would prevent sticking, this has been proven to be incorrect.

Through studying the interaction of different surface textures it has been established that the standard specification for tablet punch tip faces can include a range of surfaces that interact with formulations in different ways.

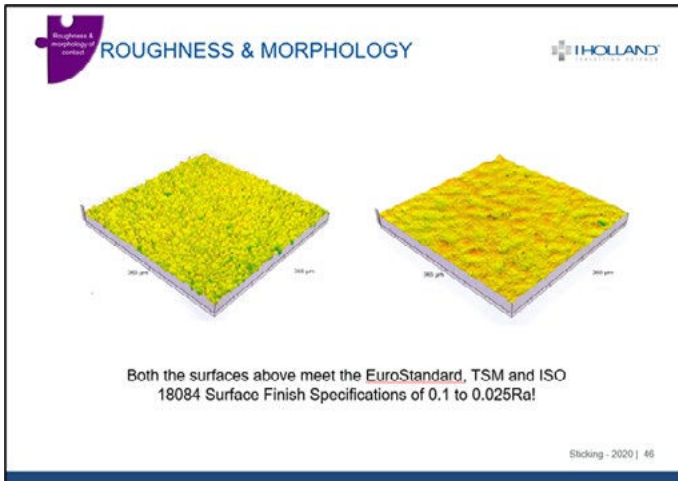
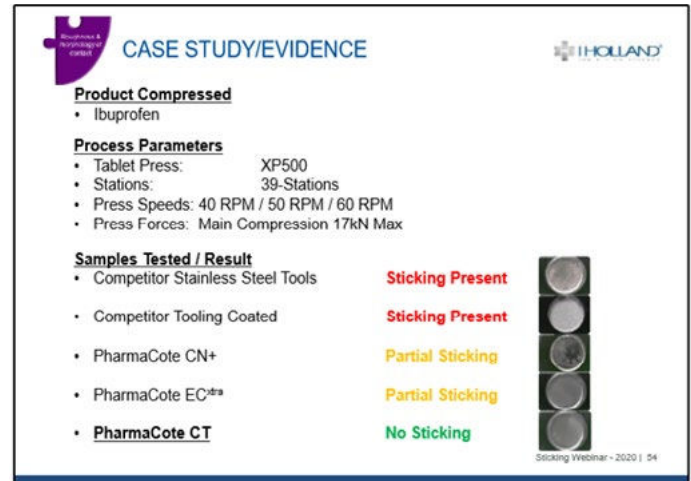


Image D – Different surface with that fit within the standard Ra value for punch tip faces

The required standard surface for a punch tip is between 0.1 to 0.025 Ra (Roughness Average). This difference can have a huge effect on sticking. Image D shows two different surfaces within the Ra parameters. On the left is tool coating PharmaCote CN and on the right is a surface engineered version with the plus applied, a unique proprietary process that modifies the coating surface, reducing the effect of formulation sticking to the punch face. The peak to valley height is the same on the CN coating as the plus process surface. When looking at the peak to peak value it is clear that they are hugely different from each other.

The surface condition of coatings all work differently to each other because of the surface roughness. It is critical to understand the effect on the interaction between the granule and the surface finish in order to stop sticking. This can be achieved through a number of methods including optical surface profilometry which measures the surface roughness after polishing takes place. Scanning electron microscopy can also be used which studies the structure of the steels and the coatings. Finally, AFM can be used to measure adhesion forces and create a nanoscale map of the surface.

A case study was recently undertaken which tested different coatings used to compress ibuprofen. It clearly showed that the surface condition of the tooling surface is critical to stop sticking.



Tool surface results on Ibuprofen

The tooling was placed in a tablet press with 39 stations, and run at three different speeds, with the main compression force of 17kN and a pre-compression force unchanged throughout the test.

Five tooling samples were tested including stainless steel and a range of PharmaCote treatments. The competitor's stainless steel and coated tooling created severe sticking, with the CN+ and ECxtra coatings presenting only partial sticking. PharmaCote CT coating was also used. This does not have a mirror finish and would once not have been used due to its Ra value, however in this instance it stopped all sticking issues in the compression of the ibuprofen formulation.

The Answer Lies in a Combination of Solutions

Sticking is detrimental to tablet production. The knock-on effect is costly as tablet press downtime and reduced productivity is inevitable. Sticking must be resolved in order to mass produce quality tablets.

There can be many reasons for the cause of sticking from Van der Waals forces, to capillary action associated with high moisture content, or conversely, from static electricity generated in very dry conditions. Because the physical properties of any sticky formulation are unique, there is no one-size-fits-all anti-stick solution. Applying a scientifically proven predictive tool which has been specifically developed to recognise the correct punch or die coating solution for a sticky formulation is the answer.

It is also one that will save a lot of time and money spent carrying out slow and costly compression trials off or on-site.

It is important to contact an experienced tooling manufacturer who understands the science behind tablet production and can introduce innovative solutions to tableting problems, therefore, maximizing production capabilities.

References

1. V. Wakis et. al., "Molecular basis of crystal morphology-dependent adhesion behaviour of mefenamic acid during tableting," *Pharm Res.* 2014;31(1):160-172.
2. J. Wang et. al., "Modelling of adhesion in tablet compression--I. Atomic force microscopy and molecular simulation," *J Pharm Sci.* 2003;92(4):798-814.



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