Leveraging Scientific Advances to Improve Tablet Manufacturing for Animal Health

In the pharmaceutical industry, prioritising product control, patient safety, and adherence to standards is crucial. This responsibility extends to maintaining the quality of solid dosage forms which are frequently utilised in veterinary medicine.

A tablet used in animal health consists of one or more active ingredients and numerous excipients and may be a conventional tablet that is swallowed whole, a chewable tablet, or a modified-release. Conventional and chewable tablets are used to administer drugs to dogs and cats, whereas modified-release boluses are administered to cattle, sheep, and goats. Tablets offer advantages in terms of physical and chemical stability compared to liquid dosage forms.[1]

Ensuring the quality and effectiveness of tablets in veterinary medicine is of utmost importance. However, there are a number of challenges that can occur during manufacture that may affect this, with the most common hurdle being sticking. Sticking issues can compromise the tablet's appearance, structural integrity, and dissolution properties, potentially affecting the delivery and efficacy of the medication.

Sticking occurs when granules build up on the punch-tip face of the tablet tooling. This issue is not only problematic for human tablets but also those used for animals and can result in considerable tablet press downtime and unpredictable production delays. Ensuring consistent tablet quality is vital for consistent mass production of quality tablets.

A Common Problem

So, why is sticking so common? The answer lies in several factors, including the formulation's physicochemical properties and the punch face's surface characteristics. These factors can be particularly challenging to manage when formulating tablets for animals, as their specific health requirements and dosage needs must be taken into account.

Fortunately, advancements in tabletting science have helped to find solutions to address sticking issues during tablet manufacturing. When these solutions are applied, they can dramatically improve production efficiency and tablet quality. It is important to prioritise proper quality control measures and adhere to dosage requirements in order to ensure the safety of animal medications. Minimising problems such as sticking during the tablet manufacturing process plays a vital role in achieving these objectives.

Distinguishing Picking from Sticking

Sticking can sometimes be confused with another common problem encountered during tablet production – picking. Picking is when the formulation becomes trapped in the embossing or design feature, leaving the finished product with visibly poor definition. Various approaches can be employed to address picking, with product design alterations such as the inclusion of embossed counters and tapered features.

To reduce picking, font styles should be designed with large open counters and no sharp corners where granule can become trapped. Additionally, the right font style can also help avoid coating problems, tooling failures, and lack of distinction.

Open islands or counters are highly susceptible to picking, and granule can easily become trapped in these areas on the face of the punch tip. To minimise this issue, the counter should be modified by reducing the depth of the stroke, thereby increasing the surface area and minimising the likelihood of picking.

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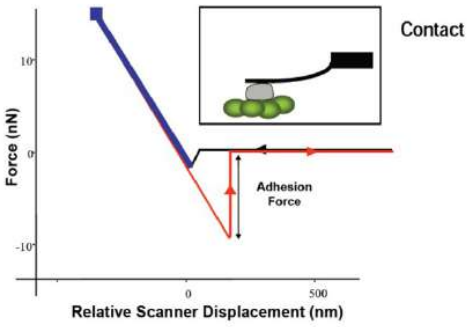


Another effective approach is the use of tapered peninsulas, which involve enhancing the corner radii in sharp, compound angles of the embossing detail. This tapered design blends the tablet face's surface with the stroke angle, resulting in a softer profile and reducing the risk of powder entrapment. By employing this method, definition can be maintained without compromising the overall stroke depth of the embossing, and ultimately helping to preserve a clear brand identity.

Understanding Sticking

Having looked at picking and its solutions, let's now focus on the most significant challenge in tablet manufacturing: sticking.

Sticking refers to the undesirable adhesion of the formulation to the surface of the punch tip face. This accumulation of granules leads to tablet defects, initially affecting the tablet's appearance and potentially progressing to issues like double compression and damage to the tooling and press.

Consequently, production is stopped while regular cleaning and maintenance are carried out on the tablet tooling to eliminate the granular build-up. This, in turn, results in costly tablet press downtime and reduced productivity.

Sticking can be understood as a battle between the cohesive forces that hold the tablet together and the adhesive forces between the ingredients in the formulation and the materials used for the tablet tooling. If the adhesive forces outweigh the cohesive forces, sticking becomes inevitable.

Where the tablet profile is a concave shape, and the core is lower in hardness, there is a tendency for sticking to occur at the centre of the punch face. This is because the concave punch tip profile applies more compression to the formulation along the tablet's edges compared to the centre, making it stick. To address this issue, incorporating a flatter profile in the tablet design and utilising a double radius can help minimise the soft area at the tablet's centre. This adjustment promotes a more uniform tablet hardness, thereby mitigating sticking problems by increasing cohesive forces.

To effectively address the challenge posed by cohesive and adhesive forces, it is crucial to delve deeper into the intricacies of both elements.

Cohesive Forces

When examining cohesive forces, it is essential to consider three key elements: Van der Waals forces, capillary forces, and electrostatic forces. Van der Waals forces occur when molecules attract each other. Within a formulation, elements naturally attract to the materials of the tablet punch. Although these forces are relatively weak, measuring only in nano-newtons, their cumulative effect on the tablet face can lead to sticking.

Capillary forces arise from moisture present in the formulation. When moisture condenses between a particle and the tool surface, it forms capillary bridges. The strength of these forces are influenced by factors such as relative humidity, gap geometry, and surface chemical conditions.

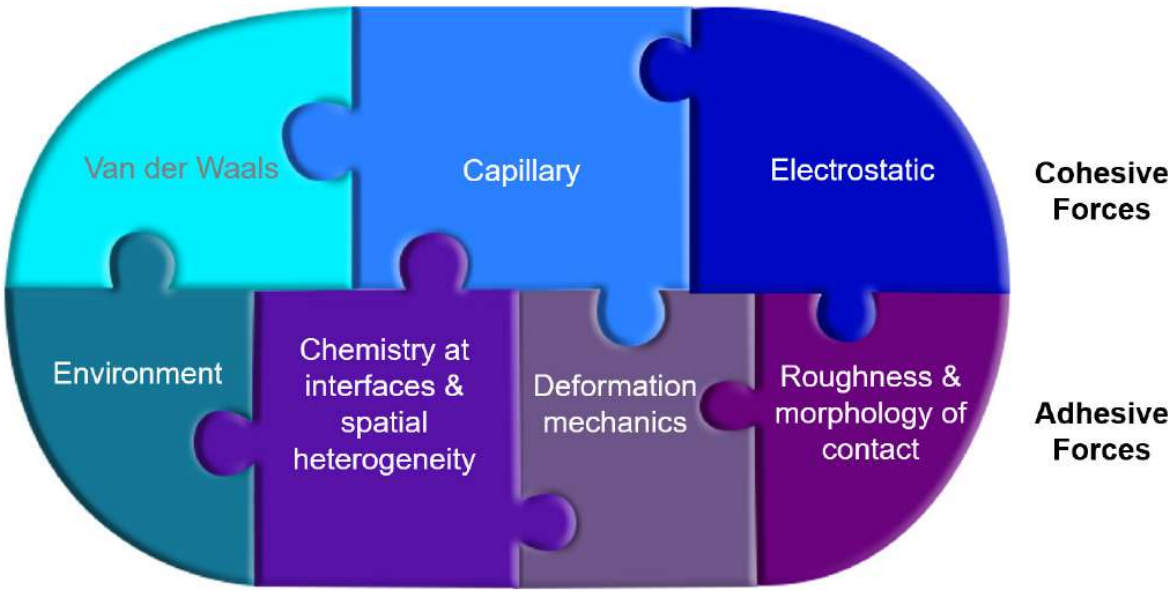
Electrostatic forces occur when there is a transfer of electrical charges between contacting materials. For instance, during pharmaceutical powder processing operations, powder particles frequently come into contact with each other and the equipment walls, leading to electrostatic charging through a process called triboelectrification Conductive or non-conductive tool coatings or treatments can also influence tribo-charging. These long-ranged and strong forces contribute to both cohesive and adhesive forces.

Adhesive Forces

Multiple factors influence the adhesive forces leading to sticking between the formulation and punch tip faces. The tablet production environment and formulation preparation process play a role. Temperature, for instance, can affect certain Active Pharmaceutical Ingredients (APIs) present in formulations. It is crucial to consider this and lower the compression room temperature during compaction to minimise sticking.

Moisture or humidity levels in the air can also increase adhesive forces, forming capillary bridges between the granule and the tablet tool face. Additionally, the chemistry at the interfaces and the spatial heterogeneity of the formulation contribute to adhesive forces. Various techniques and equipment, such as scanning electron microscopy, X-ray photoelectron spectroscopy, time-of-flight secondary ion mass spectrometry, and Atomic Force Microscopy (AFM), can be employed to investigate these factors.

Deformation Mechanics represents an additional adhesive force that can result in sticking. The granule's physical properties during compression can demonstrate either elastic or plastic behaviour. Under compression, a particle can either maintain its deformed shape or return to its original form.



Formulations with time-dependent consolidation behaviour necessitate a longer dwell time to facilitate the formation of robust bonds between the particles. Consequently, extended dwell time during the main compression phase becomes particularly crucial for formulations exhibiting predominantly elastic deformation instead of brittle fracture behaviour. The utilisation of extended dwell flat tooling (XDF) enables an adequate compression dwell time without negatively impacting the press' performance.

The correct morphology or surface roughness in tablet tooling is crucial for preventing sticking issues. While many tooling suppliers assume that highly-polished punch tip faces effectively prevent sticking, this assumption does not always hold true. By carefully examining the interaction between different surface textures, the standard specification for tablet punch tip faces can incorporate a range of surfaces that interact with formulations in diverse ways. For example, the required standard surface roughness for a punch tip typically falls within the range of 0.1 to 0.025 Ra (Roughness Average). Even this slight difference in roughness can significantly impact sticking.

Understanding the influence of the interaction between the granule and the surface finish is key to preventing sticking. Techniques such as optical surface profilometry, which measures surface roughness after polishing, can help draw conclusions. Additionally, scanning electron microscopy can be employed to study the structure of the steels and coatings, while Atomic Force Microscopy (AFM) allows for the measurement of adhesion forces and the creation of a nanoscale map of the surface. These analytical methods aid in comprehending the intricacies of the granule-surface interaction and inform effective strategies for preventing sticking.

The Solution to Sticking

Sticking is a pervasive issue in the production of solid dose forms, prompting tablet tooling experts to study anti-stick solutions extensively. The TSAR (Tabletting Science Anti-Stick Research) project investigated the reasons behind sticking and sought solutions through a predictive mathematical model. It conducted tests with various excipients and APIs, measuring the forces exerted by each against a range of tool coatings. This research provided insights into the appropriate punch or die coating for preventing sticking in specific formulations. Importantly, this approach eliminates costly and time-consuming in-the-field testing, allowing tablet production to proceed uninterrupted.

Choosing a suitable anti-stick coating is crucial, as both conductive and non-conductive tool coatings can impact cohesive and adhesive forces. Specialised punch and die coatings can significantly enhance the efficiency and output of tablet manufacturing when used alongside high-quality tooling steel. They minimise the need for tools to be removed from production for additional cleaning, thus improving tabletting efficiency.

Since the physical properties of sticky formulations are unique to each case, there is no universal anti-stick solution. Therefore, consulting with an experienced tooling equipment supplier who can accurately identify the specific reasons for sticking through tried-and-tested scientific calculations and provide a tailored resolution.

Consistent Quality

In conclusion, sticking is a common challenge faced

during tablet manufacturing, which can compromise the tablet's appearance, structural integrity, and dissolution properties, potentially affecting the delivery and efficacy of the medication. However, advancements in tabletting science, such as the TSAR project, have paved the way for effective anti-stick solutions. By understanding the complex interplay of cohesive and adhesive forces and leveraging specialised punch and die coatings, tablet manufacturers within the animal health sector can significantly improve production efficiency and maintain consistent quality.

REFERENCES

1. https://www.msdvetmanual.com/pharmacology/pharmacology-introduction/routes-of-administration-and-dosage-forms

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Since joining I Holland in 2004 Rob has been instrumental in the development of I Holland's PharmaCote® range of surface treatments and coatings for tablet compression tooling designed to improve properties such as wear resistance, corrosion resistance and antistick characteristics. He was also part of the Eurostandard steering committee and responsible for I Holland's registration to ISO 9001:2008. Rob holds multiple patents linked to solid dose manufacture and co-ordinates I Holland's close collaboration with various respected academic research bodies.