Tooling Design – How Tooling Options can Benefit Different Types of Pharmaceutical Formulations During Tablet Compression

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It can be a labour of love to get a tablet to market. With time and monetary investments made throughout the process from research to development and scale-up, one of the most challenging steps in the process can be the actual manufacture of the product. Issues range from tablet quality to equipment malfunction – all of which can result in downtime and delayed market deployment. However, there are steps that can be taken to eliminate or minimise these issues before manufacturing even begins.

Proper tooling and tablet design can greatly improve the tablet manufacturing process. But how do you know what's suitable? How is it possible to eliminate issues before they occur? Through good cross-team communication and a thorough knowledge of your product's performance characteristics.

At the point when your R&D team hands off a product to be manufactured, they are intimately aware of the formulation's physical and chemical makeup. As the formulation is granulated and prepared for compression into the final tablet, how well have the formulation's characteristics been discussed with the tablet compression team? Were they involved in the tablet and tooling design process? It's important that these experts be involved well before it's time to produce tablets, because these staff members often hold the key to your tablet's successful compression and product launch.

Powder characteristics, ambient relative humidity, tablet design – these factors may all play a part in successful (or unsuccessful) tablet manufacturing. An experienced tablet compression team can provide guidance on how to avoid issues such as sticking, picking, and potential tablet defects before any tablets are produced. The first line of defence for avoiding tablet compression problems is tablet design, which should be done with input from all team members, including an experienced tooling vendor.

The prepared powder formulation and compression tooling share a symbiotic relationship as they work together to generate your tablets. If one is not suited to the other, you may end up with unfortunate results. It's necessary for the characteristics of your tooling (material, design, etc.) to complement that of the powder (particle size, powder abrasiveness, compression ratio, tablet breaking force specification, etc.)

The three most common processing routes to prepare different powdered components for compression are direct compression blending, dry granulation, and wet granulation. Determining which route to employ is based on the tablet properties needed to meet the clinical requirements of the medicine.

Direct compression is used if the ingredients (API, excipient, etc.) are able to be blended and a tablet compressed that meets tablet dissolution and content uniformity requirements. Direct compression is a convenient (and the least costly) method to blend together the active pharmaceutical ingredient (API) and the excipients, fillers and lubricants required to make the desired tablet. Care must be taken to ensure blend uniformity is achieved before proceeding to compression.

Granulation is the process of collecting particles together and forming granules, either through compaction or by adding a binding agent.

Dry granulation is employed when ingredients in a formulation are sensitive to moisture or heat and are not amenable to direct compression blending. This is a mechanical bonding of particles without using a liquid to bind them. In this method, the particles are compacted commonly by using a roller compactor, or chilsonator. This increases their density and results in granules being formed from smaller particles. The resulting ribbon or pellets are then milled into a powder with the desired particle size distribution, which will be put through the

compression process on a tablet press.

When the physical properties of the API preclude the use of direct compression or dry granulation, then wet granulation is utilised. The API and excipients are mixed under high shear conditions and liquids are sprayed into the mixture to induce particles to stick together. Binders are added as part of the liquid or as part of the powder charge to enhance granule growth. Once the granules are formed, they are dried and subsequently milled and blended to yield the desired formulation.

Although wet granulation can be an expensive and time-consuming process, it is sometimes necessary to meet drug performance specifications. Wet granulation can cause problems during tablet compression if there is latent moisture retained in the finished powder. Capping, laminating, sticking and picking are common tableting issues that may need to be addressed and resolved before manufacturing. Often the tablet compression tooling is considered responsible for these issues, when the root cause should have been identified and eliminated during the development process.

There are an infinite number of tablet design and tooling options, including materials of construction of the compression tooling available to tablet manufacturers today. With all of the options available, it would be beneficial for tablet manufacturers to consider how their granulation method and powder preparation could influence the tablet and tool design to improve the end result.

The tablet compression tooling should be engineered and manufactured with consideration for the product being compressed. Often there is too much emphasis put on utilising a company standard tablet configuration, even though each formulation is unique. Ideally, tablet designs and compression tools should be configured for each individual product and formulation. Today, with many manufacturers utilising direct compression blends to reduce costs, the company standard tablet configuration should be modified or success is challenged.

A formulation that compresses easily with tools that have a deep or compound cup also will compress readily in a shallow or standard cup tool. The opposite is not always the case. Formulations that are difficult to compress receive better results using shallow or standard cups, not deep or compound cups.

Consider a powder made using dry granulation. These powders can experience particle segregation leading to excessive fines (dust.) Fines that recirculate around the die table are reintroduced into the feeder, causing changes in blend uniformity. This can result in tablet property variability as fines have different compaction properties.

In addition to compaction issues, there are other problems that can arise from excessive fines. First, because of their very small size, fines are more likely to result in migration of small particles into areas of the press which can be detrimental to the tableting process. As the fine particles migrate between the lower punch tip and die (see Diagram A), it may cause tip binding, lower punch tip wear, die bore wear, cam wear, excessive ejection force and heat generation, which can be a cause of sticking and tablet discolouration. Other possible tableting deficiencies that result from sifted particles are capping and lamination.

Sifted product can contaminate machine components and the lower punch guides, compromising the lubricity value for the lower punch barrel and head. This can result in the accelerated wear of various press components, leading to issues such as tool binding and resulting in manufacturing losses. Even if the press continues to run properly, the fine particles will make the press much more difficult to clean – adding time when preparing and implementing a product changeover.

While excessive fines can be addressed before tablet compression begins, if it becomes necessary to use a formulation that is prone to fine particles, there are tooling design options that can alleviate or reduce the effect of fines on the tablet compression process – thus allowing the tableting process to

be executed successfully. It's because of these issues that your tablet compression team should be involved throughout the product development process. If the final formulation's inherent characteristics may cause tablet compression issues, it may be possible to modify the tablet and corresponding tooling design to avoid them.

For instance, the tablet compression team may suggest that the lower punches be manufactured with a narrow tip width and deeper than normal relief (see Diagram B). Although it is a small adjustment to the design, narrow tip width is a good choice for dry blends because it can help to reduce and, in some cases, eliminate many of the issues relative to the fines that result from the dry granulation process. As fines have a greater propensity to adhere to the die wall, a narrow tip combined with a deeper relief provide an improved scraping action to help clear the die bore of any built-up excess granulation.

The build-up of fines in the die bore combined with the repeated linear motion of an unmodified lower punch results in increased friction between the lower punch tip and die bore. This friction causes heat which can lead to other issues, especially for heat-sensitive products or those with low melting-points. Not only will the deeper tip relief scrape excess product from the die bore more effectively, it will also cause less friction and result in less friction-generated heat. This is because the narrow tip width reduces the tip to die bore contact area.

There are many tooling options and materials available to produce robust, long-lasting punches and dies. Often, the tooling used to compress the tablets becomes an afterthought. Keeping your tablet compression team engaged can bring significant cost savings as well as increased efficiency when tablet manufacturing commences. Armed with knowledge about the powder's characteristics, tablet manufacturers are encouraged to consult with the tooling supplier to design and select the most appropriate material and tooling design.

Standard tool steels are routinely chosen for their overall balanced characteristics and for their ability to handle shock loading conditions. Some steels are only suitable for punches while others are only suitable for dies. For example, due to its high chrome and high carbon content, D3 steel exhibits high wear resistance but is very poor at accepting impact loads and compression stress. Therefore it is a preferred material for dies but a poor choice for punches. Steels with higher chromium content are good in situations where the product being compressed is corrosive or sticky, while tool steels with higher Rockwell hardness are ideal in situations where abrasive wear is a primary concern. There are tooling options such as shortened, strengthened lower tips and undercut dies that can be utilised to prevent the bending of lower tips when making very small tablets. Additionally, the punches can be designed with an extended head flat to increase dwell time for difficult to compress products.

These are just a few of the solutions available to tablet manufacturers. Tooling can be specifically designed to complement the formulation properties from which the tablet will be compressed. Even at the critical tablet design stage, pre-pick or taper of the engraving (see Diagram C), along with unique cup configurations and modifications, can be implemented to prevent issues such as sticking, picking, capping, lamination, and accommodating the desired compression force. Some products requiring a higher compression force may benefit from a shallower cup depth and/or the addition of land.

Even something as simple as changing the finish on the punch face can make a big difference on how a specific formulation runs in the press. Punch tips can be coated in chrome to improve wear resistance and other coatings can be utilised to combat other problems. Adding a coating is not the preferred method for alleviating tableting issues. Choosing the proper steel type and tooling configuration to compress marginal powders is preferred and can provide a long-term solution where coatings generally cannot. Some coatings can be cost-prohibitive and offer negligible results.

It is still best practice to ensure the delivery of a proper formulation. Often powders simply cannot be compressed effectively. Thorough, clear communication between internal departments and involving the tooling supplier throughout the tablet development process is truly the best way to ensure successful tablet production. This ensures that once the granulation reaches the tablet compression unit, the most suitable tooling has been prepared to complete the process.

Such preparation can bring measurable savings to your organisation. Not only will tablets be produced efficiently and on schedule, meeting critical launch dates, but also the equipment used for production will be subjected to less wear and likely require less unscheduled maintenance.

Some reputable tooling suppliers provide in-house scientific services and are partnered with university-based research organisations to provide unique insights into powder properties and compression profiles that offer solutions supported by data and current best practices. It is recommended that tablet manufacturers communicate with and take advantage of available resources and the experience of their tooling supplier.

As an engineer with Natoli Engineering Company, **Kevin Queensen's** experience has been focused primarily on specialty tablet/tooling designs along with determining new max compression force calculation methods and performing Finite Element Analysis (FEA). He holds a B.S. in Mechanical Engineering and was recently asked to join our Technical Support/Engineering Team to assist customers with tablet and tooling designs and solving technical issues.

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