

tableting

PREVENTION IS THE BEST CURE FOR TABLET DEFECTS

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A hands-on tableting consultant offers advice to tablet press operators and their supervisors.

I cut my teeth operating and repairing tablet presses, but it wasn't until I sold the machines that I really learned how to solve other people's problems. In those days, after a sale, I'd often get the buyer calling to tell me that the tablet press wasn't working right. (Some buyers even asked me to take the machine back.) In those cases, I would calmly ask the buyer to describe the problem. "It's not making good tablets," was a typical response, and they had concluded that, "Something must be wrong with the press," and they would ask me to come fix it. Rarely was the press at fault. In fact, most times the trouble was self-inflicted.

That's still true today. Take, for example, the call I got from someone whose company had won a contract to supply detergent tablets to Wal-Mart. That's a nice piece of business, but the company skimped and bought a used press missing all kinds of parts. When I told the caller it would take weeks to get the right parts, she actually sobbed: The company needed 4,000 samples ready in 4 days or the Wal-Mart deal was off. So I fashioned temporary parts (including an ejection cam made of oak) and got the tablet press running. Then the powder wouldn't flow. Then it wouldn't compress. Then, just for good measure, the tablets wouldn't eject. Those problems kept a group of us working with very little sleep from Friday to Monday, but we got the press running and fixed the powder problem. Most important, we met the deadline, and the company still has the Wal-Mart business.

Follow SOPs

All good tablet press operations share one important attribute: Adherence to standard operating procedures (SOPs). Companies with poor tableting operations brew their own special combinations of problems, but they, too, have something in common: They're reactive, always in repair mode. Here's a tip for those folks: The best way to solve problems is to avoid them.

That means understanding and following SOPs while employing GMPs. It boils down to "get it clean," "get it ready," and "keep it clean." Turn your tableting team into an Indy pit crew: When the race car (tablet press) comes in for a pit stop (changeover or cleaning), know what needs doing, do it well, and do it fast. If you don't, your press will be idle more than it should be, and if it's not making tablets, your company's not making money. When (not if) you encounter a problem, the first step is to disassociate



Photo shows wet, densified buildup on the blades of a mill used before final blending and tableting. If the tablet operators knew about this buildup, they could anticipate the picking and sticking that is likely to ensue. But usually, they aren't privy to information about upstream processes.

emotion and panic from the problem. Think it through. Maybe the scenarios I describe below will help you.

Ingredient-related problems

"We're having problems but nothing has changed, so we can't figure it out." Those words, "nothing has changed," are very common and almost never true. Something has changed, and many formula problems come from changing raw material suppliers or from changes that a heretofore-reliable supplier has made without informing you. Don't rely on the purchasing department to tell you about these changes. Those folks are usually given only general specifications, and when ingredients seem comparable, they often opt for the cheaper one. Meanwhile, operators on the production floor are scratching their heads, "Hm. It worked fine last week."

If the ingredients themselves are not the problem, maybe improper shipment and/or storage is to blame. You can't control shipment conditions, but once the ingredients are at your site, how you handle them may determine the success or failure of the process, because raw materials can be greatly affected by the environment in which they're stored. Many, if not most, raw materials are sensitive to temperature (heat) and moisture, and uncontrolled warehouses (fluctuating temperature and relative humidity) seldom provide the best storage. Yet many people still use them. (I've been known to suggest moving managers to the warehouse and storing the raw materials in their offices.)

Not long ago, I was at a Big Pharma site to resolve an encapsulation problem, but the point of this tale also pertains to tableting. These Big Pharma folks were convinced that the capsule filler wasn't working right. Actually, the problem was of their own making: They had stored the capsules in a hot, humid warehouse, where the capsules swelled and cooked a little, causing the caps to become "glued" to the bodies. In the production area, they simply would not feed, rectify, or fit correctly into the segments. All of this was obvious to me, yet they had spent many hours thinking of ways to fix the machine.

Powders destined for the tablet press also degrade when stored incorrectly, absorbing or shedding moisture, and sometimes forming agglomerates that are rock hard. Bad storage can influence flow, weight control, compression, hardness, friability, and sticking, to name just the most common effects. By the way, when moving ingredients from an uncontrolled environment to a controlled environment, give the ingredients time to adjust before using them. You'll have more success.

What's past is prologue

The unit operations that precede tableting are intended to make the powder ingredients work on the press. Granulating, milling, and blending are supposed to improve flow, compressibility, and ejection so that the powders can be controlled precisely to achieve accurate tablet weight, hardness, thickness, friability, disintegration, dissolution, and appearance. Recognize that the tablet press is the report card. It tells you how well you conducted the preceding unit operations.

Listen to the press. Sometimes the feedback is audible. Lack of lubricant (lube) like magnesium stearate, for instance, will make the press squeak or even lock up. An overly dry granulation will run rougher and hotter than it should, affecting compression. A good press operator can



What to make of this yellow buildup? Perhaps the product has a low melting point. Or maybe it's an inherent characteristic of the powder. It could also indicate a poorly granulated or poorly blended formula. Whatever the cause, it is sure to shorten run time on the press and, if the press is allowed to run too long, the buildup will damage the punch heads and cams because the tip is binding in the die. Ideally, the press operators and a supervisor would meet with the people in charge of the upstream process, explain what they're seeing, and devise a plan to fix it. In reality, most companies just live with problems like these. The result is less production, more downtime, and damage to the press and tooling.

often hear and feel changes in the granulation through the press. Recognize that there is no such thing as a perfect blend. Be ready for variations in the blend. Don't be surprised when they happen.

The age difference. Keep in mind that blends get old. Some deteriorate in a few days, others in a few weeks. Not many last much longer than that. I walked into one place and saw that the staging area in front of the compression department was stacked floor to ceiling with blended product "ready for compression." I knew right away that they had compression problems. If it helps you, think of blends as fresh-baked bread: Both need a rest before they're consumed, but they go stale if they sit too long. In short, don't put powders on the press right out of the blender. Let them stabilize. But don't wait too long after that to compress them. Generally speaking, wait 12 hours after blending to compress the powder, but don't wait more than 4 days. That's when they settle, de-aerate, segregate, or agglomerate. Every blend has a different window of opportunity. Watch the results and listen to the operators when they say the stuff isn't running right.

Blend sequence and lubricant. People at pharmaceutical and dietary supplement companies often misunderstand the role of final blending and its profound impact on tablet quality. There is a proper sequence to blending, and just dumping all the ingredients into the blender is a recipe for disaster. But I see that all the time. Sometimes ingredients, especially the minor ones, must be pre-blended. The powder lube (usually magnesium stearate) must be the last addition. This lube (mold-release agent would be a better term) must be lightly blended in with the rest so that, as the particles flow onto the press, they contact and coat the metal surfaces of the press and tooling.

I had a heck of a time convincing one company's management team that their idea—digging a hole into the powder blend and burying the lube—would prevent it from dispersing to the surface where it could contact the tooling surfaces. They were worried that the lube would stick to the steel. Ahem: That's exactly what is supposed to happen! Streaks on the sides of tablets are often blamed on the press and its tooling, but the real message is that the lube isn't working.

Lube usually constitutes less than 2 percent of the blend's total weight. Many formulators dilute the lube with other excipients (commonly talc) to achieve blend uniformity. That's a bad move. It hides the lube, reducing effectiveness and promoting sticking, picking, lamination, and hardness issues.

Shortcuts fall short

If you're not having problems, great. Let the press run. Only when it's loaded with fine dust and the oil dries on the punches is it time to stop and clean. Run the press longer and you run the risk of damaging the press and tooling. I repeat: Stop the press first. I caught one operator holding an oiled rag against the punches while the machine was running. Before I could enter the room, the press ripped the rag from his hand. Luckily he wasn't hurt, but I know people who have lost fingers from simi-



Damaged tooling is the result of tight punches caused by poorly processed powders. Don't blame the press operator. It more likely stems from high compression forces, high ejection forces, poor lubrication, and/or a lack of dust collection. The tablet press is the report card, laying bare the mistakes of the previous operations.

lar stunts. So why did he do it? He didn't want to stop to clean because the batch was nearly done.

Another time I saw an operator using a metal spatula to scrape powder buildup off the die table while the press was running. The press didn't balk as it transformed that spatula into perfect metal tablets. Never keep the press running just to get through a batch. It's a shortcut that can lead you right off a cliff.

Back to SOPs: They aren't for decoration. They're meant to be followed. I watched in amazement once as a die flew out of its socket and crashed into the feed frame,

causing thousands of dollars in damage. The SOP hadn't been followed. Another time, a cam was so far out of position that a punch head snapped off, fell onto the feed frame, and broke a section of turret that held six punches. No one had double-checked the setup, resulting in \$37,000 of damage, 6 weeks of repair, and an operator looking for a new job. I always tell operators, "Nobody pays you enough to get hurt." Yes, it takes time to clean and assemble a press and double-check the setup. Would you rather spend that time fixing mistakes?

In a final illustration of how shortcuts can be counter-productive, I watched as an operator used an air hose to blow dust off a running press, which sent oily, dirty granulation all over the compression zone. I couldn't resist the urge and suggested that he take the black-speckled tablets he'd made to quality control for feedback and suggestions.

Sometimes it's not a shortcut, but inattentiveness that creates problems. That was the case when a guy forgot about the black marker in his shirt pocket. It fell into the tablet press hopper and broke apart when it reached the feeder. The felt tip distributed permanent ink into a perfectly white powder, and we all discovered a new root cause for black spots in tablets.

T&C

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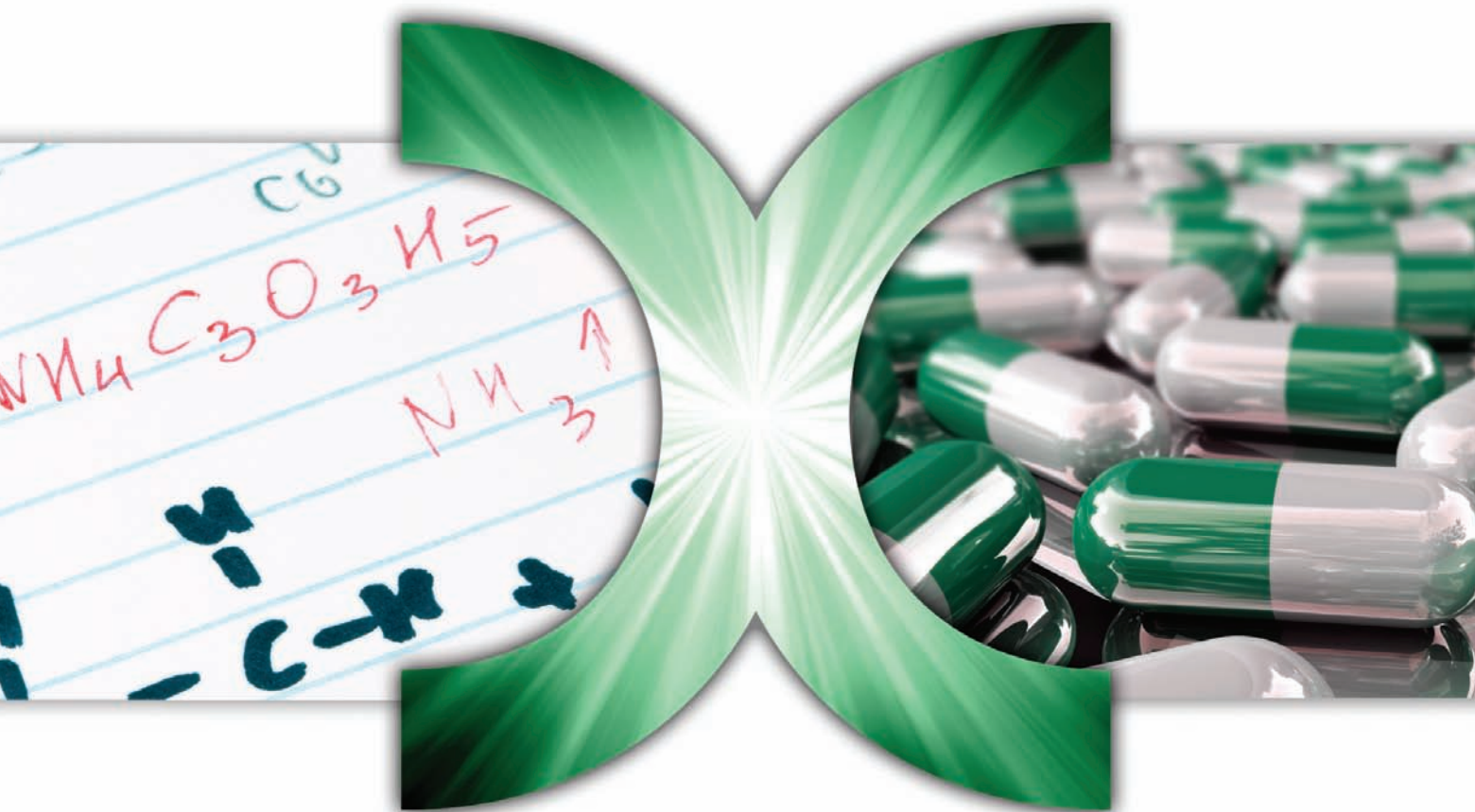
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