

# A Novel Compression-Coated Tablet Dosage Form

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The authors describe a tablet press concept for the facile production of compression-coated tablets by obviating the need to manufacture core tablets in a separate operation. Prototypes of the dosage form were produced with special tooling on a laboratory press and evaluated for their ability to form compression-coated tablets from poorly compactible substances and to control the release of drugs within the core by using suitable polymers in the coating blend.

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A new chemical entity often is first formulated as a free-flowing granulation for encapsulation within hard gelatin capsules. During the course of clinical development, the drug-containing granulation usually is modified for compaction into a tablet product. The tablet product subsequently may be film coated for taste masking, identification, or other purposes. Tablets are the most preferred and widely used dosage form because of their ease of administration, lower cost of manufacture, and elegance. In this article, we describe a means of producing tablet dosage forms (specifically, compression-coated tablets) from granulations or blends that do not readily form a compact. The compression-coating granulation or blend can be preformulated to provide desired functionalities to the coating. The only requirement for producing the compression-coated tablet dosage form described herein is that the core material should possess the ability to flow into a die during production.

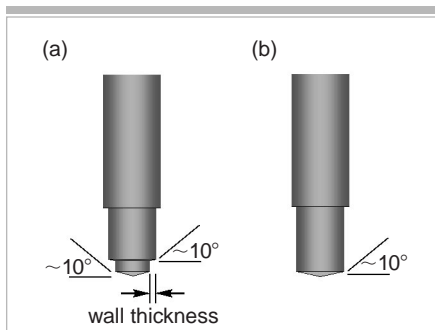
The method described may be used to produce compression-coated tablet dosage forms with minimal formulation development work. Most important, the equipment used for producing these compression-coated tablets is based on simple modifications of a traditional three-layer tablet press. Modern compression-coated products are made on specialized equipment in two separate operations: manufacture of core tablets on a traditional tablet press and the subsequent application of a compression-coating granulation. The compression-coating production process requires relatively complex machinery to encapsulate the core tablet within an outer granulation. The use of a Colton 232 tablet press is another slightly different method of making compression-

coated tablets in which the core and coated tablet are made simultaneously (1). The machinery is a relatively complex double-turret press (basically, two conjoined tablet presses) in which the core is formed on one side of the press and then transferred to the other side where the compression coating is applied. The novel compression-coated tablet process described herein does not require the separate formation of the core tablet because the core material and outer compression-coating material are formed into a tablet within the same tablet press and on a single turret.

Other advantages of the method include the capability to physically separate two incompatible drugs within the same dosage form, which is commonly achieved using multilayer tablets or compression-coated dosage forms. Multilayer tablets, however, may not have the versatility of the compression-coated tablet process described in this article, which can be modified to tailor release profiles of the drug from the dosage form. The process could allow rapid development of customizable delayed or sustained-release dosage forms as described in this article. This article presents the envisioned design of a specially adapted three-layer tablet press with modified tooling and compression rollers for the manufacture of compression-coated tablets at commercial scale.

## Materials and methods

**Materials.** The following materials were obtained: microcrystalline cellulose (Avicel PH200 MCC, FMC Corp., Philadelphia, PA); polyethyleneoxide (PEO) of various molecular weights (Union Carbide, Danbury, CT); magnesium stearate (Mallinckrodt, Phillipsburg, NJ); and theophylline and acetaminophen (Sigma Chemical Co., St. Louis, MO).



**Figure 1:** Upper punches for producing prototype compression-coated tablets on a Carver press: (a) construction of the punch used to make a cup and (b) construction of a punch used for the final compression.



**Figure 2:** Photo of the tooling used to demonstrate proof-of-concept, a cup, and a finished dosage form.

**Tooling.** To demonstrate proof-of-concept of the compression-coated tablet process, 9/16-in. tooling from a single punch press was modified (see Figures 1 and 2) to simulate the special hollow tooling with the core rod shown in Figure 3. Three punches were machined, as shown in Figure 1a, to simulate the shape of the punch tip presented to the powder bed in the die when the core rod is in the extended position shown in Figure 3a. These three punches were machined to various dimensions to produce cups with a thick wall (4.8 mm), intermediate wall (4.1 mm), or a thin wall (3.2 mm). Another punch was machined as shown in Figure 1b to mimic the shape of the punch tip in the retracted position of the tooling with the core rod as shown in front and side views in Figure 3b. Figure 2 shows the specially machined punches. The lower punch was an unmodified flat-faced punch (not shown).

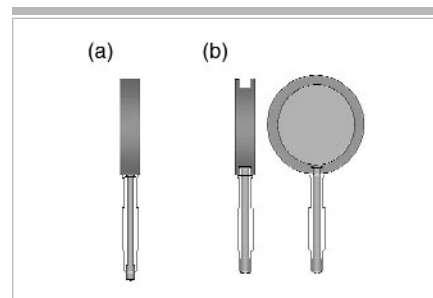
**Preparation of the compression-coated tablets.** A carefully weighed amount of powder blend (hereinafter referred to as the coating blend) was placed in the die and compressed on a Carver Press (Wabash, IN) at a known force with the tooling shown in Figure 1a to produce a cup-shaped tablet (cup). The cup was left within the die, and a known amount of either a model drug or a blend containing the drug was placed inside the cup and tamped lightly with the punch in an extended position. A weighed amount of the coating blend was placed on top of the die contents, and the cup was compressed for

a second time with the punch in a retracted position at a known force to produce the final compression-coated tablets (see Figure 1b).

**Characterization of the compression-coated tablets.** Drug release from the tablets was studied in a USP dissolution tester type 2 (Vankel Industries, Edison, NJ). Distilled water at 37 °C was used as the dissolution medium at a paddle speed of 100 rpm. The amount of drug released was monitored by automatic sampling of the dissolution media at regular intervals followed by UV spectrophotometric detection at 287 nm. The hardness of the tablets was measured on a hardness tester (Key International, Englishtown, NJ).

## Results and discussion

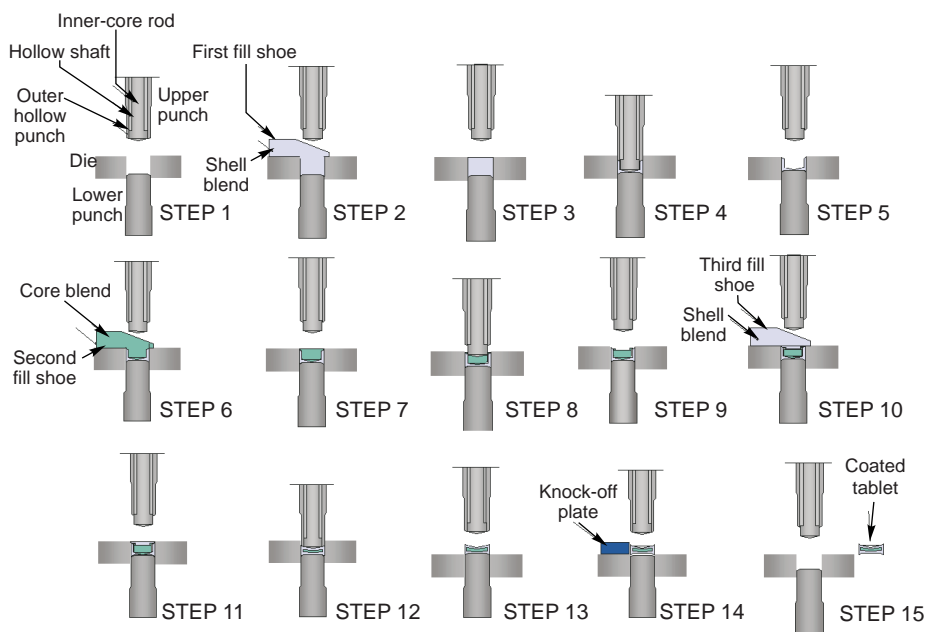
**Design concept of a commercial tablet press for the manufacture of compression-coated tablets.** The manufacturing process described in this article involves very simple modifications of a three-layer press and the use of special hollow tablet tooling somewhat similar to that described by Kilian (2). The commercial production of compression-coated tablets requires a specially modified upper punch, the construction of which is shown in Figure 3. The punch has a hollow shaft containing an inner core rod, one end of which provides a retractable tip at the compressing surface. The inner core rod runs along the length of the shaft and is longer than the shaft of the hollow punch. When the upper punch passes under a compression roller in the tablet press, the tip of the



**Figure 3:** Schematic of a hollow upper punch with a core rod showing (a) the side view of a punch tip in the extended position and a traditional solid roller and (b) the side and front views of a punch tip in the retracted position and a recessed roller.

inner rod is in the extended position at the compressing surface, and the upper end of the rod is flush with the head of the hollow punch. When the upper punch passes under a specially modified roller with a circumferential groove (see Figure 3b), the inner rod retracts into the recessed groove, and the tip of the inner rod and the annular tip of the hollow punch are flush with each other.

Figure 4 shows a sequence of events in the manufacture of the compression-coated tablets on a conventional three-layer tablet press fitted with a modified compression roller and upper punches. The sequence consists of six distinct stages — three filling and three compression. Steps 1–5 depict the formation of the cup. At the first filling station, the coating granulation is fed into the die, and in the first compression event the extended tip of the punch forms a cup, which remains within the die. The cam tracks on the press should be adjusted such that the cup is formed very close to the top of the die (i.e., the lip of the cup should be close to the upper surface of the die). At the second filling station, the core blend (drug or granulation containing drug) to be encapsulated in the compression-coated tablet is fed into the cup. At the second compression station, the core material is tamped lightly by the upper punch, which remains in the extended position as shown in steps 7–9. In step 10, at the third filling station, the coating granulation is again layered over the die contents to serve as a lid. At the final compression station, the



**Figure 4:** Schematic of production sequence of the compression-coated dosage form on a three-layer tablet press.

tip retracts because the upper punch passes under the special recessed or grooved roller, thereby allowing the entire contents of the die to be compressed to form a compression-coated tablet as shown in steps 10–15.

The tip of the punch is angled at ~10° to produce a conical punch tip. This facilitates the formation of the cup by allowing easy radial movement of the coating blend during the first compression event. In our earlier attempts to demon-

strate proof-of-concept, we used a flat-faced punch tip (i.e., not angled). During the formation of the cup, the coating blend did not migrate in the radial direction to form a well-compacted wall. This caused the bottom part of the cup to experience very high compression pressure, and hence it was well compacted, but the wall of the cup was poorly formed. The resulting cup crumbled during withdrawal of the punch tip from the cup. Similarly, the lip of the annular hollow punch tip is angled cor-

respondingly, which makes it flush with the inner punch tip when it is in the retracted position. The angled annular lip will be required during production to allow core material deposited on the lip to slide (assisted by machine vibration) into the cup after the tamping step has occurred (see step 9 in Figure 4). The tamping step ensures that space is made for the core blend on the lip of the cup to slide into the cup.

**Demonstration of proof-of-concept of the compression-coated dosage form.** Tooling (9/16-in.) was machined as described in the materials and methods section. Compression-coated tablets were produced on a Carver press using a flat-faced lower punch and corresponding die and upper punches as shown in Figures 1 and 2. Compression-coated tablets were produced using 1000-lb com-

pression force for the cup, followed by manual tamping of the core material and final compression of the die contents (cup, core, and lid) at various compression forces. Figure 2 shows a cup and a compression-coated tablet made of Avicel PH200 using tooling shown in Figure 1a.

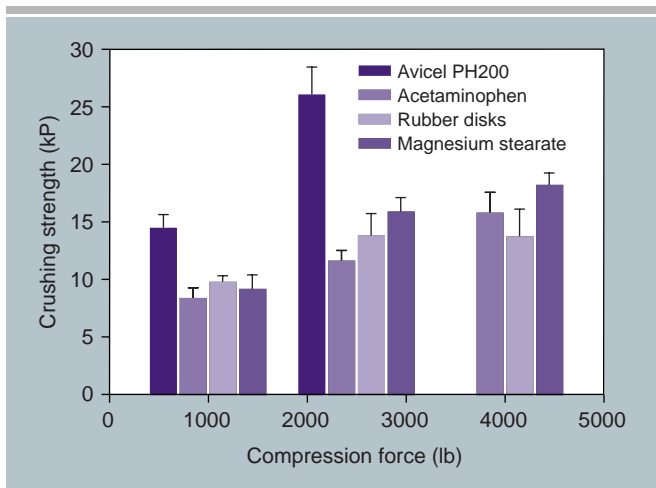
Tableting of poorly compactible materials within compression-coated tablets. Using the tooling described previously, compression-coated tablets containing three poorly compactible substances — magnesium stearate, acetaminophen, and rubber disks — were prepared on a Carver press. In each case, a highly compactible substance, Avicel PH200, was used as the coating blend. The cups were formed at a force of 1000 lb, and the final compression was performed at either 1000, 2500, or 4000 lb. Table I lists the amounts of core, coating, and lid material for each of these experiments. Figure 5 shows the crushing strength of these compacts at various compression forces compared with compacts made from only Avicel PH200 MCC. Compacts made from Avicel MCC also were made in a three-step process similar to the compression-coated tablet process. The compression-coated tablet process demonstrates the ability to form intact compacts from poorly compactible materials. The crushing strength of acetaminophen and magnesium stearate com-

**Table I: Compression-coated tablets containing various core materials.**

Core Material	Coating Material	Lid Material	Primary Compression	Secondary Compression
40 mg magnesium stearate	400 mg Avicel PH 200	100 mg Avicel PH200	1000 lb	1000, 2500, and 4000 lb
150 mg acetaminophen	400 mg Avicel PH200	100 mg Avicel PH200	1000 lb	1000, 2500, and 4000 lb
Rubber disks (1.8 mm thickness, 10.2 mm diameter)	400 mg Avicel PH200	100 mg Avicel PH200	1000 lb	1000, 2500, and 4000 lb

**Table II: Coating blends used to prepare the compression-coated tablets.**

Coating Blends	PEO Grades	PEO Amount (%)	Fast-Flo Lactose 316 (%)	Magnesium Stearate	Total
A	WSRN-1105	35.0	64.5	0.5	100.0
B	WSRN-60K	35.0	64.5	0.5	100.0
C	WSRN-301	35.0	64.5	0.5	100.0
D	WSRN-1105	50.0	49.5	0.5	100.0



**Figure 5:** Crushing strength of compression-coated tablets containing poorly compactible core materials.

pacts increased with an increase in compression force from 1000 to 4000 lb but was significantly lower than that of compacts made only from Avicel PH200 MCC at the same compression force. Avicel compacts made at 4000 lb exhibited hardness values beyond the range of the hardness tester. The crushing strength of rubber compacts did not appear to increase with an increase in compression force beyond 2500 lb. This is suggestive of higher elastic energy stored within the tablet at higher compression forces, which reduces the strength of the compact.

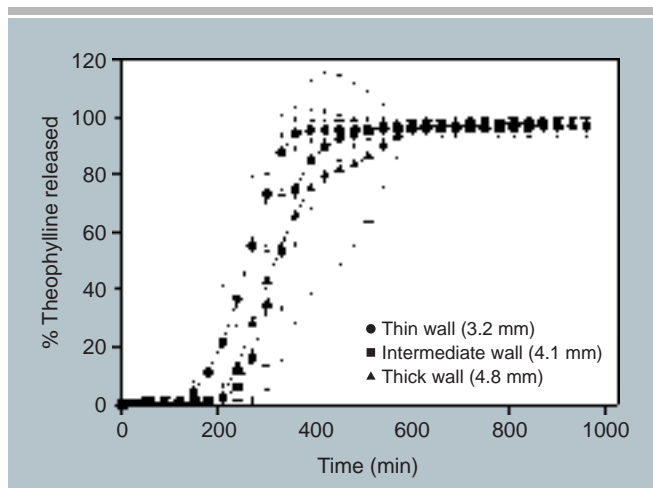
Application of compression-coated tablets to produce controlled-release tablets. Compression-coated tablets were prepared on a Carver press using coating blends that contained various amounts and types of PEO as a rate-controlling hydrophilic polymer (3). Fast-Flo Lactose 316 was used as a filler, and 0.5% magnesium stearate was added to each blend to serve as a lubricant. The core material was composed of either theophylline only or a blend of theophylline with PEO. Table II lists the various coating blends that were used to prepare the compression-coated tablets.

Figure 6 shows the effect of the thickness of the cup wall on the release of theophylline from compression-coated tablets. Wall thickness of 3.2, 4.1, and 4.8 mm could be produced by using upper punches machined to various dimensions as described in the materials and methods section. Increasing amounts of coating blend for the cup and the lid were used for punches with increasing wall thick-

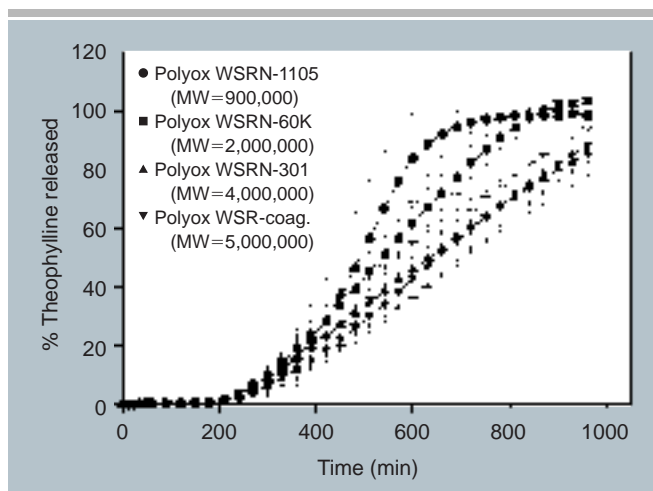
ness. Tablets with a thin wall released the drug during a shorter period of time (~120 min) than did tablets with an intermediate or thick wall (~200 min). In an attempt to obtain better control of the delay (i.e., lag) period before release of the drug begins, the molecular weights (MWs) of the polymer in the coating were varied.

Figure 7 shows that the dissolution medium took twice as long to breach, and begin drug release, the coatings containing PEO of MW 2,000,000 than it did to breach the other coatings. The coating containing PEO of MW 4,000,000 does not appear breached for the release period studied; instead, the drug seems to be diffusing through the coating barrier.

Another approach to control the delay period before drug release begins was the use of various concentrations of polymer in the coating blend. Figure 8 compares coatings containing 35% and 50% of PEO of MW 900,000. As expected, higher concentrations of the polymer delayed the release of the drug for a longer period of time.

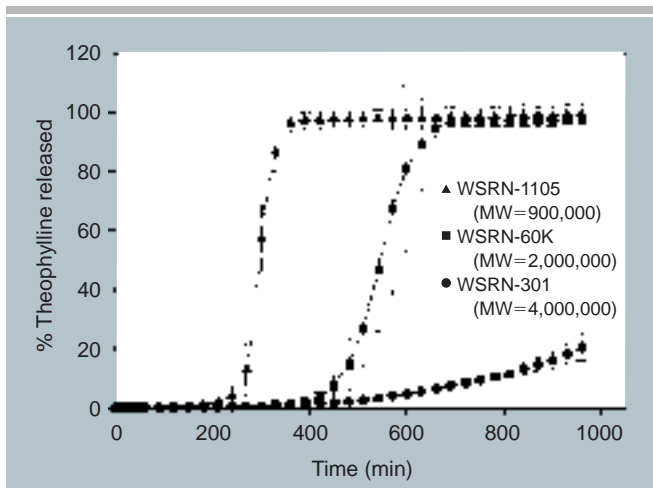


**Figure 6:** Drug release from compression-coated tablets of various radial coating-wall thicknesses. Coating is 550 mg of blend A; core is 100 mg of theophylline; and lid is 100, 150, and 200 mg of blend A for thin, intermediate, and thick walls, respectively.

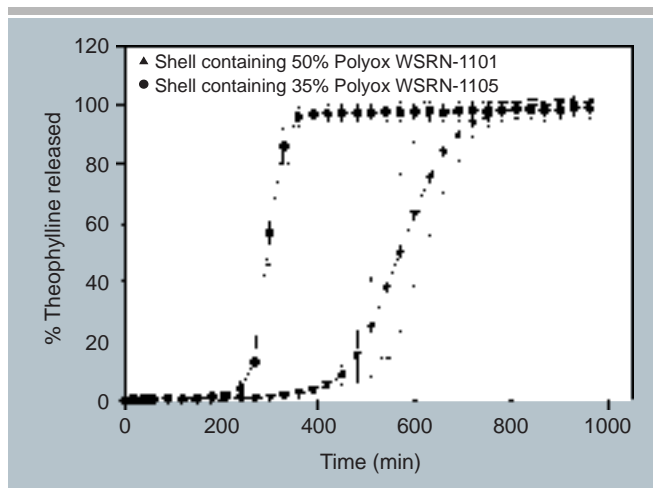


**Figure 7:** Release profiles from compression-coated tablets containing a core composed of a 2:1 blend of theophylline and PEO of various molecular weights (MWs). Cup is 750 mg of blend A; core is 150 mg of drug/polymer 2:1 blend; and lid is 200 mg of blend A.

This study examined the effect of including polymer in the core blend in addition to incorporating it in the coating blend (see Figure 9). The coating blends in these experiments were composed of PEO of MW 900,000, and the cores contained 2:1 blends of drug and PEO of various molecular weights. In each case, the release of the drug began at approximately the same time but was followed by slower release of the drug at relatively constant rates. As expected, compression-coated tablets containing polymers of lower MW in the core released the drug slightly faster. However, no appreciable difference was



**Figure 8:** Release of drug from compression-coated tablets composed of coatings of various molecular weights (MWs) of PEO. Coating is 750 mg of polymer blends A, B, or C; core is 100 mg of theophylline; and lid is 200 mg of polymer blends of A, B, or C.



**Figure 9:** Release of drug from compression-coated tablets containing various amounts of PEO in the coating. Cup is 750 mg of coating blend A or D; core is 100 mg of theophylline; and lid is 200 mg of coating blend A or D.

observed between the release rates of the drug from tablets containing PEO of MW 4,000,000 and 5,000,000.

Other possible applications of the compression-coated tablet process. Many other applications of the compression-coated dosage form may be possible. Pure drug crystals, drug–excipient blends, granules, microspheres, or beads can be readily encapsulated inside the core of the dosage form. If the neat drug has good flow characteristics, it may be filled directly in the cup during the compression-coated tableting process. This process thus may provide an inexpensive alternative to filling granulations into preformed, conventional hard gelatin capsules because the drug or drug-containing particles are encapsulated within a previously formulated and prepared coating blend instead of within a hard gelatin shell. As described in this article, even the most poorly compactible substances can be presented as a tablet if a sufficiently compactible coating granulation is used.

Various other applications of this technology are possible. It already has been shown that the release of the drug from the core can be readily modulated to produce timed-release dosage forms. Similarly, if a suitable polymer is used in the outer coating, it is possible to manufacture enteric, compression-coated dosage forms (4). The compression-coated tablet process makes it feasible to taste-mask unpleasant drugs and blind them for clinical

studies (5). Orally dissolving tablets also could be easily formulated by using a coating blend consisting of rapidly dissolving sugars with a core containing the drug as suitably taste-masked particles. Combination drug products also could be formulated by using a coating blend containing a drug different from that in the core (6). Finally, repeat-action tablets could be produced by including the drug in the coating as well as in the core blends to achieve pulsatile delivery.

### Conclusion

The compression-coated tablet process provides a means of compression coating by simple modifications to a three-layer press. There are many advantages of this process over traditional compression coating. Separate formation of a core is not required, and therefore no transfer mechanism is required for the core. Similarly, centering of the core is not a problem in this process, thereby leading to better reproducibility of release profiles in controlled-release applications. Also, the core is not required to be compactible nor is adhesion between core and coating a prerequisite. A simple and noncompactible but flowable capsule granulation could be made into a tablet as long as the coating blend is sufficiently compactible. Engineering details may need some careful attention while designing a tablet press for making compression-coated tablets.

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