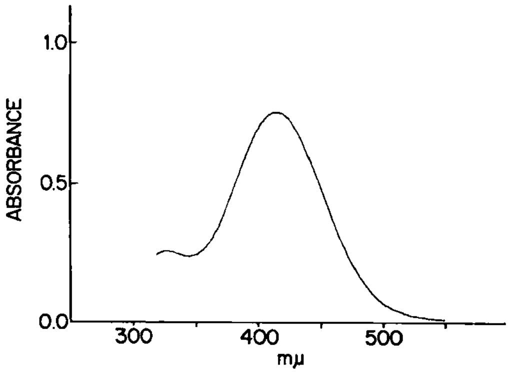

Fig. 2—Spectrum of acid-dye complex of gallamine triethiodide.

The absorption spectrum of the acid-dye chloroform extract was determined on a Cary model II recording spectrophotometer. Figure 2 shows the absorption spectra in the region 550–350 for the gallamine acid-dye extract. The wavelength where maximum absorption occurred was 416 mμ.

Various concentrations of gallamine triethiodide were evaluated by the acid-dye extraction procedure for the purpose of preparing a standard calibration curve. A typical linear Beer's law plot was obtained when the absorbance of the acid-dye extract *versus* concentration of gallamine triethiodide was plotted in the range of 2 to 10 mcg./ml.

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Keyphrases

Gallamine triethiodide—analysis
Titration, nonaqueous—analysis
Bromophenol blue—indicator
Perchloric acid—titrant
Colorimetric analysis—spectrophotometer
Bromocresol green-gallamine triethiodide—complex

Technical Articles

Instrumentation of a Rotary Tablet Machine

By FRANK W. GOODHART, GUSTAVO MAYORGA,
MORTIMER N. MILLS, and FRED C. NINGER

The Manesty 45 station Rotapress was instrumented to measure compressional force, ejection force, and lower punch pulldown force. Various positions in the pressure linkage were monitored to determine the optimum location for compressional force measurement. The upper part of the compression column just below the link to the upper roller carriage was chosen for installation of strain gauges for compressional force measurement. Ejection force was measured by installing a force washer beneath the head of the bolt which holds the ejection cam in place. The ejection cam was not modified in any way. Lower punch pulldown force was measured by using a bolt containing internally mounted strain gauges to replace one of the three bolts normally holding the pulldown cam in position. Examples of the results obtained by compressing antacid tablets at various speeds and forces are given. Data collected over a 24-day period on the compression of these tablets under regular production conditions are given.

Rotary tablet machine instrumentation has been described by Knoechel (1–3) and Wray (4). Sites for gauging and methodology have been developed for certain types of American-made machines such as the Stokes BB-2, Stokes 541, and other similar presses. It has become apparent that measurement of tableting forces is a helpful tool in the development of tablet formulations and trouble shooting. Furthermore, the use of tablet machine instrumentation makes for better production control thus giving

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more uniform, better quality products. Causes for variabilities in weights, hardness, and gauge can be found and minimized. Instrumentation is the first step in the development of a fully automated tablet press.

The Manesty 45 Rotapress has been used for several years by this production department on high volume items. Normally the press is run at 3,000–4,000 tablets per minute (TPM). Since this press was achieving more importance in the daily operation, it was appropriate to choose it for instrumentation studies. The mechanism of tablet compression of the Rotapress is somewhat different from other machines, thus experimentation on gauging sites for compressive force measurement on this machine was necessary. In addition, methods for measuring strain on cams were developed.

INSTRUMENTATION OF THE MACHINE

Compressional Force—A schematic diagram of the compression mechanism is shown in Fig. 1. The large metal column shown on the right-hand side of Fig. 1 supports one end of both the top and bottom roll carriages. The column in turn is bolted at two places to the corner post. It is not attached to the horizontal part of the machine which supports the turret. The left-hand side of Fig. 1 shows the upper roll carriage is attached to the top pressure link and the bottom roll carriage to a different support, the bottom pressure link. Thus one side of the pressure mechanism is fixed (the right side in Fig. 1), and the other side is variable. Connection of the top and bottom linkages on the left by various parts allows pressure adjustment (tablet thickness) and variable penetration of the upper punch. When a tablet is produced the force is exerted through the column and through the pressure links. Therefore, strain gauges were attached to various positions on these parts as illustrated in Fig. 1.

Location A, top pressure link above eye. Location B, bottom pressure link at the narrowest point. Location C, upper section of compression column. Location D, lower section of column just above the table. Location E, upper section of column just below the pin supporting the upper roll carriage. Location F, at the bottom of the compression column just above pin that supports lower roll carriage.

These positions are shown in Fig. 1. Half bridge configurations were used for all screening work. Actually at some positions on the column it is impossible to place gauges on both sides because of the abutment with the corner post. It is best to split the placement of the full Wheatstone bridge circuit between two sides of a column in order to eliminate measurement of column bending.

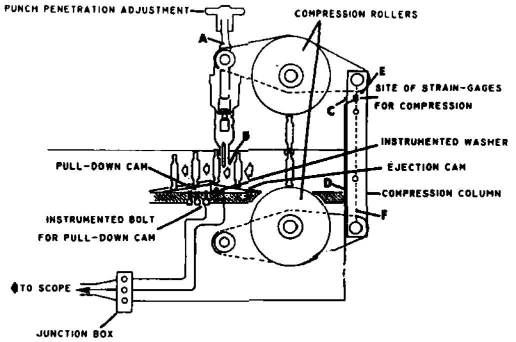

Fig. 1—Schematic diagram of the compression mechanism of the Manesty 45 Rotapress. Note various sites for placement of strain gauges for compressional force measurement. Sites for placement of force washer and instrumented bolt are indicated for measurement of ejection force and lower punch pulldown force, respectively.

Of the six positions monitored, Location E in Fig. 1 was the most promising. Judgment was made on the uniformity of the signal, the accessibility for installation of a full bridge on both sides of the member being monitored, and the signal strength. All positions except E and C showed varying degrees of harmonies or extraneous signals aside from that resulting from the compression stroke. These signals from the upper position of the compression column, Locations E and C, give readings of about one-tenth the force reading on a punch. The sensitivity was thought to be satisfactory since readings of 20 to 40 microstrain (μst.) were obtained during ordinary tableting operations. Opposite Position C, the pressure bar is butted against the corner post of the machine and is thus inaccessible. For this reason, Location E, the position just beneath the upper roll carriage pin, was chosen. The column at this position is accessible from both sides and allows installation of a half bridge on both sides of the column. During the experimentation on finding the best location, it was thought that the deep milling marks on the pressure bar might be the cause of poor signal. Because of this, Location E was smoothed down to a fine mirror finish before the final gauge installation was made. This resulted in the achievement of excellent signals from this position.

It was necessary to calibrate the compressional response from the column to actual pounds of force. To do this an upper and lower 1.59 cm. ($^5/_8$ in.) FFBE punch was instrumented with strain gauges in a full Wheatstone bridge configuration. The lower shank portion of the punches was machined away to give four flat surfaces for strain gauge installation. These punches were statically compressed on a Carver press and a linear relation was obtained by plotting punch response in microstrain to applied pressure in pounds. The Carver press was fitted with Bourdon type gauges of various ranges which had been checked for calibration by a dead weight tester. The punches were then fitted into the tablet machine and a simultaneous reading from the punches and compression column was recorded in microstrain. This was also a linear relationship. It was then possible to relate the column microstrain reading to pounds using the gauged punches as a secondary standard.

Calibration Results—Graphs of compressional force *versus* the microstrain reading obtained from the compression column were made and are shown in Fig. 2. The results of the co-variance analysis are

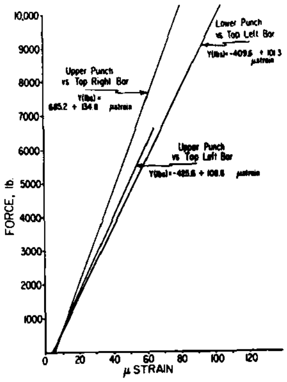

Fig. 2—Calibration of compressional force.

given below and shown in Fig. 2 also.

Upper punch *versus* top left bar
$$Y\text{ (lb.)} = -425.6 + 108.8\,X\ (\mu\text{st.}) \qquad \text{(Eq. 1)}$$

Lower punch *versus* top left bar
$$Y\text{ (lb.)} = -409.6 + 101.3\,X\ (\mu\text{st.}) \qquad \text{(Eq. 2)}$$

Upper punch *versus* top right bar
$$Y\text{ (lb.)} = -685.2 + 134.9\,X\ (\mu\text{st.}) \qquad \text{(Eq. 3)}$$

Close agreement in response of the left bar to equal pressures on upper and lower punch was achieved. At 4,000 lb., for instance, there is a 250-lb. deviation of the upper punch from the lower punch. The response of the right bar was calibrated only against the upper punch. The right bar is less sensitive than the left bar, thus giving a substantially less μstrain reading. The reason for this at present is unaccountable.

The response from the right bar was monitored for antacid tablets. Thus Eq. 3 was used for calculation of force. For example, if an average reading of 40 μ-strain is obtained on compression of these tablets, then the force is calculated as follows:

$$\text{Force in lb.} = -685.2 + 134.9\ \text{lb.}/\mu\text{st.}\ (40\ \mu\text{st.})$$
$$\text{Force} = 4711\ \text{lb.}$$

The negative intercept obtained in the above equation is not physically meaningful. Lower pressure readings would indicate the lines in Fig. 2 would actually go through the origin. Therefore Eqs. 1, 2, and 3 may be used for calculation of true force, but are not truly definitive because of the negative intercept.

Ejection Force—Because of the high operating speeds of the Manesty press and for the sake of maintaining a conventional machine, an attempt was made to measure ejection forces without fabrication of a special ejection track. It was theorized that the use of a force washer under the bolt holding the ejection track in place might be a satisfactory method. A photograph of the ejection track and force washer is illustrated in Fig. 3. When tested this method was found to work satisfactorily.

The force washer is a product of Lockheed Electronics (Houston, Tex.). It measures 2.16 cm. (0.85 in.) in diameter and is 0.81 cm. (0.32 in.) thick. Thus it is small enough to insert under the bolt and not interfere with machine performance to the slightest degree. One drawback of the washer is that it employs only one active strain gauge in the circuit. Additional active gauges would provide better electrical balance and temperature compensation. Similar force washers using a full Wheatstone bridge circuit have been obtained from Lockheed and have operated satisfactorily.

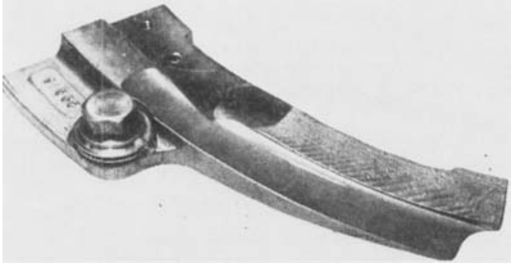

Fig. 3—Photograph of ejection track and force washer.

Ejection Force Measurement—The force washer was installed beneath the bolt that holds the ejection cam in place. Two plastic shims were used beneath the cam to obtain proper ejection height. The cam was shimmed uniformly throughout its length.

Three experiments were used to test the usefulness of this method. First, the ejection response was monitored during the run-in period. At this time no tablets were being produced. The plungers holding the lower punches were tightened to normal. Under these conditions, no ejection response was noted. This meant that the ordinary travel of the punches over the ejection cam gave no strain measurement when tablets were not being made. Next, tablets were made by hand turning the machine. The force washer was monitored for response at the time of compression. This tested whether or not compressional force was transmitted through the machine to the force washer. No response was recorded at the time of compression, thus verifying the feasibility of the force washer.

An experiment was run on an antacid tablet in which the upper punch penetration was deep, medium, and shallow. In order to compensate for the various penetrations, the lower roller was moved up or down by use of tablet thickness adjustment. Tablets of about the same hardness and thickness were produced under all three conditions and ejection forces were monitored. It was found that at deep penetration the lower punches were striking the ejection cam at a very early point and no ejection response was apparent. However, at medium and shallow penetration, good ejection responses were achieved.

Lower Punch Pulldown Force (LPPF) Measurement—The utility of this force measurement had been demonstrated for the Stokes BB-2-27 and will be described in a separate paper (5). Frequently, while making prolonged runs, lower punches may begin to bind and stick either on the punch shank or at the punch tip and die wall interface. Among conditions causing sticking are inadequate removal of overflowing granulation, excessive binding properties of the material being tableted, and poor or faulty lubrication of the formulation or the machine. Strains resulting from the above conditions are often the cause of excessive punch and cam wear or tooling and machine failure.

An instrumented bolt was made for the Manesty 45 Rotapress and is the same design as reported in

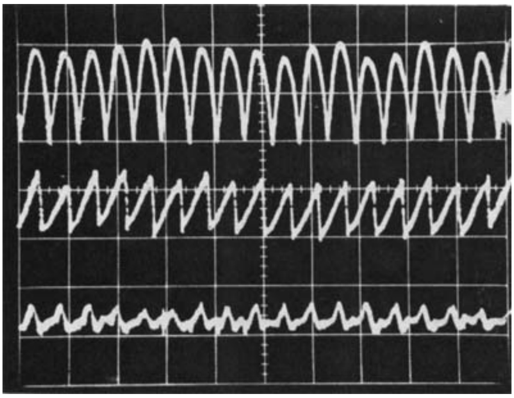

Fig. 4—Oscilloscopic tracing of various force measurements obtained on Manesty 45 Rotapress. Uppermost tracing: compressional force measurement; each large division is about 2,000 lb. of force. Middle tracing: ejection force; each large division is 10 μstrain. Lower tracing: lower punch pulldown force; each large division is 10 μstrain.

Reference 5. The bolts used for holding all cam tracks in the Manesty 45 press are 1.27 cm. ($^{1}/_{2}$ in.) in diameter and have 12 threads to the inch (Whitworth thread). Bolts having this thread system are difficult to obtain in this country. The bolts which were instrumented were obtained from Manesty. Later, when it was decided to obtain bolts having internally mounted gauges, it was necessary to buy bolts of slightly longer lengths in order for the bolts to be calibrated. These bolts were sent to Strainsert, Bryn Mawr, Pennsylvania, for installation of strain gauges.

The instrumented bolt was placed in the position nearest the ejection cam. This position gave the most sensitive and reproducible result (5). Therefore, this position was adopted for permanent measurement.

TESTING OF THE INSTRUMENTATION AND THE NATURE OF THE DATA OBTAINED

Compression, Ejection, and Cam Track Force Measurement—All data reported pertain to antacid tablets weighing about 1.33 g. produced from 1.59 cm. ($^{5}/_{8}$ in.) flat-faced bevel-edged punches and dies.

Typical data resulting from compressional force and various cam strains are shown in Fig. 4. The uppermost tracing in Fig. 4 is the typical compression response. A reading of about 40 μstrain was obtained in this instance; this is equivalent to about 4,700 lb. of force. The middle tracing represents the response obtained from ejection force measurement using the Lockheed force washer. The ejection force was not transposed to pounds of force, but was normally read and recorded as μstrain. The particular washer used in this work has a rating of 0–250 lb. The lowermost tracing in Fig. 4 is normal LPPF as seen at the beginning of a run or during good running conditions. The average response in this particular tracing is about 6 μstrain. Force rating of the Strainsert bolts which were eventually used was 0–100 lb.

Monitoring Antacid Tablets at Various Machine Settings—In order to determine the extent of several machine factors on the compression of antacid tablets, a number of short runs were made at different machine settings. The factors studied were speed, pressure setting, and depth of upper punch penetration. The summary of the results is shown in Table I.

It was found that the depth of upper punch penetration has a major effect on magnitude of ejection force. During deep penetration the lower punch strikes the ejection cam at its foremost position. This occurs because the lower roller carriage is moved downward to compensate for the deeper penetration of the upper punch. At medium or shallow penetration of the upper punch into the die, the lower punch will strike the ejection cam at a higher position. It was found that at shallow penetration an ejection response of about 30 μstrain was obtained while at deep penetration a response of about 8 μstrain was obtained. If the ejection cam had been shimmed at the furthermost point, an increased response may have been obtained. Normally tablets are produced using only minimal penetration of upper punch, so a satisfactory response was obtained under conditions of machine usage.

The data indicate that both higher ejection force and higher LPPF are obtained under higher compressional forces. This concurs with results of other studies (3, 5). Faster speeds generally show increased ejection force and LPPF as compared with slower speeds.

Tablet hardness (average of four determinations) was plotted against compressional force (Fig. 5) for this single batch of granulation and a generally linear relationship was found. Without mathematical treatment of the data it can be seen that a

TABLE I—SUMMARY OF ANTACID TABLET COMPRESSION DATA

Condition	Compression Force, lb.[a]	Ejection Force, μst.[a]	Lower Punch Pulldown Force, μst.[a]	Weight, g.[a]	Hardness, kg.[b]
Shallow penetration, high pressure, fast speed	4,653	36.1	6.5	1.326	13.8
Shallow penetration, high pressure, slow speed	4,572	32.9	6.1	1.323	13.9
Shallow penetration, low pressure, fast speed	3,844	29.8	5.5	1.335	8.9
Shallow penetration, low pressure, slow speed	3,709	26.4	4.7	1.336	9.4
Deep penetration, high pressure, fast speed	4,302	8.0	6.5	1.335	11.4
Deep penetration, high pressure, slow speed	5,057	9.6	5.4	1.334	14.8
Deep penetration, low pressure, fast speed	4,006	8.4	5.4	1.331	10.9
Deep penetration, low pressure, slow speed	3,574	8.0	3.2	1.323	7.1

[a] Average of 10 readings. [b] Average of four readings.

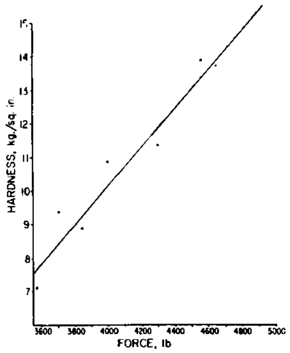

Fig. 5—Tablet hardness as a function of compressional force for a single lot of granulation.

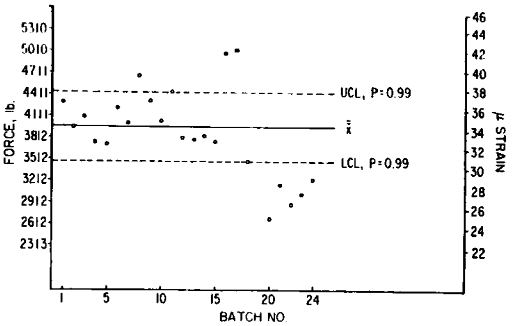

Fig. 6—Average compressionl force for various batches of antacid tablets. Eight of the 24 consecutive batches fall outside the p = *0.99 control limits.*

compressional force range of 3,550–4,650 lb. produces tablets in the 7.5–14 kg. hardness range. Compressional force of 3,800–4,150 lb. produced tablets in the 9–11 kg. hardness range.

ROUTINE MONITORING OF TABLETS IN PRODUCTION

Experimental Design—The normal production of antacid tablets in the plant was monitored by means of the instrumented Rotapress. The study was carried out for 24 working days which provided data for 24 separate batches of granulation produced from a continuous process. Usually photographs of the oscilloscopic tracings were taken at four equally spaced intervals throughout the day. Five peaks were read for compressional force analysis. At the same time tablets were collected. The weight and hardness of four tablets at each time interval were measured. The weights were determined analytically, and hardnesses were measured using an air actuated Strong-Cobb hardness tester.

Results of Daily Monitoring the Production of Antacid Tablets—The means and variabilities of the compressional force, weight, and hardness were calculated. Three separate variabilities were considered: (*a*) variability of single observations; (*b*) variability of time period averages; and (*c*) variability among batches.

Coefficients of variation of compressional force have been reported to range between ±5% and ± 40% (2). It has been shown that small deviations in tablet weight will account for similar small deviations in compressional force (6). Additional factors such as overload setting, machine speed, force flow feed *versus* standard feed, and a multiplicity of granulation factors greatly add to the variability of compressional force. Usually weight is controlled very precisely, therefore contributing little to overall compressional force variability. Of more significance may be the nature of the granulation itself and its level of loading into the machine.

A summary of compressional force means and variabilities is given in Table II. A relatively low coefficient of variation, 5.2%, is obtained for individual compressional force readings. However, the coefficient of variation of time period averages is 9.0% and for batches is 27%. An F ratio test (p = 0.01) shows significant differences for any two variabilities tested in Table II. In Fig. 6, the average compressional force per batch is plotted using control limits of p = 0.99. The limits were calculated from the standard deviation of time period averages. It can be seen that eight of twenty-four batches or 33% fall outside the limits. Five of the batches that are outside the limits were also the last five batches studied. The variability of compressional force (2,350–4,450 lb.) during these runs seems unusually high. The tablets prepared were satisfactory with respect to weight and hardness specifications. It is apparent that the granulation process being continuous adds the majority of the variability to compressive force. The precise nature of this variability has not been determined. Granulation properties such as mesh size, bulk volume, and flowability may be varying enough during normal processing to affect compressional force. Other tablet properties which might be of importance, *i.e.*, density and porosity, were not measured. However measurement of these factors may elucidate to some degree other basic correlations which are not reported in this study.

In Fig. 7, the average tablet weight is seen to be within the control limits (p = 0.99 using the time period standard deviation). The coefficient of variation for tablet weights is about 1% thus indicating that weight has a relatively small contribution to compressive force variability. Tablet hardness is shown in Fig. 8. It shows a long downward trend and subsequent fall (Batch 16) below the control limits (p = 0.99). It also shows some cyclical variation which occurs every 4 or 5 days. The lack of more detailed processing data precludes an accurate

TABLE II—SUMMARY OF COMPRESSION FORCE DATA OF TWENTY-FOUR BATCHES OF ANTACID TABLETS

Type of Observation	No. of Observations	Compression Force Average, lb.	*SD*, lb.	Coefficient of Variation, %
Individual	565	3,497	216	5.2
Time period	113	3,497	378	9.0
Batches	24	3,497	1150	27

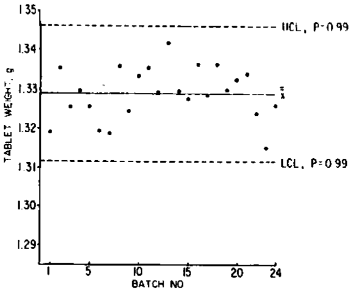

Fig. 7—Average tablet weight for various batches of antacid tablets. None of the batches fall outside the p = 0.99 control limits.

explanation for this cyclical performance. Tests for correlation between pairs of responses, compressive force, weight, and hardness were made. The only significant correlation was between hardness and weight.

CONCLUSION

The instrumentation of the Manesty 45 Rotapress was described. Locations for the measurement of compressional force were investigated, and the top of the compression column was found to be a satisfactory location. A method for the measurement of ejection force and lower punch pulldown force was developed. Compression of antacid tablets at various machine conditions was described, and it was found that compressional force (CF) has a measurable effect on tablet properties. The results of monitoring CF, weight, and hardness during routine production were reported. A wide variability in CF was found but tablet weight and hardness were nevertheless positively correlated.

The instrumentation of this machine has provided a means of better understanding the tableting process as well as the drawing of correlations between machine conditions and tablet characteristics. It is thought that overall product quality might be improved by employing an instrumented tablet machine in regular production runs. The instrumented machine will help bridge the gap between pilot scale-ups and actual production runs. The combined use of smaller instrumented rotary tablet machines for pilot sized lots together with the use of the instrumented Rotapress in actual production provides a means of formulation scale-up not previously available. Formulation characteristics and defects are better understood with the use of tablet machine instrumentation.

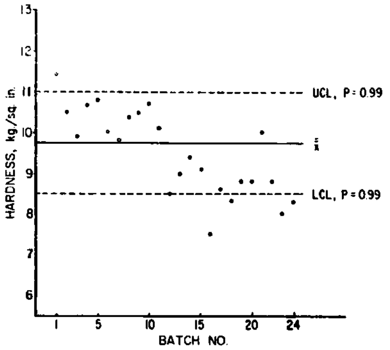

Fig. 8—Average tablet hardness for various batches of antacid tablets. Note downward trend and cyclical variation which occurs every 4 or 5 days.

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Keyphrases

Rotary tablet machine
Instrumentation—Manesty 45 Rotapress
Compressional force—determination
Ejection force—determination
Punch, lower—pulldown force
Diagram—tablet machine instrumentation