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THE EFFECTS OF CHROMIUM NITRIDE ION BOMBARDMENT TREATMENT OF TABLET TOOLING ON TABLET ADHERENCE

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ABSTRACT

During product development and scale-up of a generic tablet formulation, the problem of tablet sticking and punch filming was encountered. This report details the various methods that were evaluated to solve this problem and the results achieved. A study was undertaken that examined the use of Chromium Nitride Ion Bombardment, Chromium Electroplating, and alternate cleaning and storage techniques for tablet tooling. The results of the study indicate that the Chromium Nitride treatment significantly improves the tablet adherence problem in compression of the formulation in question. Surface analysis of the tooling was performed to attempt to describe a mechanism for the observed results.

INTRODUCTION

During formulation development studies for a generic tablet formulation, two persistent problems were encountered. The first of these was prolonged disintegration which was overcome by adjusting the excipient levels and processing parameters. The other problem was tablet sticking during compression that ranged in severity from filming of the punch faces to severe sticking and picking. The two problems were interrelated to the extent that in order to make tablets having suitable disintegration and dissolution properties, it was necessary to use somewhat low compression forces. At these low forces the filming and sticking was immediate and uniformly distributed over all stations and both upper and lower punches.

The emphasis to correct this problem during the early development of this product was in lubricant selection and particle size distribution of the granulation. These efforts were partially successful in that elegant tablets with good dissolution properties were prepared. However, start up of the compression process was difficult and required tedious steps to overcome the initial tendency of the tablets to stick and film the punch faces.

This study evaluated the use of chromium electroplating, chromium nitride ion bombardment, conditioning of punch faces, and alternate cleaning and storage techniques for tablet tooling as alternatives to eliminate this problem.

MATERIALS AND METHODS

The granulation was prepared in a planetary mixer by blending the drug, a portion of the microcrystalline cellulose (MCC) and sodium starch glycolate (SSG), and the povidone for a period of time. The blend was then granulated with purified water to a suitable consistency and wet milled through a Comil 0.156"

Tablet Formulation

	% w/w
Drug	41.67
Microcrystalline Cellulose, NF[1]	46.83
Sodium Starch Glycolate, NF[2]	8.00
Povidone, USP[3]	2.75
Magnesium Stearate, NF[4]	0.75

1 Avicel PH102©, FMC Corp., Philadelphia PA

2 Explotab©, Roquette Freres (Edward Mendell Co., Carmel NY)

3 Povidone K-29-32©, GAF Chemicals Co., Wayne NJ

4 Mallinckrodt, St. Louis MO

screen. The granulation was dried in forced air ovens at 60°C to a moisture content of <2.0%. The dry granulation was milled through a Comil 0.055" screen and blended with the remainder of the MCC and SSG for 10 minutes in a V-Blender. The magnesium stearate was added and blended for an additional 5 minutes.

This process was successfully scaled up from 2kg screening batches to 10kg pilot plant batches, and subsequently to 100kg production batches.

Placebo Blends

Placebo blends were either untreated Avicel PH102 or Avicel PH102 and 0.75% magnesium stearate.

Compression

For the experimental portion of this study compression was performed on a Kilian RTS 16A tablet press that had been instrumented with strain gauges by the manufacturer to monitor compression, ejection, pre-compression, and take-off forces. Only compression and ejection forces were monitored in this study. Data acquisition was performed by a Tablet Press Monitor (Metropolitan Computing Corporation, West Orange NJ). During development and scale up to production, tablets were also compressed on a Stokes RB2 and a Manesty BetaPress.

Tooling Preparation

The tooling was prepared from 408 steel by Natoli Engineering, St. Louis MO, and were the same sets used during product development and clinical supply production. The dosage form is available in two strengths that are dose proportional and are compressed from the same granulation at two different tablet weights. The lower strength is compressed with 9/32", flat face beveled edge, debossed 'SEARLE' lowers, and bisected uppers. The higher strength is compressed with 11/32", flat face beveled edge, plain lowers, and debossed 'SEARLE' uppers.

Four sets of upper and Lower punches of each size were sent to Natoli Engineering for conventional chrome electroplating treatment. Four other sets of each size were also sent to BeamAlloy Corporation, Dublin OH, for chromium nitride ion bombardment treatment. The remaining eight sets were not treated but were used as controls and for study of alternate cleaning and storage techniques.

EXPERIMENTAL

The tooling was cleaned prior to setting up the press with either isopropyl alcohol 99% or analytical grade hexane. Some punch tips were liberally dusted with magnesium stearate to simulate an alternate storage condition. These punches were placed in the

TABLE 1
Press Station Distribution

Tooling Type	Isopropyl Alcohol Cleaned	Hexane Cleaned
Chrome Plated	1 , 9	5 , 13
Chromium Nitride Treatment	2 , 10	6 , 14
Untreated, Plain	3 , 11	7 , 15
Untreated, Magnesium Stearate Stored	4 , 12	8 , 16

press without cleaning off the magnesium stearate. The press was tooled using the station distribution shown in Table 1.

The Kilian RTS press was first tooled with the 9/32" tooling, followed by the 11/32" size. After adjusting the press to obtain the proper tablet weights (120mg and 240mg respectively), compression was carried out at a machine speed of 40,000 tablets per hour which is approximately 40% of the Kilian RTS 16A output capacity.

Tablets were compressed at varying hardnesses and for varying time periods as described later. Then the press was stopped and each individual punch face was inspected for evidence of filming or sticking. The punch faces were cleaned where necessary with isopropyl alcohol and a soft rag. Results were recorded according to the following grading system:

- 0 = clean, no filming or sticking
- + = film present
- ++ = film to some sticking observed in embossing or bisect
- +++ = severe sticking

Tablet Tooling Surface Analysis

One upper and one lower punch of each size tooling and of each three tooling treatments (chromium electroplating, chromium nitride implantation, or no treatment) were submitted to McCrone Associates, Westmont IL, for surface analysis. The analysis consisted of microscopic examination by visual and scanning electron microscopy, and scanning Auger microprobe surface analysis.

RESULTS AND DISCUSSION

Formulation Activities

The formulation of this product, as is true for most generic formulations, is based on the innovator's published inactive ingredient list to optimize assurance of stability and eliminate extensive formulation screening activities. It was desirable from a marketing standpoint to maintain a tablet shape similar to the innovator's since it is a standard shape and is not proprietary. Physical examination of several lots of the innovator's product revealed somewhat soft tablets (3.0 - 4.8kp for the 9/32" and 2.7 - 5.1kp for the 11/32" tablets), and wide ranges of disintegration times (30 - 570 seconds).

Magnesium stearate is the preferred lubricant because it possesses excellent anti-adherent and true lubricant properties.[1,2] Magnesium stearate levels of 0.25% - 2.0% were investigated with several other lubricants. After numerous trials a lubricant level of 0.75% magnesium stearate was chosen for the final formulation.

It was felt that the efficiency of the lubricant could be increased by minimizing the level of fines in the granulation. Multiple attempts were made to achieve this goal by varying the particle size distribution through changing the processing parameters, primarily in the milling steps. None of these experiments were dramatically successful in circumventing the sticking problem, although the milling process was optimized to produce granulation with good flow properties and tablets with good disintegration and dissolution profiles.

It became obvious at this point that the active ingredient itself, which has a 'sticky feel', was the probable cause of the problem. Dilution of the active ingredient by decreasing its concentration in the formulation also can be an effective means to relieve sticking, but this was not considered in the present case because of the desire to match closely the innovator's product. It was observed that once the punches had been wiped clean several times and tablets were successfully compressed, the filming and sticking never recurred, even over extended runs.

The observations made during formulation development were confirmed during production of clinical batches using manufacturing scale equipment. When filming of the punches occurred during the clinical production several additional trials were performed to attempt to correct the problem within the framework of the formulation. These attempts included using higher compression forces for an extended period, prolonged blending time of the final granulation blend, and increasing the level of magnesium stearate to 2.0%. Mitrovej and Augsburger reported successful results when using the latter two techniques in microcrystalline cellulose based formulations.[3] None of these alternatives was successful in the present case. Finally, a placebo blend of Avicel PH102 and 0.75% magnesium stearate was prepared and run through the press using high compression force. This procedure conditioned the punch faces and tabletting of the active granulation could be started and completed without any evidence of sticking or picking. These were extended runs of at least 100,000 tablets and no filming or sticking was observed after successful start-up. This is contrary to an earlier report that adhesion force increases with increasing running time even though there is no evidence of picking or sticking.[3]

In summary, the tablet adherence problem could not be totally overcome by formulation adjustments so it was felt that the formulation was adequate and the problem was related to tooling or equipment. Since this product was eventually compressed on four separate tablet presses (Stokes RB2, 16 station; Manesty BetaPress, 16 station with 3½" lowers; Manesty BetaPress, 16 station with 5¼" lowers; Kilian RTS 18, 16 station press), and the sticking and filming problems were observed on all of them, it was felt that the tablet tooling should be examined.

Tooling Considerations

A search of the literature and an informal poll of tooling manufacturers and pharmaceutical companies indicated that this problem is common and can be difficult to overcome. Possible remedies that were identified as a result of this search were: chrome plated tooling, chromium nitride ion bombardment of tooling, conditioning or 'running in' of tooling, electro-alloying with a nickel-chromium-boron alloy, and alternate punch cleaning and storage methods.

Conditioning of tooling can either be done as in the present case using a placebo blend of excipients in the active granulation or, as was reported by another pharmaceutical company, use of direct compression grade calcium sulfate. Another company admitted the use of a "cloth sock" filled with magnesium stearate that the operators use to dust the punches when necessary, a practice that may be difficult to justify or validate in a manufacturing procedure.

Further discussions with other manufacturers disclosed that one company has altered their routine cleaning and storage procedures for tablet tooling. Following normal washing of the tools with alcohol, rather than oiling the tools as is commonly done to guard against corrosion during storage, they store the tools without oil in a controlled humidity environment. Their experience has been that the oil is difficult to remove entirely from the tooling faces and this contributes to any inherent sticking problems. This premise led to the exploration of cleaning the tools with hexane as a less polar solvent than isopropanol and storage with a dusting of magnesium stearate rather than oil.

Two papers from 1982 by Shah, et al., and Tsiftsoglou and Mendes explored the use of an electro-alloying process using a nickel-chromium-boron alloy.[4,5] This process is provided by Lectro Alloys, Jersey City NJ, at a cost of about $20 per tool. Little is published about the actual process, but it is a surface coating that is subject to wear. These papers both concluded by subjective observation that tablets prepared with this tooling were superior in appearance than controls, but attempts to quantify these observations were inconclusive. This treatment was tried on another formulation that was under development in our lab during the same period and it offered no improvement over results seen with traditional tooling. That problem was eventually solved through formulation adjustments.

The use of chrome electroplating was explored with Natoli Engineering. It has been reported in the literature that tablet tooling coatings of chrome and Teflon have met with limited success because of high cost and wear.[4] Since these coatings are external surface treatments, they will certainly erode with use. However, Natoli claims that their electroplating technique has advanced with experience and that this approach has been successful in some cases. Therefore, it was decided to investigate this treatment. The cost for chrome plating is $3.50 per tool.

As a result of personal communications another option known as chromium nitride ion bombardment or chromium nitride implantation was considered. This process offered by BeamAlloy is extensively described in their company literature and in trade publications.[6] The process is carried out in two steps. First, the tools to be treated are placed in a high vacuum chamber and a thin coating of chromium (1000 Angstroms or less) is deposited on the surface of the tool. At relatively low temperatures (below 300°F) the tools are then subjected to a beam of ionized nitrogen gas produced by a small linear accelerator. This portion of the process implants chromium nitride into the surface of the tool to a depth of 0.01 to 1 micron, depending on the energy of the nitrogen atom. The chromium is implanted within the surface of the tool as chromium nitride, effectively changing the alloy composition of the steel. There is no external surface deposition of any material. This process can be used with any number of treatments using different ionic species depending on the desired end use of the product. Ion Nitride treatment alone purportedly imparts strength and wear characteristics. Chromium Nitride imparts strength, extended wear, and anti-adherent properties. According to BeamAlloy product literature, their most exacting application has been for the U.S. and Canadian mints in treatment of the plates used for stamping coins. Those tools are subjected to extreme stress and the specifications for the finished products are very critical. The cost of this treatment in quantities greater than 50 pieces is $8 each.

Experimental Results

The observations and results of the individual runs in the current experiment using the tooling array described in Table 1 are summarized by the subjective scores shown in Tables 2 & 3. Tablets were made by starting with compression force sufficient to make tablets with a hardness of 6-7 kp. Pressure was gradually reduced to prepare tablets having a hardness of 3-5 kp. The 9/32" tooling was used for a total of 5 separate runs of 5-10 minutes using active granulation with 2 placebo runs interspersed. Unlubricated Avicel PH102 was compressed for 5 minutes at relatively high pressure between Run 3 and Run 4. Lubricated Avicel placebo tablets were compressed between Run 4 and Run 5. Run #5 lasted in excess of 15 minutes.

The 11/32" tooling was used for 3 runs of 10 minutes each compressing active granulation. The same procedure used with the 9/32" tablets was followed.

TABLE 2
9/32" Tablets
Punch Tip Observation Scores

Station/Treatment	Run #1 U	Run #1 L	Run #2 U	Run #2 L	Run #3 U	Run #3 L	Run #4 U	Run #4 L	Run #5 U	Run #5 L	TOTALS U	TOTALS L
1 Chromium/IPA	+++	0	+	0	+	++	0	+	0	0	5	3
9 Plated/ "	++	++	+	++	0	++	0	+	0	0	3	7
5 " /Hexane	++	0	+	+	0	++	0	+	0	0	3	4
13 " / "	++	++	+	+	+	+++	0	++	0	0	4	9
2 Chromium/IPA	0	+	0	0	0	0	0	0	0	0	0	1
10 Nitride/ "	+	0	0	0	0	0	0	0	0	0	1	0
6 " /Hexane	0	+	0	0	0	0	0	0	0	0	0	1
14 " / "	0	+	0	0	0	0	0	0	0	0	0	1
3 Untreated/IPA	+++	++	+	++	0	+	0	0	0	0	4	5
11 (Control) "	++	+	+	++	0	+	0	0	0	0	3	4
7 " /Hexane	+++	++	0	0	0	+	0	0	0	0	3	3
15 " / "	+++	++	0	++	0	++	0	+	0	0	3	7
4 Mg Stearate	+++	++	+	++	0	+	0	+	0	0	4	6
12 Dusted /IPA	+++	++	+	++	0	+++	0	+	0	0	4	9
8 "	++	+	0	0	0	0	0	+	0	0	2	2
16 " /Hexane	+++	++	0	++	0	+	0	+	0	0	3	6
TOTALS	32	22	8	17	2	19	0	10	0	0	42	68

U = Upper Punches L = Lower Punches
0 = clean, no filming or sticking
\+ = film present
++ = film, some sticking observed
+++ = severe sticking

The lubricated Avicel placebo blend was compressed between Run 2 and Run 3. Run #3 lasted in excess of 15 minutes.

The compression characteristics as collected and analyzed by the Tablet Press Monitor were inconclusive and shed little light on the present problem. As described by earlier work, physical observation was more meaningful than quantitation of adherence forces.[4,5] As reported by earlier studies, measurement of take-off and ejection forces does not consider adherence to the upper punch faces which was a significant problem in the present case. Also, the anti-adherent activity of magnesium stearate could not be correlated with true lubricant properties as measured by ejection forces.[2] For information purposes, the compression force required to prepare tablets of the target hardness ranges were around 300kg for the 9/32" tablets and 350kg for 11/32" tablets. The ejection forces were so low, about 10-12kg, that sufficient meaningful data could not be collected. This suggests that the lubricant level is more than sufficient and die wall friction is minimal.

The results of the physical observations of the individual punch faces are displayed in Tables 2 & 3. The totals at the bottoms of the tables indicate the score (total number of +'s observed) for that run and give some measure of changes from run to run. The totals at the right of each table indicate the total score for that individual station. The scores for each configuration are totaled in Table 4 and allow for a way to recognize tendencies. In summary, the following observations were made with regard to each tooling treatment:

<u>Chromium Nitride Treatment</u>

This treatment is by far the most effective in overcoming the sticking and filming problems of the subject tablets. The only positive scores that were recorded for these tools occurred after the first run of the 9/32" tablets when slight filming on one upper and three lower punch faces was observed. It is suspected that this happened because the first run was not started at a high enough pressure and then decreased as was done in other runs. This is further evidenced by the fact that the 11/32" tablets were started at high pressure, then decreased, and no

TABLE 3
11/32" Tablets
Punch Tip Observation Scores

Station/Treatment	Run #1 U	Run #1 L	Run #2 U	Run #2 L	Run #3 U	Run #3 L	TOTALS U	TOTALS L
1 Chromium	0	+	++	++	+	+	3	4
9 Plated /IPA	0	0	+	+	0	0	1	1
5 "	+	+	++	0	++	0	5	1
13 " /Hexane	0	+	+	+	0	0	1	2
2 Chromium	0	0	0	0	0	0	0	0
10 Nitride/IPA	0	0	0	0	0	0	0	0
6 "	0	0	0	0	0	0	0	0
14 " /Hexane	0	0	0	0	0	0	0	0
3 Untreated	+	+	++	+	0	0	3	2
11 (Control)/IPA	+	0	++	0	0	0	3	0
7 "	++	0	+	0	0	0	3	0
15 " /Hexane	+	0	++	0	0	0	3	2
4 Mg Stearate	+	+	+	0	0	0	2	1
12 Dusted /IPA	+	0	+	0	0	0	2	0
8 "	0	+	0	0	0	0	0	1
16 " /Hexane	+	0	+	0	0	0	2	0
TOTALS	9	6	16	7	3	1	28	14

U = Upper Punches L = Lower Punches

0 = clean, no filming or sticking
+ = film present
++ = film, some sticking observed
+++ = severe sticking

evidence of filming of these punch faces was observed. After the first 9/32" run no filming or sticking of the chromium nitride tools was observed.

Chrome Electroplating Treatment

This treatment offers no advantage over untreated tooling, and in fact appears to have slightly poorer performance though the significance is not known. It was noted that these stations were showing more tendency to film and stick in the later runs as compared to the untreated tools.

TABLE 4

Punch Tip Observations - Total Scores

Treatment	9/32" Tablets Uppers	9/32" Tablets Lowers	11/32" Tablets Uppers	11/32" Tablets Lowers
Chromium Nitride	1	3	0	0
Chrome Plating	15	23	10	8
Magnesium Stearate Dusted	13	23	6	2
Untreated (Control)	13	19	12	4
Isopropyl Alcohol Washed	24	35	14	8
Hexane Washed	18	33	14	6

Untreated Tooling, Magnesium Stearate Dusted

This treatment offers no clear improvement over plain, untreated tooling. Any positive effects would be observed in the first run with either dosage strength as the magnesium stearate is quickly dispersed. No such effects were seen.

Untreated Tooling (Control)

The results observed for the untreated tooling are similar to what was expected based on previous experience.

Isopropyl Alcohol vs Hexane Wash

The observations clearly show no correlation between the solvent used to clean the tooling and the tendency toward sticking.

Avicel and Avicel/Magnesium Stearate Placebo Treatment

An interesting observation is that a plain microcrystalline cellulose placebo run was ineffective in conditioning the punches. This occurred between Run #3 and #4 of the 9/32" size and filming was still observed on several lower punches following Run #4. The Avicel/magnesium stearate run did condition the punches and eliminate filming in the 9/32" size. This is also true for the 11/32" size except for 1 lower and 2 upper punches which were chrome plated.

Upper Punches vs Lowers, 9/32" vs 11/32" Tablets

In the 9/32" tablet runs it can be observed that the upper punches cleared themselves much more rapidly than the lowers. This may be because the lowers are debossed with the SEARLE logo which provides more surface area and sites where sticking can start. The uppers contain a bisect that, while it is of greater height than the lettering of the logo, provides less surface area and no tight corners.

In the 11/32" tablet runs the lower punches clean up more quickly, no doubt because these are plain while the uppers contain the logo. No clear differences between the two sizes of tooling are apparent.

Surface Analysis

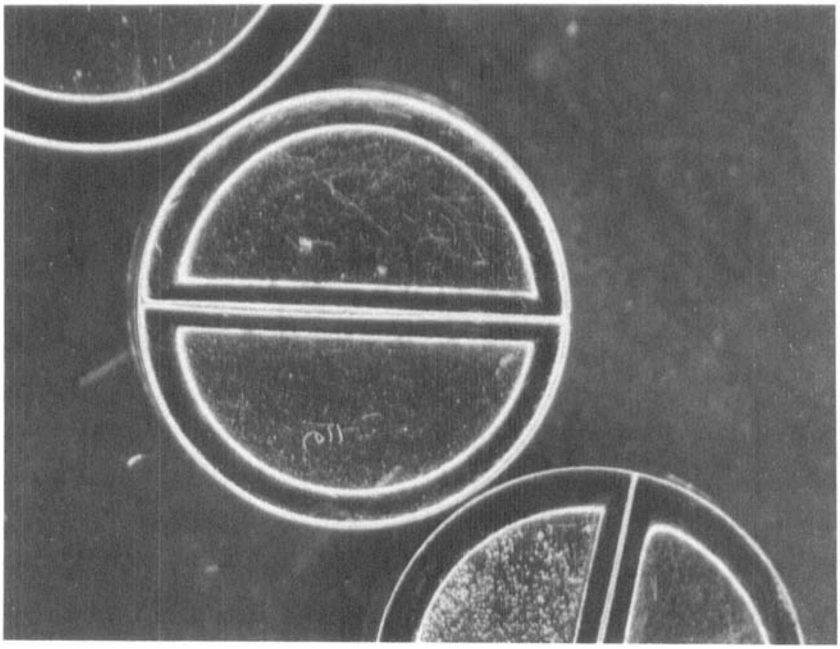
The results that were obtained were very promising and indicated that the chromium nitride implantation would eliminate the sticking problem. In an effort to describe a possible mechanism to explain the observed success, samples of tooling were sent to McCrone Associates for surface analysis.

Visual inspection of the treated tools reveals that the chromium plated tooling is bright and shiny while the chromium nitride treatment leaves the tools with a 'bronzed' or 'antiqued' appearance. Optical and scanning electron microscopy reveal some very surprising and perhaps unexpected results. Photomicrographs (Figures 1-3) taken at 7.5X magnification reveal that the chromium plated tooling is the only surface that is totally smooth. The chromium nitride treated tool is notably rough, almost appearing to be pitted. Untreated tooling at this magnification also appears to have surface imperfections.

The SEM's (Figures 4-9) confirm the observations of the optical microscopy. At magnifications of 30X and 4000X the chromium plated tools still obviously exhibit the smoothest surface although some random and very infrequent imperfections were observed. The untreated tools appear to have pits in the range of 1-2μm diameter and a swirled pattern that is imparted by the polishing process at the manufacturer. The swirled polishing pattern also can be observed in both of the treated tooling samples at higher magnifications (4000X). The chromium nitride tools exhibit very noticeable pits and crevices and even raised areas that are roughly 10-50μm in diameter. These imperfections are evenly distributed through the face of the tools.

Auger surface analysis and electron microprobe of the three tooling types were performed. These analyses revealed the percentage of atomic elements as found in Table 5. The Auger analysis was performed using Argon etching to a further depth of 100 to 500 Angstroms. These results are indicative of the surface of the

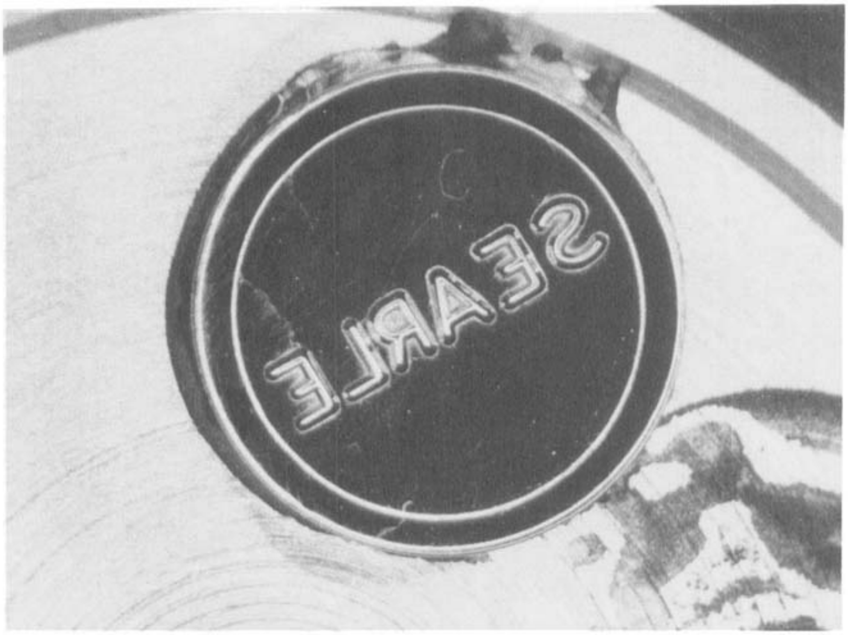
1



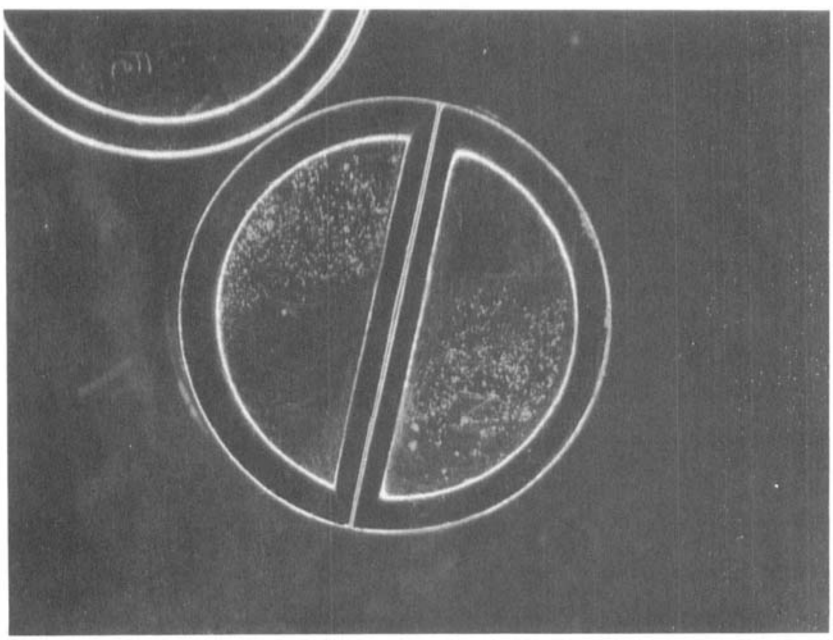
FIGURES 1,2,3 Photomicrographs (7.5X) of Untreated (Figure 1), Chrome Plated (Figure 2), and Chromium Nitride Treated (Figure 3).

tools only, so the data do not match exactly with what may be expected for the total alloy composition. This is because of the high levels of oxygen reported due to the thin layer of oxides present. The data do indicate the presence of low alloy steel for the untreated tools, primarily chromium in the chrome plated tools, and chromium and nitrogen (probably chromium nitride) in the chromium nitride treated tools. Further analysis of the pits in the chromium nitride samples revealed high concentrations of carbon with traces of sulfur, chlorine, and aluminum, probably polishing residues that are entrapped in the surface of the tool during the final polish by the tooling manufacturer.

2



3



4

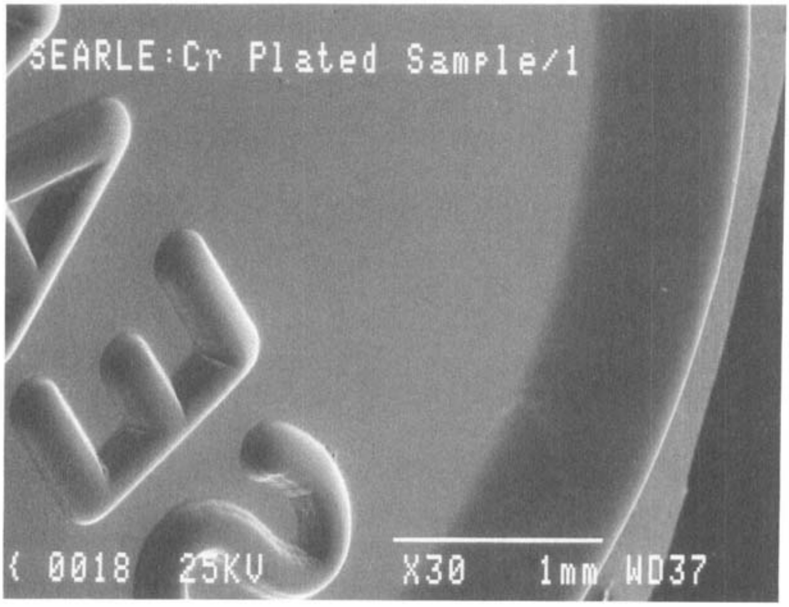
FIGURES 4,5,6 SEM's (30X) of Untreated (Figure 4), Chrome Plated (Figure 5), and Chromium Nitride Treated (Figure 6).

These residues are then "burned into" the face of the tooling during the ion implantation process. These residues were also detected in the untreated and chrome plated tools.

Mechanism

The relatively rough surface of the chromium nitride treated tooling as compared to the totally smooth surface of the chrome plated tools suggests that the experimental results should have been reversed. The success of the chromium nitride treatment may be due to either or both of two mechanisms. First, it may be possible that the microscopic pits and imperfections in the tooling face provide loci that "break" the

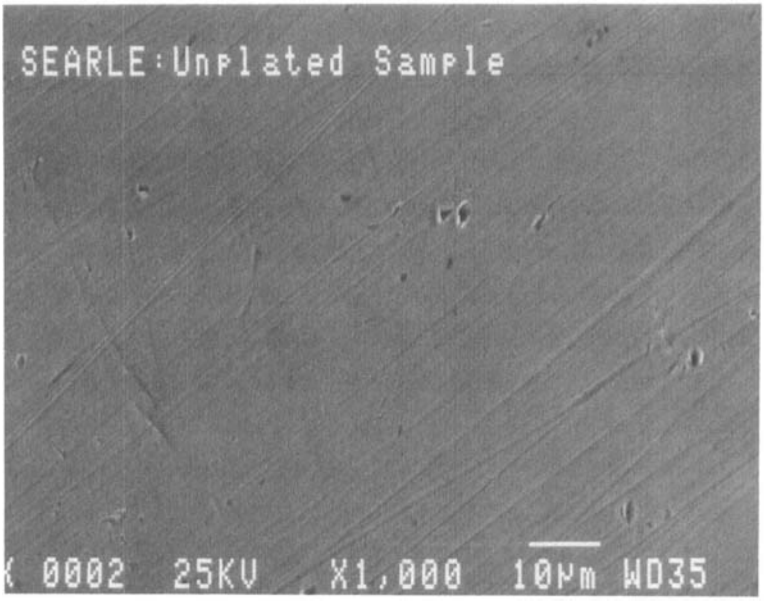
5


SEARLE:Cr Plated Sample/1
(0018 25KV X30 1mm WD37

6


RLE:Implanted Sample/2
(0014 25KV X30 1mm WD37

7

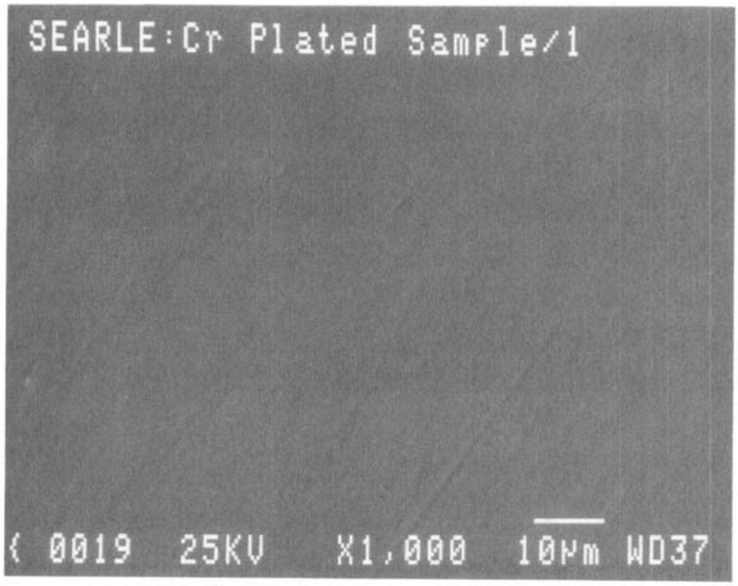


FIGURES 7,8,9 SEM's (1000X) of Untreated (Figure 7), Chrome Plated (Figure 8), and Chromium Nitride Treated (Figure 9).

suction and allow the tablet face to pull away from the tooling. On the contrary, the tooling face of the chrome plated tools is so smooth that the force of suction is greater than the cohesive force of the tablet and therefore portions of the tablet face break away in order to break the suction force. This premise is described more fully by Mitrovej and Augsburger.[2] Due to the soft nature of this tablet formulation this mechanism is likely. Apparently, there is a threshold limit of adherence force to overcome and once this is achieved the punch faces are conditioned by the granulation.

Secondly, one purported attribute of the BeamAlloy chromium nitride treatment is a decrease in chemical

8


SEARLE:Cr Plated Sample/1
{ 0019 25KV X1,000 10μm WD37

9

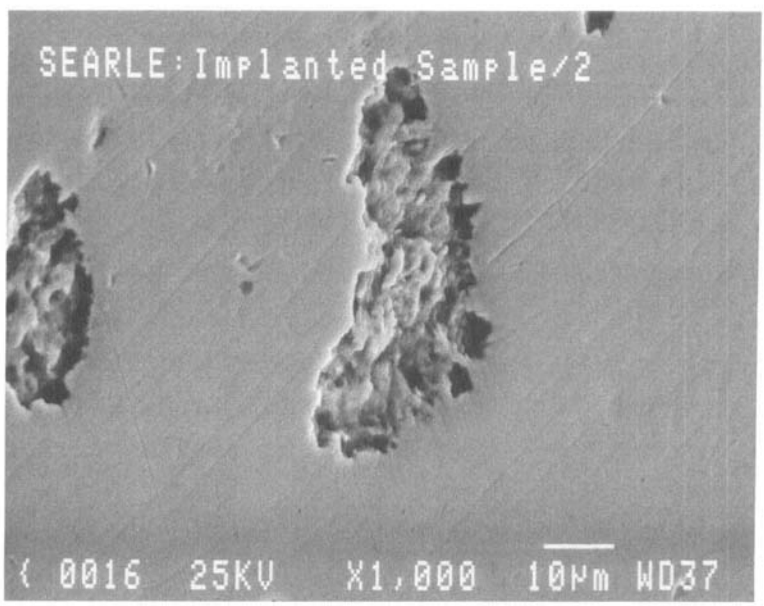

SEARLE:Implanted Sample/2
{ 0016 25KV X1,000 10μm WD37

TABLE 5
AUGER SURFACE ANALYSIS
ATOMIC % OF ELEMENTS ON SURFACE

Sample	Fe	Cr	C	Ni	Mn	Si	O	S	Cl	Ca	N
408 Steel[7]	*	.75	.50	3.0	.50	.25	-	-	-	-	-
Untreated	50.0	0.9	12.6	-	-	-	25.7	5.3	3.1	2.4	-
Chromium Plated	-	55.2	3.5	-	-	-	16.4	16.0	7.7	1.2	-
Chromium Nitride Implanted	-	50.4	1.6	-	-	-	29.6	-	-	-	18.4

*Not listed but may be assumed to be balance of Atomic % if surface oxides are ignored

reactivity of the steel. In some instances this mechanism may be beneficial and plausible but it does not seem likely in the present study.

As a result of this study full sets of production tooling were obtained and subjected to the chromium nitride ion bombardment treatment. The full sets of tooling were utilized in a production environment using the same granulations as used in this study. No sticking or filming was encountered when high compression force was used for start-up and then decreased to normal levels. The results of these production trials confirmed the findings of this study and as a result this treated tooling will be used for production of this product.

CONCLUSIONS

This study has compared several alternatives for alleviation of tablet sticking and punch filming with a problem granulation. As a result of this study chromium nitride ion bombardment has been shown to eliminate punch filming in the case of the subject granulation. Scale-up to full size production batches has shown that this treatment is successful and will be used for commercial production of these tablets.

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REFERENCES

1. T.A. Miller, P. York, IJP 41, 1, (1988).
5. A. Mitrovej, L.L. Augsburger, Drug Dev. Ind. Pharm., 6 (4), 331, (1980).
3. A. Mitrovej, L.L. Augsburger, Drug Dev. Ind. Pharm., 8 (2), 237, (1982).
4. K.B. Shah, L.L. Augsburger, R.F. Shangraw, Pharm. Tech., 31, April 1982.
5. T.B. Tsiftsoglou, R.W. Mendes, Pharm. Tech., 30, April 1982.
6. A.H. Deutchman, R.J. Partyka, C. Lewis, Industrial Heating, 32, January 1990.
7. "Tabletting Specification Manual, Third Edition", APhA, Washington DC, 1990.