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1 **Lamination of pharmaceutical tablets: classification and influence of process**
2 **parameters**

3 V. Mazel*, P. Tchoreloff

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5 Univ. Bordeaux, CNRS, Arts et Metiers Institute of Technology, Bordeaux INP, INRAE,
6 I2M Bordeaux, F-33400 Talence, France

7 *corresponding author: Université de Bordeaux, CNRS, I2M Bordeaux, 146 rue Léo
8 Saignat, F-33000 Bordeaux, France ; tel:+33 5 57 57 92 60 ; E-mail address:
9 vincent.mazel@u-bordeaux.fr

10

11 **Abstract**

12 Lamination is a common industrial problem during the production of pharmaceutical
13 tablets. It corresponds to a failure of the tablet in one or several planes parallel to the
14 surface and passing through the tablet band. But different kinds of lamination exist, and
15 a classification of the different cases is proposed in this work. Type 1 corresponds to a
16 multiple fracture caused by air entrapment. Type 2 occurs because of the shear stresses
17 developing when the tablet goes out of the die. Type 3, which is limited to convex
18 tablets, is due to a tensile stress developing at the center of the tablet at the end of the
19 unloading that further propagates toward the band. One case of each type was studied
20 experimentally in order to test three solutions classically used at the industrial level:
21 slowing down the press, using a precompression and using a tapered die. Results
22 shows that, in coherence with the proposed mechanisms, lamination type 1 can be
23 mitigated by slowing down the press or using a precompression. For type 2, only the
24 tapered die solution stopped lamination. None of the solutions completely solved

25 lamination type 3. Nevertheless, the use of a tapered die decreased the severity of the
26 problem avoiding the propagation of the crack until the surface.

27 **Keywords:** lamination, tablet, compression, precompression, tapered die.

28

29 **1. Introduction**

30 Tablet defects are a major concern during the manufacturing of pharmaceutical tablets.

31 Sticking, capping and lamination are among the defects the most commonly and the

32 most often described in the literature. Capping and lamination both refers to a problem

33 of tablet failure after the ejection of the tablet from the die, but they, in fact, correspond

34 to different phenomena. Capping refers to the separation of the surface of the tablet and

35 is especially observed on convex tablets even if it can also sometimes happen on flat

36 tablets. Lamination refers to a failure of the tablets in planes normal to the compaction

37 direction passing through the band of the tablet¹. Capping and lamination correspond

38 thus to different failure patterns which comes from the fact that their causes and

39 mechanisms are different. The mechanism for capping can be found in the literature²⁻⁴.

40 As it corresponds to a phenomena different from lamination, it will not be considered in

41 the present work that will focus on the case of lamination.

42 In fact, even lamination does not correspond to a single phenomenon. There are

43 different kinds of lamination that correspond to different mechanisms. This was long

44 recognized in the pharmaceutical literature. In 1960, Long published two important

45 articles, one about the evolution of die wall pressure during compaction⁵ and one about

46 problems of air entrapment during compaction⁶. In both articles, laminated tablets are

47 shown but their failures are attributed to different causes. In the case of wax tablets⁶,

48 cracks are attributed to the presence of air in the compact and at the end of this article
49 authors made this conclusion: “The cracks observed in wax compacts (...) are very
50 similar in appearance to those produced by residual radial pressures in the die, but the
51 conditions required for the production of cracks of the latter type are much less
52 restrictive”. This means that even if the patterns look similar, their origin is different. And
53 of course, if the origin of lamination is different, it can be foreseen that the different kinds
54 of lamination might not be solved using the same technical solution.

55 In order to solve lamination problems, it is thus important to understand correctly the
56 phenomena and to be able to distinguish between the different kinds of lamination.
57 Nevertheless, there is, to our knowledge, no published article that, based on the existing
58 literature, tries to classify the different kinds of lamination and to understand how they
59 could be solved. The aim of the present work is thus, first to present a classification of
60 the different lamination phenomena and to describe, based on the literature, the
61 mechanisms that promote each case. Then, taking an experimental case study of each
62 kind of lamination, the influence of various process parameters (compaction speed,
63 precompression and use of tapered die) will be studied in order to confirm the
64 mechanisms involved and to help to propose useful strategy to solve lamination
65 problems at the industrial level.

66 **2. Lamination classification**

67 According to a survey of the literature and to the authors experience, there are at least 3
68 different cases of lamination occurring during the production of pharmaceutical tablets.
69 They will be called lamination type 1, 2 and 3 in the following text. It is worth noting that
70 other kinds of lamination might exist that will not be described in the present text.

71 Lamination type 1 corresponds to the case where lamination is due to air entrapment as
72 described by Long *et al.* for the compression of wax⁶. In the cited article, it is said that
73 this phenomenon occurs for high speed compression in the case of materials that are
74 very compressible, i.e. that can be compressed very close to their true density. This is
75 for example the case for materials characterized by a very ductile behavior
76 under pressure. In this case, air can be entrapped in the tablets and the increase of air
77 pressure can lead to a breakage of the tablet during unloading. This phenomenon was
78 also described more recently using microcrystalline cellulose^{7,8}. One of the distinctive
79 characteristics of this kind of lamination is that it seems that the pattern of failure is
80 relatively random, i.e. failure does not always occur at the same place in the band ^{7,8}.

81 Lamination type 2 was also described by Long and is due to the die wall pressure and to
82 the shear stresses occurring when the tablet goes out the die⁵. In fact, when the tablet
83 goes out of the die, due to the elastic recovery and to the residual die wall pressure,
84 shear stresses develop at the edge of the die as shown more recently by numerical
85 simulation⁹. In this case, the shear stresses can promote the development of cracks that
86 will then propagate from the exterior to the interior. As it can be seen on the numerical
87 simulations presented by Garner *et al.*⁹, the shear stresses are very concentrated on the
88 band. So, as in the case of capping which is also due to a concentrated stress,
89 lamination type 2 should more affect products that present a great sensitivity to stress
90 concentration². It is interesting to note that this phenomenon seems to be more severe
91 without lubrication ^{5,10}. It seems also that the pattern of failure is reproducible from one
92 tablet to the other.

93 Finally, lamination type 3 affects specifically biconvex tablets and correspond to a single
94 failure plane in the middle of the band¹¹. It is due to the development of tensile stresses
95 at the center of the tablet at the end of the unloading. This means that the failure starts
96 at the center of tablets and then propagates towards the exterior¹¹. It is favored by a
97 small band thickness. Due to the mechanism, this kind of failure is also favored by a
98 high residual die wall pressure. Finally, as for any kind of failure, crack propagation will
99 be favored in the case of products presenting a brittle fracture behavior.

100 As the three types of lamination arise from different mechanisms, it can be foreseen that
101 they will not be always influenced by the same process parameters. All the three types
102 of lamination are favored by a high compaction pressure but, for example, it was found
103 that a high tablet thickness increases lamination tendency for type 1⁸ but decreases
104 lamination tendency for type 3¹¹. Among the classical technological solution that are
105 often adopted in case of lamination occurrence at the industrial level, three were studied
106 in the present work. The first is to slow down the press, i.e. studying the influence of
107 press speed on the defect occurrence. The second is precompression and the third is
108 the use of a tapered die. Upper punch penetration level is another factor which is often
109 used to solve lamination. Nevertheless, due some limitations of the compaction
110 simulator used, it was not possible to change this parameter without affecting the
111 kinematic of the rest of the compaction cycle. This parameter was thus not studied in the
112 present work.

113 In the following text, three examples of lamination situations, each representing one of
114 the 3 types presented above, were studied, and the influence of the three classical

115 solutions (speed, precompression and tapered die) on each case of lamination was
116 assessed.

117 **3. Materials and method**

118 **3.1. Powders**

119 Three different formulations were considered in the present work, each one representing
120 one type of lamination. Their choice was based on previous studies and on in house
121 knowledge^{8,11}. The products used were Microcrystalline cellulose “MCC” (Vivapur 12,
122 JRS Pharma, Rosenberg, Germany), Anhydrous calcium phosphate “ACP” (Anhydrous
123 Emcompress, JRS Pharma, Rosenberg, Germany) and Tricalcium phosphate “TCP”
124 (Tricafos 500, Chemische Fabrik Budenheim, Budenheim, Germany). Each product was
125 mixed with 2% (w/w) of Magnesium stearate (LIGAMED MF-2-V , Peter Greven France,
126 Rueil Malmaison, France). This percentage, which is relatively high especially for MCC,
127 was chosen for the sake of the demonstration. In the case of MCC, it makes it possible
128 to emphasize the lamination defects as shown elsewhere⁸. For ACP and TCP, this
129 percentage is needed to avoid sticking problems. Formulation blending was performed
130 for 5 minutes at 49 rpm in a Turbula mixer (Type T2C, Willy A. Bachofen AG, Muttenz,
131 Switzerland).

132 **3.2. Tablet manufacturing**

133 All tablets were manufactured on a compaction simulator Styl’One Evolution
134 (Medelpharm, Beynost, France). This device is a single station instrumented tableting
135 machine. It is equipped with force sensors (strain gauges) on both punches and on the
136 die wall, and the displacements of the punches are monitored using incremental

137 sensors. It is equipped with one engine for each punch. The compaction cycle was set to
138 simulate a Korsh XL 100 tableting press. Three speeds were simulated: 1 rpm, 10 rpm
139 and 60 rpm. At these speeds, the maximum punch velocities during compaction were
140 respectively 1.5 mm/s, 14 mm/s and 80 mm/s.

141 **3.2.1. Lamination experiments**

142 First, process parameters were chosen for each product to obtain lamination. The
143 manufacturing parameters were adapted for each product for the sake of the
144 demonstration, i.e. parameters were chosen to obtain laminated tablets. MCC and TCP
145 tablets were manufactured using 11.28mm round flat punches and ACP tablets using
146 11.28R11 round concave punches (i.e. punch diameter of 11.28 mm and radius of
147 curvature 11 mm). Two dies were used (ACM, Avilly-Saint-Léonard, France). A straight
148 die and a tapered die with taper depth of 4.76mm and a total enlargement of 0.08mm
149 (i.e. a taper angle around 0.3°). Filling height was 10 mm for MCC, 9.2mm for TCP and
150 8 mm for ACP. Manufacturing pressure was set to 230 MPa for MCC, 100 MPa for TCP
151 and 200 MPa for ACP. All compaction experiments were performed using a symmetrical
152 compression with a tablet center positioned at 6mm inside the die (this position ensures
153 the symmetrical compression on the machine used)

154 Precompression was added for some experiments as explained below. For each
155 formulation, different levels of precompression were tested. Precompression pressure
156 was set to 20, 35, 80, 112 and 130 MPa for MCC. For TCP precompression pressures at
157 20, 35, 50 and 80 MPa were tried. For ACP precompression levels at 15, 30, 60, 115
158 and 160 MPa were used.

159 For each condition, 10 tablets were made and scrutinized to assess lamination.

160 **3.2.2. Characterization experiments**

161 These experiments were performed to determine the tableability profiles for all the
162 products. For this purpose, 11.28 mm flat round punches were used. A straight die was
163 used for MCC and ACP and the tapered die previously described was used for TCP, as
164 no intact tablets could be obtained using a straight die. Tableability was measured,
165 using, as in the lamination experiments, the cycle of a Korsch XL-100 at three
166 compaction speed: 1rpm, 10 rpm and 60. The filling heights were the same as in part
167 3.2.1. For each product and each speed, tablets were manufactured at 6 pressure points
168 between 40 and 260 MPa. Three tablets were manufactured for each pressure point.

169 **3.3. Mechanical tests**

170 The diametral compression test was used in two cases. First, it was used to detect
171 lamination type 3 in the cases where the tablet was not visually laminated. It was
172 previously seen that this methodology was well suited to detect internal lamination
173 cracks by comparing the results with images obtained using X-ray micro CT on the tablet
174 before the breaking test¹¹. Second it was used to break the tablets made to build the
175 tableability profiles.

176 The diametral compression test was performed using a TA.HDplus texture analyzer
177 (Stable microsystems, Surrey, United Kingdom). Compacts were compressed between
178 two flat surfaces at a constant speed of 0.1 mm.s⁻¹ with an acquisition frequency of 500
179 Hz.

180 For the tableability profiles, the tensile strength, σ_r , was calculated for each test using
181 the following equation¹²:

$$182 \quad \sigma_r = \frac{2F}{\pi Dh}$$

183 where F is the breaking force, D the diameter of the tablet and h its thickness.

184

185 **4. Results and discussion**

186 **4.1. Lamination behavior of the formulations**

187 At a compaction speed of 60 rpm, without precompression and in a straight die, all the
188 products studied presented lamination after the ejection. A photograph of a laminated
189 tablet for each product is presented in Figure 1.

190 The failure pattern for MCC is similar to the one presented in a previous publication⁸. It
191 corresponds to a multi-breakage with a random pattern from one tablet to another and
192 can be classified as type 1⁸.

193 The pattern obtained for ACP was already described elsewhere¹¹ and corresponds to a
194 breakage into two halves in the middle of the band that we classified as type 3.

195 TCP tablets presented a very reproducible failure pattern with a thin layer detaching
196 from the bottom of the tablet at the end of the ejection. The reproducibility of the pattern
197 and the fact that it was near one end of the tablet seemed to indicate that it
198 corresponded to a type 2. Nevertheless, as the failure occurs in the band but near the
199 edge of the tablet, this defect could be confused with capping. In order to ensure our
200 identification of this defect as lamination type 2, some tests with a lower lubrication were

201 performed. Indeed, as mentioned above, the cases found in the literature are usually
202 obtained on unlubricated tablets ^{5,10}, which seems to mean that a lower lubrication
203 should increase the defect. A first try was performed using TCP with only 0.5% of
204 Magnesium stearate. Figure 2 shows the comparison between the failure pattern
205 observed with 0.5% and 2% lubricant in the powder. The patterns look similar, i.e. a
206 layer is detached at the bottom of the tablet, but in the case of 0.5% of lubricant, this
207 layer is thicker and the defect cannot be confused with capping anymore. This confirms
208 that the defects observed was indeed lamination, and, as said above, the reproducibility
209 of the pattern points towards a type 2. Note also that this pattern is very similar to the
210 one presented by Anuar et al. for unlubricated paracetamol tablets compressed at
211 moderate pressure ¹⁰. It is important to remark that in the cited article, the detached
212 layer is near the top of the tablet but the tablet was ejected downwards, i.e. with the
213 bottom part exiting first. So the broken layer is situated near the face that last exits the
214 die, like in the present case.

215 A further try was made without any lubricant. It led to completely destroyed tablets after
216 ejection as presented in Figure 3. Cracks are occurring in multiples directions so the
217 failure pattern is difficult to describe precisely. Nevertheless, among the fractures, several
218 laminations level can be seen, as expected from the literature ^{5,10}, which confirms,
219 again, that for this product, a lamination type 2 is observed.

220 **4.2. Influence of the process parameters**

221 As described above, three solutions were tested to solve the lamination problem:
222 reducing the tableting speed, adding a precompression and using a tapered die. The
223 results obtained are presented in Table 1. The number in each cell of the table

224 corresponds to the percentage of laminated tablets among the 10 tablets produced for
225 each condition.

226 The first parameter studied was the compaction speed. As said above, in a straight die
227 at 60 rpm, 100% of the tablets were laminated for the three products. The compaction
228 speed was first reduced to 10 rpm. As reported in Table 1, at this speed, all the tablets
229 of TCP and ACP were still laminated. On the contrary, MCC tablets showed no sign of
230 lamination. To further test the effect of speed on the lamination of ACP and TCP, the
231 press was then slowed down to 1 rpm. Again, all the tablets showed defects.
232 Nevertheless, if for ACP the lamination pattern was exactly the same, in the case of
233 TCP, the defects looked slightly different as shown in Figure 4. At 1 rpm, the lower part
234 of the tablet did not separate completely, like at higher speed, but only a part of it was
235 detached and it was necessary to pull it a little bit to detached it.

236 In a second step, effect of precompression was studied at 60rpm with a straight die. In
237 the case of MCC, using a precompression made it possible to suppress completely the
238 problem. For the main compression pressure used, 230MPa, levels of precompression
239 between 35 and 115 MPa made it possible to obtain intact tablets. On the contrary with
240 precompression pressures at 20 and 130MPa, the tablets were laminated. There is thus
241 a minimum and a maximum level of precompression between which precompression is
242 effective to suppress this type of lamination. For ACP and TCP, various levels of
243 precompression were also tried as described above, but in each case, 100% of the
244 tablets were still laminated, whatever the precompression pressure.

245 Finally, the effect of a tapered die was also studied at 60 rpm. For MCC, under the
246 conditions used, no effect was found, all the tablets being laminated after the ejection.

247 On the contrary, for TCP, the use of a tapered die made it possible to suppress
248 completely the problem as no sign of lamination was detected on the produced tablets.
249 Finally, the case of ACP gave another situation. Directly out of the die, the tablets
250 showed no external sign of lamination as mentioned in Table 1. The ten tablets were
251 then submitted to the diametral compression test to verify if signs of lamination could be
252 found inside the tablet as described elsewhere ¹¹. All the tablets showed, after diametral
253 compression large signs of internal defects as shown in Figure 5. This means that the
254 use of a tapered die didn't suppress completely the lamination, as the cracks were seen
255 after the diametral compression test, but it renders the problem less severe, meaning
256 that the cracks, which are created at the center, did not fully propagate until the tablet
257 band.

258 **4.3. Tableability profiles**

259 To allow for a better interpretation of the lamination phenomena, tableability profiles
260 were determined, for each product, at 1rpm, 10 rpm and 60 rpm. As seen above, in the
261 case of TCP, no intact tablet could be obtained if a straight die was used. In order to
262 have an idea of the behavior of this product, it was thus decided to use a tapered die.
263 Nevertheless, a straight die was used for MCC and ACP. The results are presented in
264 figure 6.

265 As expected, MCC makes it possible to obtain strong tablets at low speed. It also
266 showed signs of strain rate sensitivity as weaker tablets were obtained, at the same
267 pressure, when the press speed increased. This is especially visible between 60 rpm
268 and 10 rpm. It can also be noticed that, at 60 rpm, no tablets are presented above 125
269 MPa. The reason is that, above this pressure, all tablets were laminated using this

270 compaction speed. Finally, it can be seen that the level of pressure chosen for the
271 lamination study, 230 MPa, correspond to a case where the tensile strength seems to
272 reach a limit, i.e. it is closed to what is sometimes called “over-compression” in the
273 literature.

274 TCP also makes it possible to obtained very strong tablets (e.g. the tensile strength of 2
275 MPa which is often recommended is already overpassed at a compaction pressure of
276 100 MPa). No sign of strain rate sensitivity could be seen for this product. Contrary to
277 the case of MCC, the pressure chosen for the lamination study, 100 MPa, is far from a
278 tensile strength plateau. At 100 MPa, the product cannot be considered as over-
279 compressed.

280 Finally, among the three products presented, ACP gives the weakest tablet at one
281 compaction pressure. It is interesting to note that some strain rate sensitivity can be
282 found for this products despite its known brittle nature. As for TCP, for the pressure used
283 in the lamination study (200 MPa), the tensile strength has not reached a plateau and
284 the product is not over-compressed.

285 **4.4. Discussion**

286 The different technical solutions commonly used to solve tablets lamination had some
287 effects as presented in Table 1. Nevertheless, the effect was dependent on the type of
288 lamination. It would thus now be interesting to discuss the reasons why some of the
289 solutions might have an effect and why they made it possible to mitigate or not the
290 different kinds of lamination.

291 Let's first consider the influence of tableting speed. Considering the literature, two main
292 effects can be foreseen. First, increasing the tableting speed will leave less time for air
293 to escape during the compression so it will favored the increase of air pressure during
294 compression and as such it should influence the occurrence of lamination type 1 ^{6,7,13}.
295 So it is logical to find that the lamination of MCC, i.e. lamination type 1, which is due to
296 air entrapment can be solved by slowing down the press. The second effect is that
297 increasing the compaction speed generally lowers the tableability, i.e. the tensile
298 strength obtained for a given compaction pressure ¹⁴. Results presented above showed
299 that both MCC and ACP presented some strain rate sensitivity (Figure 6). This effect
300 might thus participate also in the resolution of lamination Type 1 and could also
301 influence, in our case, lamination type 3. Nevertheless, even if an influence of speed on
302 lamination type 3 cannot be completely ruled out, the results presented above showed
303 that, even at very low speed, tablets still presented defects. Slowing down the press
304 seems thus not to be an option to avoid lamination 3 in the present case. As no impact
305 of the speed on the tensile strength was found in the case of TCP, this could explain the
306 lack of efficiency of speed reduction in our case for lamination type 2. Nevertheless, in
307 the case of TCP, it was observed, at very low speed, that the defects pattern was
308 slightly different. It is difficult to give a definitive explanation for this phenomena.
309 Nevertheless, one reason could come from the friction. As said above, it is well known
310 that lamination type 2 is influenced by the friction between the tablet and the die, i.e. the
311 phenomena seems worth when the frictions are high ^{5,10}. More precisely, the results
312 obtained above for various lubrication levels indicate that decreasing the friction moves
313 the location of the defect toward the lower face of the tablet. It is also known that the
314 friction coefficient increases with the sliding speed¹⁵. So decreasing the speed, because

315 it lowers the friction coefficient, moves the initiation of lamination toward the tablet edge.
316 A crack which initiate near the tablet edge would lead to a very thin layer which is likely
317 to break due to the granular structure of the tablet. This could explain why only
318 incomplete layers are detached.

319 The role of precompression has been debated in the literature. On the one hand it
320 seems to have a desaeration role, i.e. it reduces the amount of air in the tablet during
321 the main compression step ¹⁶⁻¹⁹. On the other hand, it increases the time under pressure
322 and as such it could allow for stronger bonds in the tablet ¹⁸⁻²⁰. It is a mean that is often
323 used in case of tablet defects, i.e. lamination and capping. There is no definitive proof in
324 the literature about the way precompression could solve defect problems, but in the case
325 of capping, it was shown that the increase of the time under pressure was, at least in
326 certain cases, not the reason for problem solving ²¹. In the present case,
327 precompression only made it possible to suppress lamination in the case of lamination
328 type 1, i.e. MCC. In this case, it was found that between a minimum and a maximum
329 pressure, the use of precompression made it possible to obtain intact tablet. The results
330 for MCC is coherent with the proposed mechanism, i.e. air entrapment. Precompression
331 makes it possible to release air from the formulation. A minimum precompression
332 pressure is needed. This means that, to be effective, a threshold quantity of air must go
333 out of the tablet during precompression. If the pressure during the precompression is too
334 high, porosity will be closed during precompression, so air will not escape and
335 lamination might occur during precompression. This explains the existence of a
336 maximum pressure value. This is confirmed by the tableability results presented in
337 figure 6. As said above, for pressures higher than 125 MPa, no intact tablets were

338 obtained for MCC at 60 rpm. The precompression pressure 130MPa is thus in the range
339 where lamination starts without precompression. It is logical to find the upper limit of
340 precompression in this range. Concerning the two other cases of lamination, there is no
341 proof in the literature that precompression changes the structure of the tablet (e.g.
342 density distribution) or the stresses applied to it (e.g. residual die-wall pressure). So
343 considering the mechanism described above, it is not surprising that precompression
344 had no impact on lamination type 2 and 3.

345 Finally, the effect of tapered die, as presented in the literature, seems to rely on two
346 main effects. The first one is that the larger gap between the punch and the die on the
347 upper part of the die makes it easier for air to escape¹³. The second one has to do with
348 the release of the die wall pressure during unloading. Because the slope of the taper is
349 small, the release of the die wall pressure is much more gradual (or slower) than in the
350 case of a straight die. The shear stresses at the edge of the die are then smaller and it
351 was shown that this made it possible to limit defects seen on the tablet band ⁹. Results
352 presented in Table 1, indicate that the tapered die had no effect on the lamination of
353 MCC. This means that, even if the impact of the tapered die on air escape cannot be
354 ruled out, the effect obtained in our case was marginal and did not allow for a mitigation
355 of lamination. On the contrary, for TCP, the use of a tapered die suppressed completely
356 lamination. This is very logical if we consider that TCP corresponds to a lamination type
357 2. In this case, lamination is due to a shear stress acting on the tablet band when the
358 tablet goes out of the die. But these shear stresses are due to the die wall pressure and
359 to the elastic recovery of the tablet. The tapered die makes it possible to smoothly

360 release the elastic strains and the die wall pressure and, as a consequence, it lowers the
361 shear stresses that can promote lamination during ejection ⁹.

362 Finally, the effect of a tapered die on ACP gives an interesting insight on this case of
363 lamination. As described above, this defect comes from tensile stresses at the center of
364 the tablet that develop at the end of the unloading and that propagate from the center
365 towards the surface of the band ¹¹. Considering this mechanism, it is thus not expected
366 to have significant effect of the tapered die on the occurrence of this defect as it does
367 not change the unloading part of the cycle (note that the whole band is below the taper
368 during unloading in the conditions used in this study). Nevertheless, the results showed
369 that, contrary to the case of the straight die, the tablets were not laminated out of the die.
370 After diametral compression, the tablets showed nevertheless large lamination defects,
371 meaning that the use of tapered die did not eliminate the initiation of the defects but that
372 it more likely played a role on the growth of the defects toward the surface. This seems
373 to indicate that the ejection process and especially the friction occurring during ejection
374 play a role in the propagation of the central defect toward the surface. As a tapered die
375 lowers the die wall pressure during ejection it also lowers the friction forces, reducing, by
376 this way, the growth of the central crack of the tablet. So in the case of lamination type 3,
377 tapered die did not suppress the lamination cracks but it limited their propagation

378 **5. Conclusion**

379 At least three different kinds of lamination of pharmaceutical tablets can be described.
380 Each type corresponds to a different mechanism and as such is influenced differently by
381 the process parameters.

382 On the one hand, in the case of lamination type 1, which is due to air entrapment,
383 slowing down the press and using a precompression were shown to be efficient means
384 to mitigate the problem. On the other hand, these two solutions had no effect on
385 lamination type 2, which is promoted by shear stresses developing upon the ejection of
386 the tablet from the die. Nevertheless, we found it possible to suppress lamination type 2
387 by using a tapered die, solution that had no visible influence on the case of lamination
388 type 1 studied in this work. Finally, none of the three proposed solutions had a definitive
389 effect on lamination type 3. Only the tapered die was found to lower slightly the severity
390 of the defects without suppressing them completely. In the case of this defects, solution
391 can come from changes in the tablet geometry in order to increase the band thickness
392 as already presented elsewhere¹¹.

393 These results show that, at the industrial level, when lamination problems occur, it is of
394 primary importance to correctly identify the type of lamination during the root cause
395 analysis in order to use the adapted technical solution for troubleshooting.

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447

448 **Legend to figures**

449 Figure 1: Photographs of laminated tablets: MCC(left), TCP (center) and ACP (right)

450 Figure 2: Comparison of the fracture patterns of TCP with different lubrication levels:

451 0.5% (left) and 2% (right)

452 Figure 3: Example of tablet obtained for unlubricated TCP

453 Figure 4: Tablets obtained for TCP at 1 rpm

454 Figure 5: Photograph of the interior of a tablet of ACP after the diametral compression

455 test

456 Figure 6: Tabletability profiles (a) MCC; (b) TCP and (c) ACP.

457 **Legend to tables**

458 Table 1: results of the observation of lamination for the different conditions used. The

459 number in one cell indicates the percentage of laminated tablets among the 10 tablets

460 produced for these parameters.











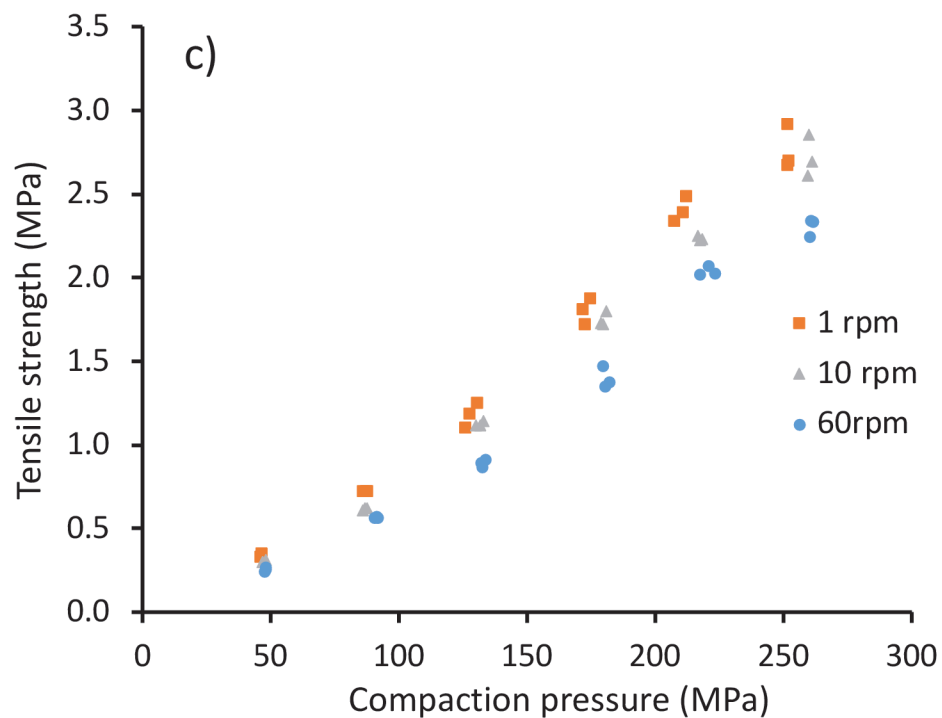
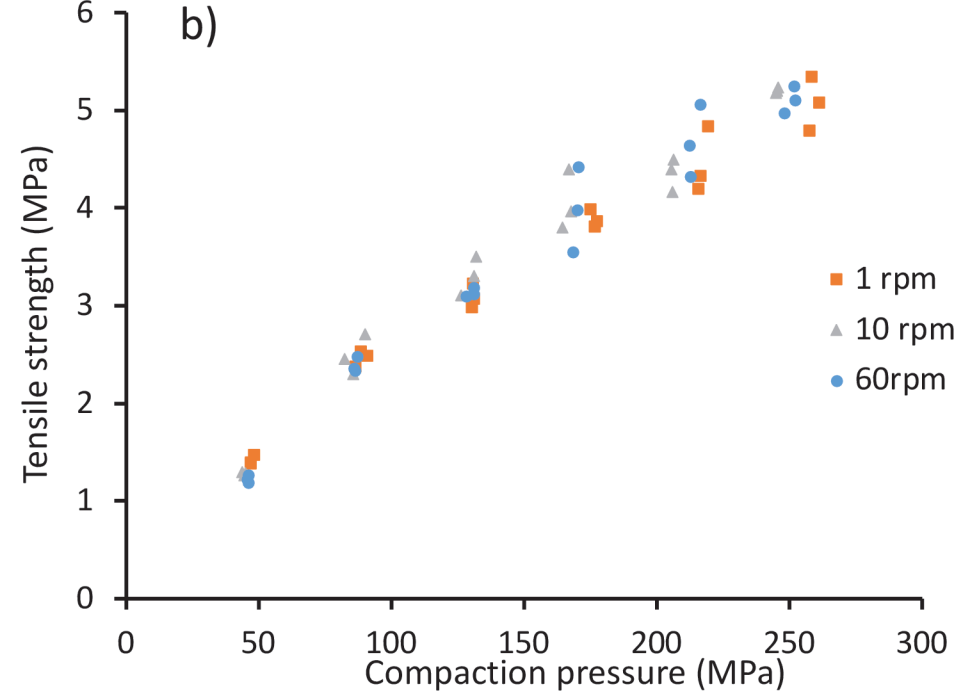
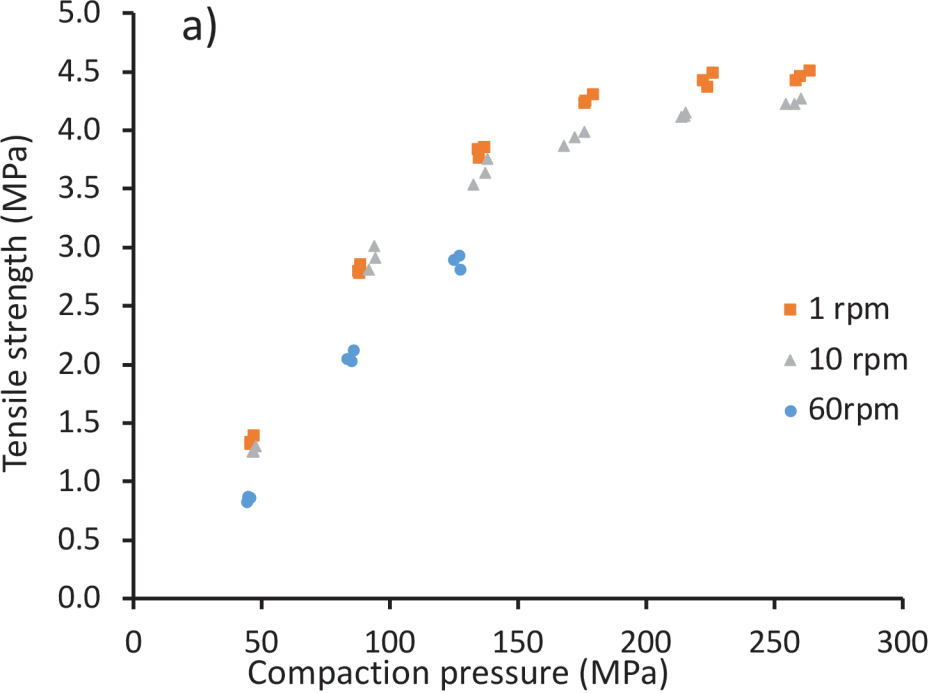


Table 1: results of the observation of lamination for the different conditions used. The number in one cell indicates the percentage of laminated tablets among the 10 tablets produced for these parameters.

Product	Lamination type	1rpm	10rpm	60 rpm		
		Straight die	Straight die	Straight_die	Tapered die	effect of precompression
MCC	1	x	0%	100%	100%	yes
TCP	2	100%*	100%	100%	0%	no
ACP	3	100%	100%	100%	0%**	no

*defects on all the tablets but the lower face of the tablet was not completely detached. ** no lamination out of the die, but strong internal lamination after diametral compression.