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Review article

Breaking of scored tablets: a review ☆

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Abstract

The literature was reviewed regarding advantages, problems and performance indicators of score lines. Scored tablets provide dose flexibility, ease of swallowing and may reduce the costs of medication. However, many patients are confronted with scored tablets that are broken unequally and with difficulty, reducing compliance and reliance on the drug. Possibilities to reduce breaking difficulties are breaking instructions, tablet-splitters and breaking in advance. Factors influencing the performance of score lines are shape, size, curvature and thickness of the tablet and the form and deepness of the score line. Performance of score lines can be defined by breaking ease, uniformity of mass of subdivided tablets and loss of mass by the subdivision. For breaking ease, an in-vivo reference test and a routinely applicable *in-vitro* test need to be established. For the uniformity of mass of subdivided tablets a requirement has recently been set by the European Pharmacopoeia. Loss of mass upon breaking can be limited to not more than 1%.

Keywords: Scored tablets; Score lines; Breaking tablets; Splitting tablets; Subdivision of tablets; Tablet-splitters

1. Introduction

Very recently, the European Pharmacopoeia (Ph.Eur.) [1] included a test on the subdivision of scored tablets, being the first Pharmacopoeia to do so. Therefore, it is now clear that badly performing score lines are a quality defect. This review summarises the literature on tablet score lines, focussing on their advantages and problems. Possibilities to overcome the problems associated with scored tablets are discussed. Finally requirements for the performance of score lines are proposed. The databases searched were Medline, Embase, Biosis, International Pharmaceutical Abstracts, Scisearch, Chemical Abstracts and the Derwent ringdoc files up to January 2001.

2. Advantages of scored tablets

The advantages of score lines are summarised in Table 1. Dose flexibility is the most important advantage of scored tablets. This was reported to be particularly important for tablets with a dose schedule that has to be dosed up or down, like for instance ACE-inhibitors [2]. In paediatrics and geriatrics, doses are used which may not be available in marketed strengths [3–5]. Footitt [3] considers for small dosage requirements a well breakable tablet preferable to a reformulation into a liquid dosage form, or a powder. Powders involve the risk of contaminating others than the patient. Liquid preparation may involve formulation and stability problems. Moreover, an often-used diluent in liquid preparations is syrup, resulting in an increased sucrose intake [3]. On the other hand, Sedrati et al. [4] state that the use of half tablets cannot replace elegantly prepared suspensions and other liquid preparations for paediatric patients. Dose flexibility is also important when tablets are prescribed 'if needed' and the experienced patient may wish to dose a part of a tablet [2].

The second important advantage of scored tablets is ease of swallowing. This may especially be important for big-sized tablets [6,7].

A third advantage of scored tablets is cost savings. Score lines on tablets reduce the number of tablets strengths needed, reducing costs both for the producing industry as well as the pharmacy and the patient. No data are available on the economical benefits of score lines. Savings were reported when patients broke tablets with a double dose to take half a tablet, instead of taking a whole tablet of the right dose [8,9]. The rationale for the savings reported was that

☆ This paper does not necessarily reflect the opinion of the Medicines Evaluation Board in The Netherlands.

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Table 1
Advantages of scored tablets

Ease of swallowing
Dose flexibility in geriatrics and pediatrics
Dose flexibility for dosing on need
Dose flexibility on increasing and decreasing dosage schedules
Cost reduction

the tablets in different strengths cost about the same [8,9]. However, the cost-saving effect of splitting tablets could be undone by increased non-compliance caused by bad functioning score lines [9–11]. Fawell et al. [9] investigated the relationship between tablet splitting and compliance; no significant difference in compliance was reported between patients who split tablets and those who did not. Finally, no over- or under dosing caused by unequal broken tablets has been reported in the literature.

3. Problems with scored tablets

Reported problems with scored tablets are difficulty of breaking, unequally breaking and loss of mass upon breaking, see Table 2.

3.1. Difficulty of breaking

Difficulty of breaking scored tablets is frequently reported [2,12–17]. Breaking scored tablets is particularly difficult for older persons [2,14,18]. Small scored tablets appear difficult to break [13,14,19]. Kristensen et al. [12] tested uncoated and filmcoated scored tables with a claim that the tablets may be subdivided before administration. However, in some cases the tablets were difficult to break. In a study of German commercial ACE-inhibitor scored tablets, 25% of the brands included in the study were considered not breakable [16]. In Spang's study [13] volunteers assessed the breaking ease of commercial scored tablets; 22% of these were assessed as 'hard to break'. Stimpel et al. [17] found that 15% of commercial antihypertensive scored tablets could only be divided by carving. Wilson et al. [18] reported difficult breaking and pain with two different glyburide brands in diabetic patients, which were over 70 years old. Further, considerable differences between the breakability of the two brands were found and it was suggested that besides an effect on bioavailability, this may have an effect on patient-compliance, because a bad performance of the score line may be experienced by the patient as a quality defect.

3.2. Unequal parts

Another problem with scored tablets was that tablets are broken unequally [3–5,11–13,16–22]. Unequally breaking tablets may result in dose variability. The risk of dose variability may be larger when tablets are split in advance because of the risk of taking subsequently light or heavy halves [20]. Bad score lines producing unequal parts may also be experienced as a quality defect by the patient and this might have consequences for the reliance on the drug-product and the compliance. Kristensen et al. [12] found that no correlation existed between tablets that are broken with difficulty and the standard deviation of the masses for the broken tablets.

McDevitt et al. [11] studied the manual breakability of 6 mm-diameter, round, scored tablets, by volunteers. Of the subdivided tablets, 41% parts showed deviations of more than 10% from the target weight and 12% deviated by more than 20%. Stimpel et al. [17] found for six of 34 commercial antihypertensive tablets that many of the subdivided tablet parts showed weight deviations of more than 10% from the target weight. Kristensen et al. [12] tested uncoated and filmcoated tablets with a claim that the tablets may be subdivided before administration. The relative stan-

Table 2
Problems associated with scored tablets, possible solutions and their limitations

Problem	Possible solutions	Limitations to solutions
	Without change of tablet	
	Instructions to patient	No limitations
	Tablet-splitters	Breaking accuracy not improved Cross-contamination if different tablets are broken with the same splitter Positioning the tablet may be difficult Sharp blade
	Pre-breaking in pharmacy	Safety concerns with hazardous substance Stability concerns of subdivided tablets Risk of taking subsequently heavy or light halves
Breaking is difficult Unequal parts Loss of mass		
	With change of tablet	
	Improve functioning of score line	Change of appearance of tablet Reformulation Conflicting formulation parameters
	Remove score line	Loss of advantages of score-line and change of appearance of tablet

dard deviation (RSD) of the weight of the subdivided tablets was up to 14% and almost all the tablets would be rejected if the test for uniformity of mass of single-dose preparations of the Ph.Eur. was applied to the broken tablets and only about 50% of the investigated tablets would meet the test proposed by the investigators. For twelve commercial ACE-inhibitors the RSD of the masses of the manually subdivided parts ranged from 2.1 up to 23.2% [16]. Gupta and Gupta [19] found in 60% of the investigated tablets that the majority of subdivided tablet weights deviated by more than 10% from the theoretical weight. The smallest tablet was most difficult to break accurately and 44% of the weights of the subdivided tablets deviated by more than 20% of the theoretical weight. Elongated tablets that were scored deeply on both sides broke most evenly and 97% of the weights of the tablet halves did not deviate by more than 10% from the theoretical weight. Wilson et al. [18] conducted a study in which tablets were broken by diabetic patients of 70 years or older and over 15% of one of the two studied tablets showed a mass variance of the subdivided parts of more than 15%. Hecker-Niedick [22] investigated whether subdivided tablet parts of six formulations would comply with the requirements Ph.Eur. for uniformity of mass of solid dosage forms and only one formulation complied. Also, problems are reported with two crossed score lines intended to break the tablet into quarters. Kristensen et al. [12] state that breaking in quarters should be avoided since it is expected that the variability of the mass of the broken tablets will be significantly higher than the variability demonstrated for the halved tablets. Indeed, Biron et al. [21], studying six anticoagulants, found that no tablet quarters would pass the test Ph.Eur. for uniformity of content whereas tablets divided into halves did meet this test. However, Schumann [2] as well as Müller and Kublik [14] showed that the quarters of a tablet formulation can comply with the Ph.Eur. requirements for the uniformity of mass.

3.3. Loss of mass

A third problem reported for scored tablets is loss of mass, due to powdering and fragmentation at the score line when a tablet is broken. Loss of mass leads to loss of dosage, contamination and health hazards for others than the patient. Some studies show that the loss of mass can be considerable [3,5,19,21]. In the study of Biron et al. [21] weight losses up to 14% were reported when breaking tablets into halves and up to 27% when breaking tablets into quarters. Horn et al. [5] found that a chewable tablet crumbled into multiple pieces when split into parts.

Footitt [3] found losses of mass as high as 6% when tablets were broken in two. Gupta and Gupta [19] found a weight loss of up to 2.6% for round tablets but a negligible weight loss for elongated tablets. Other studies report very little loss of mass [11,12,15,17,23,24]. For 39 tablet-preparations it was found that the loss of mass per tablet was usually less than 1 mg when breaking one tablet in two [12]. McDevitt et al. [11] found that 1.1% of the weight was lost in splitting scored 6-mm diameter tablets.

Lüdemann and Moest [23] optimised the breakability of a phenytoin tablet-formulation by changing the shape of the tablet and score-line without changing the composition of the tablet-formulation. The breakability of the optimised tablet-form was compared to the previous tablet-form and another comparative phenytoin tablet-formulation. The loss of weight after breaking was 0.4, 0.5 and 0.7% for the comparative-formulation, previous-formulation and optimised formulation, respectively. Stimpel et al. [17] found that for all the 34 tablets included in their study the loss of weight upon breaking was not important.

4. Possibilities to overcome problems with scored tablets

Possibilities and limitations to cope with score line problems are shown in Table 2.

4.1. Instructions to patients

Different breaking methods may result in different outcomes for breaking ease and the uniformity of mass of tablet parts. Therefore, instructing the patient on how to break tablets may be helpful. Janknegt and Ten Harmsen van der Beek [20] applied two different manual breaking methods on 10 different tablet formulations. For three tablet formulations, the average deviation of the weight of the tablet halves from the theoretical weight differed a factor of about three for the two breaking methods. For 70% of all the tablets included in the study the results differed significantly. In the study of Wilson et al. [18] the tablet breaking performance of two groups of diabetic patients of 70 years or older were compared. One group received written and verbal instructions on how to break the tablets, whereas the other group did not. Uniformity of mass of subdivided tablets, pain and ease of tablet breaking were assessed. The instructed group scored for uniformity of mass up to nearly three times better than the non-instructed group, breaking ease scored up to nearly two time better compared to the non-instructed patients. The instructed patients also scored less pain compared to the not-instructed patients. Spang [13] found that three different breaking methods as depicted in Fig. 1 resulted in different results for breaking ease, although the uniformity of mass only differed slightly for the three methods. Method b seemed to be the most convenient method but this method can only be used for curved tablets [2].

4.2. Tablet-splitter

A tablet-splitter may relieve the difficulty of breaking tablets by hand, see Fig. 2. The patient's acceptance of tablet-splitters was studied by Carr Lopez et al. [6]. Most patients reported that the tablet-splitter was easy to use, did not waste medication and did not affect their compliance.

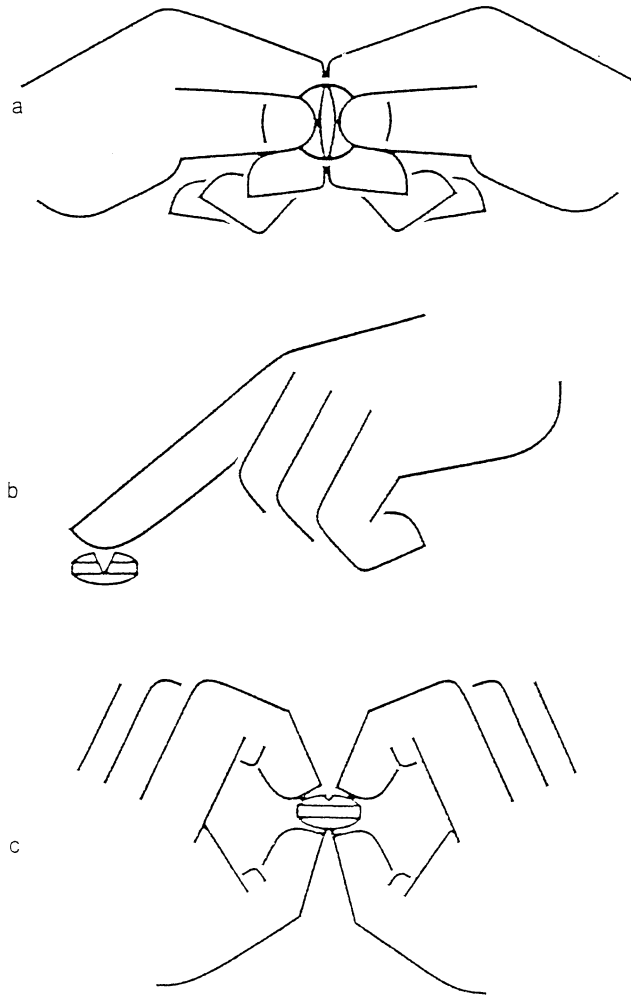

Fig. 1. Methods for breaking tablets by hand. Source: Pharmaceutica Acta Helvetica 1982;57(4)99-111. Reproduced with permission of the copyright holder.

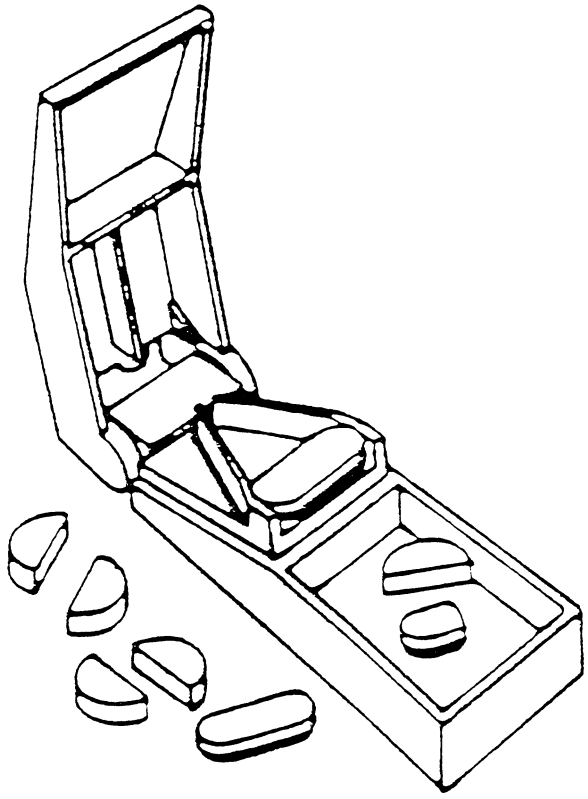

Fig. 2. Tablet-splitter. Source: American Journal of Hospital Pharmacy 1994;51(4)548-550. Reproduced with permission of the copyright holder.

However, 6% reported that the tablet-splitter was not easy to use, that they would not use one even if it would save them money and that the tablet-splitter discouraged them from complying with their prescribed regimen. The concern most frequently cited was that the tablet-splitter did not consistently produce two equal doses. In the study of Fawell et al. [9] patients that used a tablet-splitter indicated that tablet splitting was not detrimental to medication compliance. McDevitt et al. [11] found that it was difficult to place round, 6-mm diameter tablets in the tablet-splitter and concluded that the use of a tablet-splitter did not improve the accuracy of splitting. Horn et al. [5] investigated the performance of two different tablet-splitting devices. No splitter demonstrated satisfactory results when cutting quarters. Both tablet-splitters split only 19% of the tablets into halves within 15% of the theoretical weight and its was concluded that neither splitter reproducibly cut tablets into the desired parts. Sedrati et al. [4] evaluated a tablet-splitting device for accuracy. For 20% of the tablet brands included in this study all subdivided tablets were within 15% of their mean weights. For 27% of the brands, up to 3% of the subdivided parts deviated over 15% of its mean weight and for the remaining 53% of the brands up to 50% of the subdivided tablets deviated over 15% of their mean weight. The best results were obtained with the larger tablets and those that were coated, were oblong and had flat edges. Problems reported regarding tablet-splitters are potential injury due to the sharp steel blade and the possibility of cross contamination when different tablets are split [11]. It can be concluded that a tablet-splitter may make breaking easier but also might cause difficulties and does not improve accuracy of breaking.

4.3. Pre-breaking by the dispensing pharmacy

Pre-breaking by the dispensing pharmacy is a third possibility to cope with score line problems. Although pre-breaking may be hazardous to others than the patient in view of contamination, pre-breaking tablets in the pharmacy is advantageous since breaking is performed by professionals under controlled conditions. Pharmacists broke mercaptopurine tablets more accurately than parents of children did [3]. However, tablets split in advance and returned into the pill bottle may be subject to stability problems: increased friability and fragmentation, hygroscopic adsorption of water and altered shelf-life due to, for example, a break in the tablet's protective coating [11].

4.4. Change in tablet shape or formulation

Producers of tablets have possibilities to counteract breaking problems by changing the shape of the tablets, see Table 2 and below. Changing the composition of the formulation to one with a better breakability requires a significant amount of development work, e.g. stability and validation studies. An important disadvantage of reshaping may however be the change in a well-known and recognised appearance of tablets that are already on the market.

5. Requirements for the performance of score lines

5.1. Requirements for breaking accuracy

Kristensen et al. [12] proposed requirements on mass uniformity of tablet parts: from 40 subdivided tablets with an average mass of up to 250 mg not more than four parts should deviate more than 15% of the average mass and none more than 30%. For subdivided tablets with an average mass of 250 mg and more, deviations of 10%, resp. 20% were proposed. The authors showed that about 50% of the investigated scored tablets would fail to meet these criteria. A Ph.Eur. draft monograph for the mass uniformity of subdivided tablets required compliance of the subdivided tablets to the Ph.Eur. test for content uniformity [25]. This requirement was restricted to tablets with active substances having a critical dosing. This draft monograph was not adopted.

Very recently, March 2001, the Ph.Eur. adopted a change in the monograph on TABLETS, including under PRODUCTION a paragraph requiring subdivided parts of scored tablets to comply either with the Ph.Eur. test for uniformity of content or uniformity of mass. This requirement is not restricted to substances with a critical dosing. The adoption of this requirement is a milestone: for the first time a pharmacopoeial requirement on score lines is set. However, this requirement raises also questions. It is not clear when the requirement for compliance to content uniformity prevails and when the requirement for compliance to mass uniformity. Furthermore, the breaking method is not defined. However, the results of breaking depend on the breaking method and the person(s) who carry out the breaking (see above). From a technical point of view, the requirement for compliance to uniformity of mass is a very strict one and most scored tablets now on the market will fail to meet this requirement. The requirement for compliance of subdivided parts to uniformity of content is less strict but many scored tablets at present marketed will also not comply with this requirement and the position of these non-complying tablets on the European market is yet not clear.

Finally, when subdivided tablets are required to comply with the uniformity of content, testing will involve chemical assays. This procedure to determine the breaking accuracy may be considered overdone.

5.2. Requirements for ease of breaking

Although an increasing attention is paid to breaking ease by the Health Authorities, no formal regulatory requirements exist for this quality issue of scored tablets. Recently, the Dutch Medicines Evaluation Board rejected the score line of parallel imported Zocor® 20 mg tablets from France, mainly because these tablets were hardly breakable by hand [26].

A test including a panel which scores for breaking ease may be suitable for assessing the ease of breaking. In Spang's study [13] volunteers broke tablets and scored the breaking ease on a four-stage scale as very well breakable, well breakable, hard to break and not breakable. Also Taillens and Keuser [15] used this four-category scale. Wilson et al. [18] used a 10-category scale to assess pain and ease of tablet breaking. Spang [13] found a correlation between mechanical breaking force and manual breakability. He concluded that the only possibility to assure a good manual breakability of tablets is to establish limits for the breaking force based on mechanical measurements. Taillens and Keuser support this finding [15]. Measuring the breaking ease mechanically was described in several papers [13,15,27,28]. All these methods use modified hardness testers and are based on a frequently described three-point bending test [13,15,27–33]. In the three-point bending test, the tablet is supported with two supports. At the unsupported side, a load is applied at the center of the tablet, which will break the tablet on the scoring line. Spang [13] fixed the distance of the two supports at two thirds of the tablet diameter when testing round tablets. Gold et al. [33] tested oblong tablets using a distance between the supports of 80% of the tablet length. Endicott et al. [27] also used adjustable supports. Other studies have been described in which non-adjustable supports of one size were used [15,32].

5.3. Requirements on loss of mass

No regulatory requirements for the maximum loss of mass upon breaking exist up to now. In view of results reported for loss of mass on breaking and in line with Ph.Eur. requirements on friability, the authors consider a loss of 1% acceptable.

6. Formulation aspects of score lines

Some tablets have been designed to be broken easily, e.g. the so-called 'Snap-Tab' tablets [2,13]. Snap-Tabs are curved on one side, see Fig. 3 and a special breaking method should be used, see Fig. 1b. Oblong tablets appear to be better breakable than round tablets regarding breaking ease as well as uniformity of mass, also when using a splitter [4,13,19]. Spang [13] states that scored tablets should be at least of 8 mm diameter to be well manageable. This is in line with the finding of Müller and Kublik [14] who found in four commercial formulations that the smallest tablet, with 7 mm diameter, was the most difficult to break. Gupta and

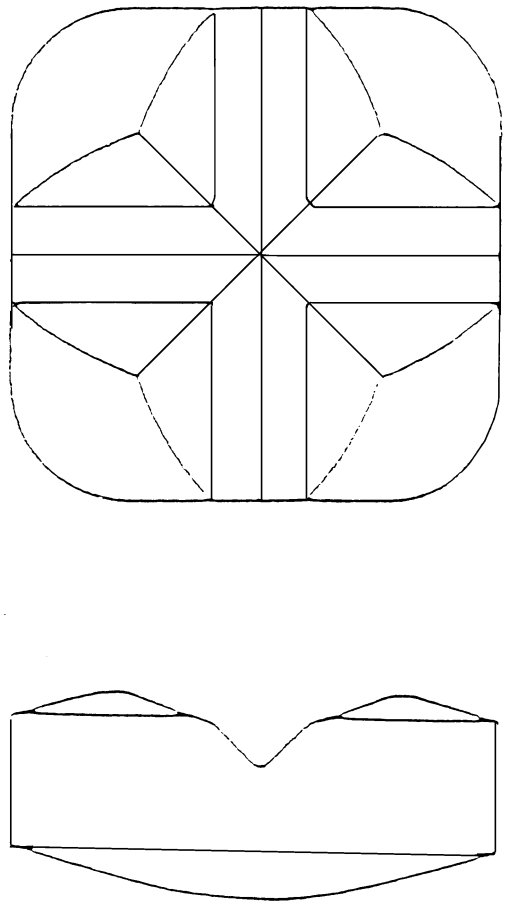

Fig. 3. View from above and side-view of a Snap-Tab. Source: Deutsche Apotheker Zeitung 1995;135(4)3099-3102. The tablet form is protected by Azupharma D 9415022.2 Reproduced with permission of the copyright holder.

Gupta [19] suggest scored tablets to be elongated in shape, be scored deeply on both sides and be large enough to permit a firm grip on each end. Thick tablets are generally harder to break compared to thinner tablets having the same diameter [2,13]. Tablets with rounded edges were difficult to place properly in the tablet-splitting device [4]. The design and depth of the score have an important effect on the breakability [13,14,34]. Spang [13] demonstrated that a deepened score facilitated manual breaking and reduced weight variation of the halves. The angle of the score and the sharpness of the score edge turned out to be of little importance for tablet breakability.

Schumann [2] found a correlation between mass uniformity and hardness; when tablets are pressed at a higher force, this results in a higher hardness and a better uniformity of mass. However, a higher hardness makes it more difficult to break tablets [13].

Lüdemann and Moest [23] found for one tablet formulation that merely deepening the score line was unsuccessful to improve the breakability. This was because increasing the depth of the score increased the hardness at the center of the score line, resulting in fracture beside the score line. A coating appears to have a negative effect on the manual breakability. However, the uniformity of mass of coated tablets seems to be better than of uncoated tablets [4,13]. Spang [13] states that a coating increases the hardness and makes that the tablet breaks neatly whereas higher hardness makes it more difficult to break. Also, the composition of the tablet influences the breakability [13,14]. Ito et al. [35] investigated the relationship between the dividing properties of scored tablets and the characteristics of the powder mixtures from which the tablets have been compressed. A more uniform and denser packing resulted in a better uniformity of mass of the subdivided tablet parts. From a theoretical point of view, filler and binder excipients with only a limited elastic recovery after compaction are more suitable for breaking tablets.

7. Breakability as a batch to batch release test of versus a development item

The EU Note for Guidance on Development Pharmaceutics suggests that accuracy of breaking is a development matter [36]. Also the inclusion of requirements for uniformity of mass of subdivided tablets under PRODUCTION in the monograph TABLETS of the Ph.Eur. indicates that this is a development parameter. However, Stimpel et al. [17] found for one brand that 86% of the tablets could be divided by hand, whereas 14% could not. This suggests that within one brand the breakability can differ, i.e. breakability being variable from batch to batch. This might be caused by batch to batch differences for example in hardness, water content, or storage time.

8. Discussion

Scored tablets bring added value to solid dosage forms both with respect to their possibility for flexibility of dosing and for cost savings of medication. It may be worthwhile to quantitatively assess these advantages.

Most problems encountered with scored tablets come from bad functioning score lines. Although score lines can be designed to break well, not every patient will always be able to break a scored tablet himself, even with a very good score line design. However, the pharmacist has a number of possibilities to help his patients with breaking problems. Proper instructions, dispensing tablet-splitters and pre-breaking in the pharmacy are possible solutions, but the effectiveness of these interventions need further study.

Although regulations for breaking accuracy have been set recently, regulatory standards are still missing for breaking ease and loss of weight. On breaking ease an in-vivo reference test need to be established in a way similar to the test of NEN 1740 on child resistant packages [37]. Also a regulatory mechanical test for breaking ease is needed. Specifications for breakability by this mechanical method need to be validated against the in-vivo reference test.

The Ph.Eur. test on mass uniformity of subdivided tablets

Table 3
Proposed criteria for scored tablets

Ease of breaking at subdividing
An in-vivo reference test and specification need to be established using a breaking panel. A surrogate in-vitro mechanical test needs to be defined and the specifications for in-vitro ease of breaking derived by cross-validation versus the reference test
Uniformity of mass of subdivided tablet parts
According to monograph TABLETS Ph.Eur. after breaking by the test for ease of breaking
Minimal loss of mass at subdividing
Not more than 1% after breaking by the test for ease of breaking

needs to be expanded by an instruction on the breaking of the scored tablets under investigation. It is rational to use the mechanical test on ease of breaking as the breaking procedure for the test on uniformity of mass of subdivided tablets.

Regulatory requirements for a maximum loss of mass are also needed. Limiting the loss of mass to 1% is in line with the Ph.Eur. requirement on friability and studies show that such a requirement is realistic.

The proposals of the authors for score line requirements are shown in Table 3 and from a technological point of view score lines that comply with these requirements are possible but many tablets on the market presently fail to meet the proposed criteria.

Finally, more data are needed on the batch to batch variability of these three parameters to decide on testing at release or on development only.

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