COMPARISON OF SOME PHYSICAL PARAMETERS OF WHOLE AND SCORED LISINOPRIL AND LISINOPRIL/ HYDROCHLORTHIAZIDE TABLETS

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Abstract

Tablets are one of the most popular and preferred solid dosage forms because they can be accurately dosed, easily manufactured and packaged on a large scale, have good physical and chemical stability, and can contribute to good patient compliance given their ease of administration. The ability to match doses to patients depends on the availability of multiple dose sizes and adequate dose-response information. These are not always provided, so splitting of the tablets is sometimes necessary. Tablet splitting is an accepted practice in dispensing medication. It has been used when a dosage form of the required strength is not available commercially. The aim of our study was to compare some physical parameters of whole and scored lisinopril and lisinopril/hydrochlorthiazide tablets and to accept or exclude their influence on the obtaining of required dosage.

According to the results obtained, we may conclude that tablets from batch "I", "II", "III" and "IV" satisfied pharmacopeial requirements concerning crushing strength, friability, disintegration time and mass uniformity. The hardness testing showed acceptable reproducibility and indicate that the data variation was primarily from the irreversible changes in the structure of tablet samples. The act of compacting powders stores energy within the tablets, by shifting or compressing the intermolecular bonds within the particles. The tablets have a natural tendency to relax once pressure is removed, and this tendency works against the interparticle bonding formed during compression. Hardness testing procedure causes irreversible changes in this structure.

KEY WORDS: physical parameters, scored tablets

Introduction

Tablets are one of the most popular and preferred solid dosage forms because they can be accurately dosed, easily manufactured and packaged on a large scale, have good physical and chemical stability, and can contribute to good patient compliance given their ease of administration (1). The ability to match doses to patients depends on the availability of multiple dose sizes and adequate dose-response information. These are not always provided, so splitting of the tablets is sometimes necessary (2). Tablet splitting is an accepted practice in dispensing medication. It has been used when a dosage form of the required strength is not available commercially (3).

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 (4).

The process of splitting tablets cases a number of problems, some of which are patient related while others are related to the tablet or formulation. Uneven splitting of a tablet may result in significant fluctuations in the administered dose. This may be clinically significant for drugs with a narrow therapeutic range. For many drugs, especially those with long half-lives and/or a wide therapeutic range, dose fluctuations are unlikely to be clinically significant (5, 6).

Lisinopril tablets labelled strength 5, 10 and 20 mg and lisinopril/hydrochlorothiazide tablets labelled to contain 20/12,5 mg (in all cases samples were scored tablets) were used as a model for our study.

The aim of our study was to compare some physical parameters of whole and scored lisinopril and lisinopril/hydrochlorthiazide tablets and to accept or exclude their influence on the obtaining of required dosage. The following tests were provided: friability, tablet hardness and disintegration testing for whole and scored tablets and mass uniformity as well.

Materials and Methods

Materials

The tablets used for this study were commercially available, obtained from the same producer and purchased from the local pharmacy. Four different batches of scored tablets were used: Batch I- lisinopril tablets, labelled strength 5 mg; Batch II- lisinopril tablets, labelled strength 10 mg; Batch III- lisinopril tablets, labelled strength 20 mg; Batch IV- lisinopril/hydrochlorthiazide tablets, labelled strength 20/12,5 mg

Crushing strength testing

The tablet is placed between the jaws, taking into account the shape, the break mark and the inscription. The tablet was oriented in the same way with respect to the direction of application of the force. The measurement was carried out on 10 tablets, taking care that all fragments have been removed before each determination. The results are expressed in the values of the forces measured, all expressed in newtons. The crushing strength was determined using hardness tester (type TBH 28, Erweka, Apparatebau, Germany).

Friability testing

Twenty tablets were placed on a sieve, and any loose dust was removed with the aid of the brush. The tablet sample was accurately weight and placed in the drum. It was rotated 100 times, and the tablets were taken out. Any loose dust from the tablets was removed as before. The friability is expressed as the loss of the mass and it is calculated as a percentage of the initial mass. The friability was determined using Roche friability tester (Erweka, Apparatebau, Germany).

Breakability test methods

The following manual breakability test was performed; the tablet was held between the thumb and the index finger of each hand on either side of the score line, with the score line facing upwards and without using the nail. Separation into two halves was done by breaking open the tablet at the score line side.

Mass uniformity testing

Thirty tablet units were taken at random and weight individually. Additional 30 tablets were taken at random

and broken manually. All the parts obtained from one tablet were used for the test. Each of the thirty parts were weight individually and the average mass calculated. The same procedure was done with the remaining thirty parts.

Disintegration testing

The following disintegration test was performed; in each of six tubes, one tablet is placed. The assembly was suspended in the 1 litre beaker, containing water, and operated for 15 min. A suitable device maintained temperature of the liquid at 35-390C. The test was provided using ZT 70 disintegration tester (Erweka, Apparatebau, Germany).

Results and Discussion

The results of resistance to crushing of tablets, friability testing and disintegration time per batch are presented in Table 1, 2, 3 and 4. Mass uniformity analysis of whole and scored tablets (Batch I, Batch II, Batch III, Batch IV) is presented in Table 5.

	Resistance to crushing of tablets (N):		
	Whole tablets	1/2 tablet	2/2 tablet
Sample 1	52,8	38,0	22,1
Sample 2	63,9	32,1	42,5
Sample 3	67,7	14,8	28,3
Sample 4	71,5	13,5	25,6
Sample 5	61,5	27,6	35,2
Sample 6	62,8	32,1	29,7
Sample 7	60,8	21,1	23,1
Sample 8	61,8	28,0	48,7
Sample 9	67,0	35,2	62,8
Sample 10	60,4	16,6	62,5
$\overline{X}$	63,0	25,9	38,1
S.D.	5,06	8,84	15,45
R.S.D	8,03	34,14	40,61
min.	52,8	13,5	22,1
max.	71,5	38,0	62,8
	Friability (%)		
	Whole tablets	1/2 tablet	2/2 tablet
	0,17	0,36	0,30
	Disintegration time		
	Whole tablets	1/2 tablet	2/2 tablet
	6 min 21 sec	6 min 20sec	6 min 10 sec

TABLE 1. Resistance to crushing of tablets, friability testing and disintegration time per Batch I (lisinopril tablets- labelled strength 5 mg)-whole and halved tablets

	Resistance to crushing of tablets (N):		
	Whole tablets	1/2 tablet	2/2 tablet
Sample 1	53,2	24,9	40,4
Sample 2	47,0	20,7	23,5
Sample 3	48,7	15,9	32,5
Sample 4	55,9	39,7	11,7
Sample 5	43,2	28,0	50,1
Sample 6	47,7	16,9	30,0
Sample 7	42,8	33,5	11,7
Sample 8	45,2	31,1	20,0
Sample 9	47,0	33,5	18,0
Sample 10	53,2	15,9	63,2
$\overline{X}$	48,4	26,0	30,1
S.D.	4,42	8,47	16,92
R.S.D	9,12	32,58	56,19
min.	42,8	15,9	11,7
max.	55,9	33,5	63,2
	Friability (%)		
	Whole tablets	1/2 tablet	2/2 tablet
	0,14	0,36	0,32
	Disintegration time		
	Whole tablets	1/2 tablet	2/2 tablet
	4 min 41 sec	4 min 10 sec	3 min 50 sec

TABLE 2. Resistance to crushing of tablets, friability testing and disintegration time per Batch II (lisinopril tablets- labelled strength 10 mg)-whole and halved tablets

	Resistance to crushing of tablets (N):		
	Whole tablets	1/2 tablet	2/2 tablet
Sample 1	54,9	31,4	18,6
Sample 2	61,5	29,4	17,6
Sample 3	55,9	46,6	13,8
Sample 4	65,6	18,0	49,7
Sample 5	57,7	25,2	39,0
Sample 6	55,2	63,9	43,2
Sample 7	57,7	78,4	57,3
Sample 8	62,5	45,6	35,6
Sample 9	63,9	23,8	14,8
Sample 10	61,1	38,7	37,6
$\overline{X}$	59,6	40,1	32,7
S.D.	3,82	19,07	15,57
R.S.D	6,40	47,56	47,58
min.	54,9	18,0	13,8
max.	65,6	63,9	49,7
	Friability (%)		
	Whole tablets	1/2 tablet	2/2 tablet
	0,13	0,24	0,26
	Disintegration time		
	Whole tablets	1/2 tablet	2/2 tablet
	5 min 05 sec	5 min 00 sec	4 min 50 sec

TABLE 3. Resistance to crushing of tablets, friability testing and disintegration time per Batch III (lisinopril tablets-labelled strength 20 mg)-whole and halved tablets

	Resistance to crushing of tablets (N):		
	Whole tablets	1/2 tablet	2/2 tablet
Sample 1	59,7	61,1	26,9
Sample 2	59,0	52,5	57,3
Sample 3	65,6	68,0	17,6
Sample 4	62,8	20,4	21,1
Sample 5	62,5	47,3	51,5
Sample 6	61,8	66,0	25,9
Sample 7	69,8	43,9	30,4
Sample 8	65,3	39,7	16,6
Sample 9	66,3	58,7	42,8
Sample 10	66,6	29,4	62,8
$\overline{X}$	63,9	48,7	35,3
S.D.	3,36	15,70	17,02
R.S.D	5,26	32,24	48,22
min.	59,0	20,4	17,6
max.	69,8	68,0	62,8
	Friability (%)		
	Whole tablets	1/2 tablet	2/2 tablet
	0,24	0,27	0,26
	Disintegration time		
	Whole tablets	1/2 tablet	2/2 tablet
	6 min 38 sec	6 min 05 sec	6 min 10 sec

TABLE 4. Resistance to crushing of tablets, friability testing and disintegration time per Batch IV (lisinopril/ hydrochlothiazide tablets labelled strength 20/12,5 mg)-whole and halved tablets

Acceptable values of friability (less than 0,25%-whole tablets; and less than 0,37%-halved tablets; upper limit-loss %≤1) were obtained for all batches of tablets with suitable disintegration time values.

Hardness values, indicating good mechanical properties for whole tablets that are able to withstand handling. It is obvious from the results for the hardness value of halved tablets, that resistance to crushing of tablets showed broad variation (comparing values for relative standard deviation for whole and halved tablets). During the compaction or pressing of pharmaceutical powders into tablets, the quality of the resulting tablets depends on die aspect ratio and geometry, the forces of the upper and lower punch, the speed at which this force is applied, the length of time for which the force is applied, and the powder properties of compressibility, permeability, friction and cohesion within the powder, and friction and adhesion between the powder and the die walls and punches. In particular, excessive die wall friction may promote uneven disposition of the compressive force throughout the powder, resulting in heterogeneity of density within the tablet. The tensile strength of a tablet depends on the bonding strength between particles within the tablet. Particle size and shape can affect how particles pack together during compression, and how well the particle surfaces interact to create stronger or weaker bonds. Under compression, brittle particles may break or shatter, while softer particles may undergo deformation to fill gaps between the particles. The strength of the interparticulate bonds formed during compaction can be affected by the brittleness/elasticity of the material, and the rate of tablet compression. The act of compacting powders stores energy within the tablets, by shifting or compressing the intermolecular bonds within the particles. The tablets have a natural tendency to relax once pressure is removed, and this tendency works against the interparticle bonding formed during compression. Hardness testing procedure causes irreversible changes in this structure. Up to now, no regulatory requirements for the maximum loss of mass upon breaking exist. In view of the results reported for loss of mass on breaking (7) and in line with Ph. Eur. requirements on friability, we consider a loss of 1% acceptable. All samples (whole and halved tablets) meet this requirement (Table 5).

	Batch I			Batch II			Batch III			Batch IV		
Sample	Whole tablets	1/2 tablet	2/2 tablet	Whole Tablets	1/2 tablet	2/2 tablet	Whole tablets	1/2 tablet	2/2 tablet	Whole tablets	1/2 tablet	2/2 tablet
1	0,20907	0,10414	0,10027	0,14032	0,07791	0,07371	0,27853	0,15160	0,14810	0,21076	0,10325	0,10735
2	0,20554	0,10410	0,09903	0,14096	0,06827	0,07141	0,28191	0,14390	0,14842	0,21381	0,10548	0,10843
3	0,20582	0,09924	0,10639	0,13841	0,07382	0,06986	0,28250	0,14848	0,15160	0,21011	0,10796	0,10609
4	0,20830	0,10794	0,10416	0,14130	0,06434	0,07171	0,28259	0,12950	0,13859	0,20843	0,10535	0,10724
5	0,20929	0,10916	0,11201	0,13678	0,07057	0,06593	0,28200	0,14909	0,12609	0,20826	0,10248	0,09822
6	0,21249	0,09959	0,10556	0,13997	0,07443	0,07185	0,27907	0,14958	0,13620	0,20967	0,10614	0,10779
7	0,21066	0,10900	0,10970	0,13762	0,06448	0,07289	0,28304	0,12815	0,13398	0,21230	0,10734	0,10200
8	0,20742	0,10398	0,09641	0,13852	0,06792	0,06862	0,28141	0,14088	0,14283	0,21050	0,10375	0,10594
9	0,20914	0,10824	0,11282	0,14220	0,06570	0,07301	0,28084	0,14684	0,13458	0,21064	0,10221	0,10529
10	0,21206	0,11034	0,11294	0,13959	0,07434	0,06549	0,28417	0,13500	0,13407	0,20256	0,10793	0,10006
11	0,20941	0,09892	0,10019	0,13930	0,06493	0,06559	0,28554	0,13082	0,13862	0,20848	0,09955	0,10900
12	0,2095	0,10990	0,10242	0,13796	0,06906	0,07498	0,28750	0,15068	0,14387	0,21000	0,10460	0,10738
13	0,21306	0,10490	0,10554	0,13826	0,06947	0,07718	0,28068	0,14845	0,13320	0,20849	0,10140	0,10038
14	0,20916	0,10462	0,10126	0,14128	0,07075	0,06892	0,28276	0,14388	0,13368	0,20895	0,10100	0,10119
15	0,21227	0,10725	0,10053	0,13980	0,06960	0,07654	0,28276	0,13822	0,15251	0,21164	0,10450	0,10481
16	0,21005	0,10379	0,10924	0,13997	0,06853	0,06317	0,28508	0,14782	0,12289	0,21063	0,10390	0,10477
17	0,21212	0,09416	0,11298	0,14210	0,06543	0,06741	0,28050	0,13416	0,12659	0,20959	0,10720	0,10584
18	0,21491	0,10680	0,09736	0,13794	0,07245	0,06890	0,28338	0,12653	0,15008	0,2063	0,10371	0,09827
19	0,21097	0,10899	0,10350	0,14097	0,06566	0,06517	0,28533	0,14794	0,14783	0,20661	0,10513	0,10118
20	0,20987	0,11040	0,09511	0,13974	0,06427	0,07433	0,28041	0,13871	0,14955	0,21364	0,10244	0,10226
21	0,20786	0,10487	0,09784	0,13931	0,07374	0,06907	0,27882	0,14959	0,14139	0,20795	0,10022	0,10523
22	0,21027	0,11243	0,10166	0,13896	0,07336	0,06618	0,28295	0,13832	0,12319	0,20916	0,09957	0,10463
23	0,20529	0,09931	0,10678	0,13836	0,07148	0,06895	0,27951	0,14590	0,14404	0,21187	0,09747	0,10835
24	0,20769	0,11499	0,11003	0,14227	0,07148	0,06832	0,28471	0,14928	0,14422	0,2088	0,108	0,10595
25	0,21442	0,09880	0,10370	0,13779	0,06780	0,07084	0,28449	0,13740	0,13577	0,20891	0,10282	0,10715
26	0,21336	0,10059	0,10448	0,14017	0,07022	0,06929	0,28118	0,13901	0,1258	0,21296	0,0984	0,10328
27	0,20572	0,10089	0,10767	0,14169	0,06798	0,07112	0,27937	0,12280	0,14971	0,21365	0,1031	0,10405
28	0,20905	0,11038	0,09969	0,14097	0,07085	0,06439	0,28136	0,14191	0,13771	0,20634	0,107	0,1074
29	0,20716	0,09558	0,10959	0,13865	0,06836	0,06930	0,28578	0,13224	0,13068	0,21128	0,1061	0,10761
30	0,21191	0,10919	0,09650	0,14130	0,06842	0,06800	0,28254	0,13402	0,13115	0,21253	0,10840	0,10536
$\overline{X}$	0,20979	0,10508	0,10418	0,13975	0,06952	0,06974	0,28236	0,14069	0,13856	0,20983	0,10388	0,10475
S.D.	0,00261	0,00517	0,00536	0,00152	0,00347	0,00357	0,00228	0,00821	0,00893	0,00251	0,00303	0,00304
R.S.D	1,24532	4,92484	5,15247	1,08945	4,99865	5,12517	0,80859	5,83344	6,45092	1,19734	2,91375	2,90727

Conclusion

◊ According to the results obtained, we may conclude that tablets from batch "I", "II", "III" and "IV" satisfied pharmacopeial requirements concerning crushing strength, friability, disintegration time and mass uniformity

◊ The hardness testing showed acceptable reproducibility and indicate that the data variation was primarily from the irreversible changes in the structure of tablet samples. The act of compacting powders stores energy within the tablets, by shifting or compressing the intermolecular bonds within the particles. The tablets have a natural tendency to relax once pressure is removed, and this tendency works against the interparticle bonding formed during compression. Hardness testing procedure causes irreversible changes in this structure.

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