Tablet scoring study of enalapril maleate tablets USP 20 mg

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Abstract
The present study of tablet scoring of Enalapril Maleate Tablets USP 20 mg it is necessary form FDA Guideline for Industry – Tablet Scoring: Nomenclature, Labeling and Data for Evaluation. These tablets scoring data described results are obtained during test performed on Enalapril Maleate Tablets USP 20 mg. The results are carrying out the test on exhibit batches. Various test are performed for these tablet scoring study like Loss of Mass on low, optimum or high speed (limit NMT 3%), Friability on low, optimum or high speed (limit NMT 1%), Dissolution is done by hand and splitter in 30 min., Content Uniformity is also done by hand or splitter limit is less than or equal to 15. Each and every parameter results are found within acceptable limit.

Keywords: Enalapril Maleate, Friability, Content Uniformity, Scoring.

Introduction
The tablet dosage form is that it may be manufactured with a score or scores (Breakline). The score can be used to facilitate the splitting of the tablet in to fractions when less than a full tablet is desired for the dose. The tablet scoring is ensure that the patients able to adjust dose, by splitting the tablet. This enables the patient to switch between products made by different manufacturers without encountering the problems related to the dose. The scoring is ensuring that neither generic product nor the reference listed drug has an advantage in the marketplace because one is score and one is not.[1,2]

Tablet splitting or scoring of tablets into multiple strengths has been a usual practice across the world. Scoring of table gives various advantages such as dose flexibility and ease of swallowing in different population including geriatric and pediatric patients (wide patient acceptance) and cost saving on medications (economic advantage) The tablet products that are meant to be split and approved by the Food and Drug Administration (FDA) will have a scored line indicating the split location to ensure patient can adjust the dose by splitting and such splitting information will be included in the patient package insert. Having a consistent scored reduces difficulty in dose related problems especially when using products made by different manufacturers such as Generic compared to Reference Listed Drugs (RLD). Physical characteristics such as shape, size and tablet score may affect tablet split ability. Currently, various regulatory bodies (FDA, USP, and EP) provide consistent and useful information to the pharmaceutical industry. In this review, authors have compiled information from currently available resources on tablet scoring and scoring was done with tabletsplitter apparatus which showed in Fig. 1.[3,4]

Objectives of tablet scoring
1. The dose amount meant to be achieved after splitting the tablet should not be below the minimum therapeutic dose indicated on the approval laneling.
2. The split tablet should be safe to handle and not pose risk unintended drug exposure
3. Modified product release for which the control of drug release can be compromised by tablet splitting should not have scoring features.
4. The split tablet stored in the pharmacy dispensing containers (not sealed/not dessicants), should demonstrate adequate stability for a period of 90 days at $25^0C \pm 2^0C$/ 60 % relative humidity ± 5% relative humidity.[5]

Enalapril is an ACE inhibitor and ACE stands for angiotensin converting enzyme. Enalapril is used to treat hypertension (high blood pressure) in adults. Enalapril is also used to treat congestive heart failure. Congestive heart failure is a disorder of the ventricles (the lower chambers of the heart) which decreases the heart's ability to pump blood to the body.[6]

Materials and Methods

Product name is Enalapril Maleate Tablets USP 20 mg and label claim is Each Tablet contain Enalapril Maleate USP 20 mg and color is Iron Oxide Brown.

Methodology [7,8,9]

Following tests are to be performed for the Tablet Scoring Study of Enalapril Maleate Tablets 20 mg

Loss of Mass (LOM) – Loss of mass is carried on low, optimum and high hardness of tablets. The test carried out on 40 split portions in their 20 of each side of enalapril maleate tablets and loss of mass limit is not more than 3%.

Friability - Friability is done on low, optimum, and high hardness by Roche Friabilator and test carried out on 6.5 gm. split portion (equal part of each side) of enalapril maleate tablets. Friability of split carried out after 100 revolutions and their limit is not more than 1%.

Dissolution Profile (On Optimum Hardness) – Dissolution is carried ended 24 split portions (12 of each side) of enalapril maleate tablets with the help of USP Type II (Paddle) dissolution test apparatus with 50 rpm speed. Phosphate Buffer pH 6.8 used as medium, volume is 900 ml. Sample is withdraw in time interval of 5, 10, 15, 20, 30 minutes.

Content Uniformity – Content uniformity done on 20 split portion (10 of each side) of enalapril maleate tablets for each half / split tablet portion. The limit of test is Not less than or equal to 15.0.

Stability Study –Stability study carried on 180 split portion (90 of each side) of enalapril maleate tablets which packed in standard high density polyethylene (HDPE) bottle (40 cc) with cap (not sealed) stored at $25^{o}C$ +_ $2^{o}C$/ 60% RH +_5%RH room conditions for 90 days. Moisture Content (Loss on drying on $60^{0}C$ under vacuum), Dissolution (of any 24 split portion (12 of each side)), Content Uniformity of each half/ split portion tests performed after 90 days.

Table 1: Loss of Mass of split tablet

Loss on Mass limit: NMT 3%		
	Tablet Split mechanically with tablet splitter	**Tablet split non mechanically – by hand**
Low hardness	0.335 %	0.261 %
Optimum hardness	0.275 %	0.324 %
High hardness	0.348 %	0.240 %

*NMT – Not more than

Table 2: Friability test results of split tablet

Friability limit: NMT 1.0%		
	Tablet split mechanically with tablet splitter	**Tablet split non mechanically – by hand**
Low hardness	0.74 %	0.64 %
Optimum hardness	0.43 %	0.43 %
High hardness	0.82 %	0.81 %

*NMT – Not more than

Table 3: Dissolution profile of tablet split which split by hand and splitter

Tablet split by Hand											
Limit NLT 80 (Q) in 30 minutes											
RHS	**5 min**	**10 min**	**15 min**	**20 min**	**30 min**	**LHS**	**5 min**	**10 min**	**15 min**	**20 min**	**30 min**

1	96	102	106	106	106	**1**	82	104	103	102	102
2	79	101	101	100	100	**2**	78	98	97	97	96
3	68	102	101	100	100	**3**	72	100	100	99	98
4	55	83	96	96	96	**4**	77	104	104	103	103
5	65	92	98	96	96	**5**	71	100	98	97	96
6	78	104	104	102	102	**6**	61	102	102	102	101
7	61	97	97	95	95	**7**	66	95	98	98	97
8	86	97	96	97	96	**8**	98	98	98	98	97
9	78	97	98	96	96	**9**	71	101	101	100	99
10	65	105	105	104	104	**10**	61	91	92	91	91
11	68	99	99	98	98	**11**	59	87	90	89	89
12	60	95	95	94	93	**12**	62	92	92	91	90
Min	60	92	95	94	93	**Min**	59	87	90	89	89
Max	86	105	106	106	104	**Max**	98	104	101	102	102
Mean	70	98	98	97	97	**Mean**	71	95	94	95	94
Tablet Split by Splitter											
Limit NLT 80 (Q) in 30 minutes											
RHS	**5 min**	**10 min**	**15 min**	**20 min**	**30 min**	**LHS**	**5 min**	**10 min**	**15 min**	**20 min**	**30 min**
1	61	88	93	91	93	**1**	68	99	103	103	102
2	78	102	102	102	101	**2**	55	84	86	86	86
3	68	89	95	94	94	**3**	57	91	90	90	89
4	62	88	92	92	91	**4**	66	95	100	100	99
5	67	98	101	100	101	**5**	62	82	88	89	87
6	70	95	101	100	100	**6**	68	92	92	92	91
7	71	99	100	100	100	**7**	62	87	89	89	88
8	51	87	96	95	94	**8**	73	97	99	98	98
9	62	89	96	95	94	**9**	60	88	91	91	90
10	67	92	101	101	102	**10**	61	90	97	97	97
11	63	91	94	93	92	**11**	57	88	93	93	92
12	64	92	93	94	94	**12**	66	92	91	89	90
Min	51	86	92	93	91	**Min**	57	82	89	86	88
Max	78	102	102	101	102	**Max**	73	97	99	100	98
Mean	63	92	97	96	96	**Mean**	63	60	93	93	92

*Min. – Minimum, Max. –Maximum, Min. – Minutes, LHS – Left hand side, RHS - Right hand side

Table 4: Content uniformity results of splitted tablet by hand and tablet splitter

Sample	**By Hand Limit –** Less than or equal to 15.0		**By Tablet Splitter–** Less than or equal to 15.0	
Sample	**RHS**	**LHS**	**RHS**	**LHS**
1	97.7	99.4	93.7	98.5
2	99.1	104.9	99.2	101.8
3	96.1	89.9	98.7	92.1
4	100.6	101.3	101.1	97.2
5	89.4	88.9	96.4	97.9
6	95.9	96.6	95.2	92.2
7	96.1	93.2	97.6	92.4
8	94.7	90	97.6	95.2
9	91.4	98.1	94.8	98.3
10	94.7	96.8	96.6	106
Min	89.4	88.9	93.7	92
Max	100.6	104.9	101.1	106
Average	95.6	95.9	97.1	97.3
RSD	3.5	5.5	2.3	4.8

*Min. – Minimum, Max. –Maximum, RSD – Relative Standard Deviation, LHS – Left hand side, RHS - Right hand side

Table 5: Dissolution profile of stabilised tablet split which split by hand and splitter under stability study

Tablet splitting by hand											
Limit NLT 80 (Q) in 30 minutes											
RHS	**5 min**	**10 min**	**15 min**	**20 min**	**30 min**	**LHS**	**5 min**	**10 min**	**15 min**	**20 min**	**30 min**
1	96	103	103	104	104	**1**	85	100	101	103	102
2	76	100	104	100	102	**2**	78	97	98	98	97
3	70	101	100	100	100	**3**	73	103	102	98	99
4	59	86	98	99	97	**4**	72	104	104	99	102
5	65	95	97	97	97	**5**	71	96	96	100	96
6	74	99	102	100	102	**6**	70	103	102	102	101
7	66	97	97	94	98	**7**	62	99	95	93	98
8	80	96	97	98	97	**8**	94	100	99	100	98
9	79	99	96	97	98	**9**	73	101	101	99	97
10	69	101	106	102	102	**10**	60	92	94	93	91
11	63	99	98	98	99	**11**	60	88	92	91	87
12	63	93	93	94	94	**12**	64	92	92	91	91
Min	59	86	93	94	94	**Min**	60	88	92	91	871
Max	96	103	106	104	104	**Max**	94	104	104	103	102
Mean	71.66	97.41	99.25	98.58	99.16	**Mean**	71.83	97.91	98	97.25	96.75
Tablet splitting by splitter machine -											
Limit NLT 80 (Q) in 30 minutes											
RHS	**5 min**	**10 min**	**15 min**	**20 min**	**30 min**	**LHS**	**5 min**	**10 min**	**15 min**	**20 min**	**30 min**
1	57	87	93	94	93	**1**	59	103	104	103	104
2	79	99	104	102	101	**2**	60	82	86	88	85
3	68	87	95	93	95	**3**	64	93	92	89	88
4	66	88	93	96	93	**4**	65	94	99	102	97
5	64	96	103	103	101	**5**	66	83	87	87	89
6	74	98	102	100	102	**6**	67	97	93	94	93
7	71	96	100	100	102	**7**	69	87	88	90	88
8	53	88	98	94	93	**8**	73	98	98	96	99
9	63	90	96	96	97	**9**	61	86	92	93	91
10	67	95	99	100	105	**10**	62	89	96	98	96
11	64	93	97	94	99	**11**	58	90	95	95	93
12	66	92	96	95	97	**12**	68	94	91	92	90
Min	53	87	93	93	92	**Min**	58	82	86	87	85
Max	78	99	104	103	105	**Max**	73	103	104	103	104
Mean	66	92.41	98	97.25	98.16	**Mean**	64.33	91.33	93.41	93.91	92.75

*Min. – Minimum, Max. –Maximum, Min. – Minutes, LHS – Left hand side, RHS - Right hand side

Table 6: Content uniformity study of stabilised tablet split which split by hand and splitter under stability study

Sample	**By Hand Limit –** Less than or equal to 15.0		**By Tablet Splitter–** Less than or equal to 15.0	
Sample	**RHS**	**LHS**	**RHS**	**LHS**
1	97.7	99.3	93.4	98.4
2	99.5	104.9	98.7	101.4
3	96.3	89.8	99.2	93.1
4	99.9	101.3	101.3	97.4
5	89.6	88.8	96	98
6	95.6	96.7	95.3	92.3
7	96.9	93	97.4	93.1
8	94.1	90	97.5	94.2
9	93	98	94.7	98.2
10	94.5	97.2	96.8	99.9

Min	89.6	88.8	93.4	92.3
Max	99.9	104.9	101.3	101.3
Average	95.69	95.9	97.3	96.6
RSD	3.09	5.58	2.42	3.26

*Min. – Minimum, Max. –Maximum, RSD – Relative Standard Deviation, LHS – Left hand side, RHS - Right hand side

Fig. 1: Tablet splitter

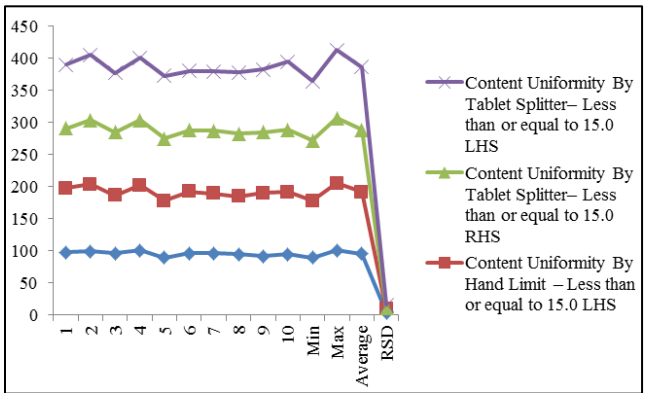

Fig. 2: Content uniformity study of Splitted tablet by hand and tablet splitter.

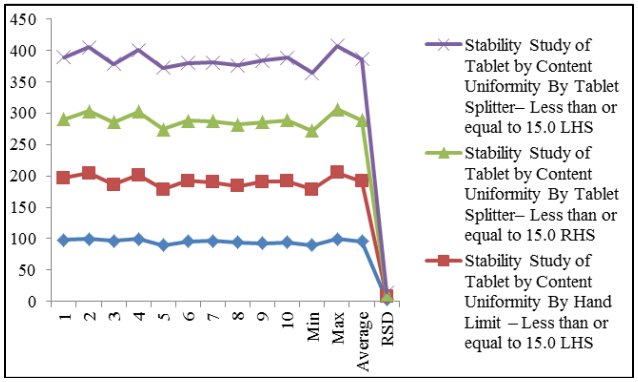

Fig. 3: Content uniformity study of Splitted tablet by hand and tablet splitter under Stability Study

Result and Discussion

Loss of Mass (LOM) – Loss of mass (LOM) carried on low, optimum, and high hardness of enalapril maleate tablets. Tablets split mechanically with tablet splitter and by hand and their their results on different hardness which depicted on table **Discussion –** The results of Loss of Mass are found within acceptable limit like not more than 3 % by mechanically or non-mechanically.

Friability –Friability done on low, optimum, and high hardness of enalapril maleate tablets with the help of Roche Friabilator. Tablets split mechanically with tablet splitter and by hand. The results of friability test was showed in table 2. **Discussion –** The results of friability test by Roche Friability Test Apparatusare found within acceptable limit at low hardness, optimum hardness and high hardness.

Dissolution Profile – Dissolution is carried ended 24 split portions (12 of each side) of enalapril maleate tablets in time interval of 5, 10, 15, 20 and 30 minutes and the results are described in table 3. **Discussion –** The results of dissolution test by LABINDIA Dissolution Test Apparatusare found within acceptable limit in different time intervals like 5 min., 10 min., 15 min., 20 min., 30 min. are found within acceptable limit.

Content Uniformity –Content uniformity done on 20 split portion (10 of each side) of enalapril maleate tablets of right hand side and left hand side. The limit of test is not less than or equal to 15.0. Splitting done with by hand and tablet splitter and their results depicted in table 4 and figure 2.**Discussion –**The results of Content Uniformityare found within acceptable limit like for by hand split tablet and by splitter splited tablet found as 3.5, 5.5 and 2.3, 4.8 respectively.

Stability Study – Stability study is performed after 90 days. Following test parameters are carried under stability study such as Assay, Moisture Content, Related Substances and Content Uniformity those all parameters results are found within acceptable limit.

Assay (By HPLC) - The assay of stabilized tablet was done with HPLC and their limit is not less than 95.0% and not more than 110.0%. The results of these assay

study of tablet which split mechanically with tablet splitter was 97.3 % and tablet which split mechanically with tablet splitter was 96.4%.

Moisture Content – Loss of Drying is done at 60°C under vacuum and LOD limit is not more than 1.5%. The results of these moisture content of tablet which split mechanically with tablet splitter was 0.66 % and tablet which split mechanically with tablet splitter was 0.68 %.

Dissolution – Dissolution Profile is carried out in time interval of 5 min, 10 min, 15 min, 20 min, 30 min time interval of splitted tablets (by hand and by splitter machine) and the results are described in table 5.

Content Uniformity –Content uniformity done on 20 split portion (10 of each side) of stabilized enalapril maleate tablets of right hand side and left hand side. The limit of test is not less than or equal to 15.0. Splitting done with by hand and tablet splitterand their results depicted in table 6 and figure 3.**Discussion –** The results of Content Uniformityare found within acceptable limit like for by hand split tablet and by splitter splited tablet found as 3.5, 5.5 and 2.3, 4.8 respectively.

Conclusion

Based on the analytical data of sample collected of Enalaprial Maleate Tablets USP 20 mg and analyzed for the split portion of tablet, Loss of mass on low, optimum, and high hardness (limit not more than 3%), Friability on low, optimum, and high hardness (Limit not more than 1%), Dissolution Profile by hand and splitter (Limit not less than 80 in 30 min.) and Content Uniformity is also by hand and splitter (Limit less than equal to 15.0)which is observed as per acceptance criteria with the respect to the parameter evaluated. This data of scoring study which support approval of a scored tablet. After confirmation of this study, splitted tablet or scored tablet does not affect on prescribed dose of tablet.[10,11]

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None.

Conflict of Interest

None.

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