Original Article

STUDY OF QUALITY ASPECTS OF DIFFERENT BRANDS OF TELMISARTAN TABLETS MARKETED IN INDIA

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Abstract

Purpose: The objective of the study was to determine the difference between commercially available Telmisartan sustained release tablets in relation to its quality studies.

Methods: Four commercially available telmisartan sustain release tablets manufactured in India were evaluated for four in vitro parameters, both official and non-official, viz., uniformity of weight, hardness test, drug content, disintegration and dissolution test. The test was followed as per I.P guidelines

Results: All the products met the requirements as per general specifications of Indian Pharmacopoeia for tablets. It is concluded that despite some apparent minor difference in tablet hardness, thickness, drug content and dissolution characteristic of various commercially available Telmisartan sustain release marketed tablets appear to be similar and not significantly different from various manufacturers.

Keywords: Telmisartan, hardness, disintegration and drug content.

INTRODUCTION

The main goal of sustained drug delivery is to improve patient compliance while ensuring safety and pharmacological efficacy. Because they keep the drug concentration in plasma above the minimal effective concentration and below the minimal hazardous level for an extended length of time, these dosage forms are increasingly used in the treatment of acute and chronic disorders. Thus, sustained drug delivery leads to optimal drug therapy with decreased frequency of dose and side effects. Various commercially available dosage forms with the same ingredients are readily available on the market, all of which are claimed to be bioequivalent. The main objective of present study was to conduct the evaluation of commercially available Telmisartan tablets marketed in INDIA.[1]

Telmisartan IUPAC name 2 - [4 -[[4 – methyl – 6 - (1 –methyl benzimidazol – 2 – yl) – 2 -propylbenzimidazol-1-yl]methyl]phenyl]benzoic acid is an anti-hypertensive drug belonging to the class of anti-hypertensive called as

Angiotensin II Receptor Blocker (ARB)[2].Angiotensin is an peptide hormone which cause increase in blood pressure due to its vasoconstriction effect. The angiotensin II type I receptors are located in adrenal gland, heart and brain. Since telmisartan has high affinity for angiotensin II type I receptor (G Protein coupled receptors) preventing the binding of angiotensin on the vascular smooth muscles preventing the rise in blood pressure. [2,3]

Telmisartan of different brands are available in INDIA having different excipients having strengths such as 20mg, 40mg, and 80mg. According to BCS classification telmisartan belongs to class II, i.e., having low solubility and high permeability.. The solubility of telmisartan is dependent on pH of solution especially in biological solution. Poor solubility in turn leads to poor dissolution of drug in solution which in turn decreases the bioavailability of the drug. [3]

DRUG PROFILE:

TELMISARTAN

IUPAC NAME: 2-[4-[[4-methyl-6-(1-methylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl]methyl]phenyl]benzoic acid **[2]**

Description: Telmisartan can be used either by alone or in combination with other medications to treat high blood pressure. The strain on the heart and arteries is increased by high blood pressure. The heart and arteries might not work correctly if it persists for a long time. Blood vessels in the kidneys, heart, and brain may be injured, which could lead to renal failure, heart failure, or a stroke. Lowering blood pressure can lower the risk of heart attacks and strokes. In patients 55 years of age and older with diabetes or cardiac issues, telmisartan is also used to reduce the risk of heart attacks or strokes.[2]

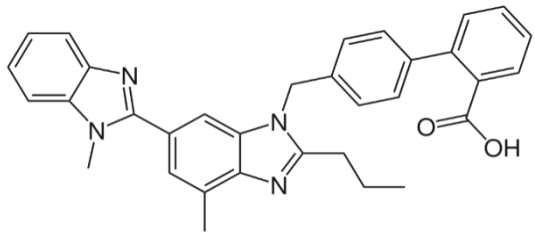
Telmisartan, an angiotensin II receptor blocker It works by blocking a bodily chemical that constricts blood vessels. Telmisartan results in relaxation of the blood vessels. The heart consequently receives more blood and oxygen. Additionally, blood pressure is lowered.

To buy this drug, you only need a prescription from your doctor.[2,3]

Molecular formula: $C_{33}H_{30}N_4O_2$[3]

Molecular weight:514.6 [3]

Structure: Chemical structure of telmisartan[3]



Category: BCS Class II [3]

Solubility: very low 0.078 mg/ml in water

Vapour pressure:9.33X10-20 mm Hg at 25 °C[3]

Melting point: 261-263 °C[3]

Pharmacology:

Mechanism of action: The renin angiotensin aldosterone system plays a key role in modulation of blood pressure. Renin is produced from Juxtaglomerular cells. The renin produced is released onto the blood which acts on

angiotensinogen. The liver produces angiotensinogen which circulates in plasma and is cleaved by renin to angiotensin I. The angiotensin I produced is inactive but is converted to active form by enzyme angiotensin converting enzyme Telmisartan prevents the binding of angiotensin II to angiotensin II receptor thereby causing vasodilation in arteriolar smooth muscle.

Telmisartan is responsible for delaying voltage gated Na+ channel inactivation which causes intracellular Na+ overload which causes prolonged action potential duration. This results in activation of reverse Na+ - Ca2+ exchange activity causing accumulation of Ca2+ intracellularly causing improvement and enhancement of cardiac contractility. Prolonged accumulation of Ca2+ causes intracellular Ca2+ overload and delayed inactivation of voltage gated Na+ channel resulting in cytosolic Na+ overload causing prolonged action potential. Both the effects combined causes myocardial infraction and cardiac cell death. [4]

QUALITY CONTROL TESTS FOR TABLETS [5,7]

In general, quality control refers to a process or series of actions used during the production of a product to guarantee that it complies with specifications and is repeatable.

Table 1: Drug profile information of 5 brands of TELMISARTAN 40 mg are coded by A,B,C,D,E

Sl.No	**Brand Code**	**Mfg. Date**	**Exp. Date**	**Price/ 10 Units**
1.	A	07/2022	12/2023	15
2.	B	07/2022 11/2021	06/2025 04/2024	36.983 36.983
3.	C	10/2021	09/2023	28.83
4.	D	1/2022	12/2023	34.8425
5.	E	06/2022	05/2024	41.495

1. Physical evaluation:

Table 2 :The different physical evaluation tests for Telmisartan tablets of different brands A,B,C,D,E.[6, 8]

General appearance	**A**	**B**	**C**	**D**	**E**
Colour	White	White	White	White	White
Odour	Odourless	Odourless	Odourless	Odourless	Odourless
Shape	Round	Oval	Round	Round	Oval
Thickness	0.39	0.67	0.37	0.47	0.71
Diameter	0.99	0.48	0.8	0.99	0.57
Width	---	1.21	---	---	1.48

2. Hardness:

The amount of pressure needed to break a tablet when compressed diametrically. The Stock's Monsanto hardness tester, which comprises of a barrel with a compressible spring, is used to assess the tablet's hardness. The barrel fracture's gauze is traversed by the pointer. The 7Kp hardness level is regarded as appropriate for handling tablets.[8]

Table 3: Date of hardness determination of different brands of Telmisartan

Brand names code:	**Avg.Hardness (Kg/cm)**
A	4.5
B	3.5
C	4
D	3
E	6

3. Friability:

Methodology: About 10 previously weighed tablets of each brands were placed in a friability apparatus and subjected to abrasion, which was rotates at 25 revolutions for 4 minutes and the tablets were dusted and were reweighed. The percent friability was calculated using formula.[8]

% Friability = [(Initial weight)-(Final Weight)/Initial weight] X 100

Table 4: :Date of friability determination of different brands of Telmisartan

Brand name code	**Initial weight (g)**	**Final weight (g)**	**% Friability**
A	2.550	2.549	0.039
B	2.555	2.554	0.0391
C	1.385	1.3847	0.0216
D	2.020	2.016	0.019
E	4.550	4.549	0.0219

4. Weight variation:

Methodology: Weight variation test is conducted to ensure uniformity in the weights of the tablet in batch. 10 tables of each brand are individually weighed and the average weight is calculated. From the average weight % Weight variation is determined.[8]

% weight variation = (average weight of tablet – weight of each tablet/ average weight of each tablet)

Table 5:The data of Telmisartan tablets is coded by a brand name A,B,C,D,E with a percentage variation rage from 13.20-45.10%.

SL.NO	A	B	C	D	E
1.	0.245	0.255	0.135	0.200	0.455
2.	0.245	0.250	0.135	0.200	0.450
3.	0.255	0.255	0.130	0.190	0.450
4.	0.245	0.260	0.130	0.195	0.455
5.	0.250	0.255	0.130	0.195	0.455
6.	0.250	0.255	0.130	0.200	0.455
7.	0.245	0.255	0.135	0.195	0.455
8.	0.245	0.250	0.130	0.195	0.450
9.	0.245	0.245	0.135	0.200	0.450
10	0.255	0.255	0.130	0.195	0.445
Total	2.481	2.535	1.320	1.965	4.510
%Weight variation	24.81	25.35	13.20	19.65	45.10

5. Disintegration:

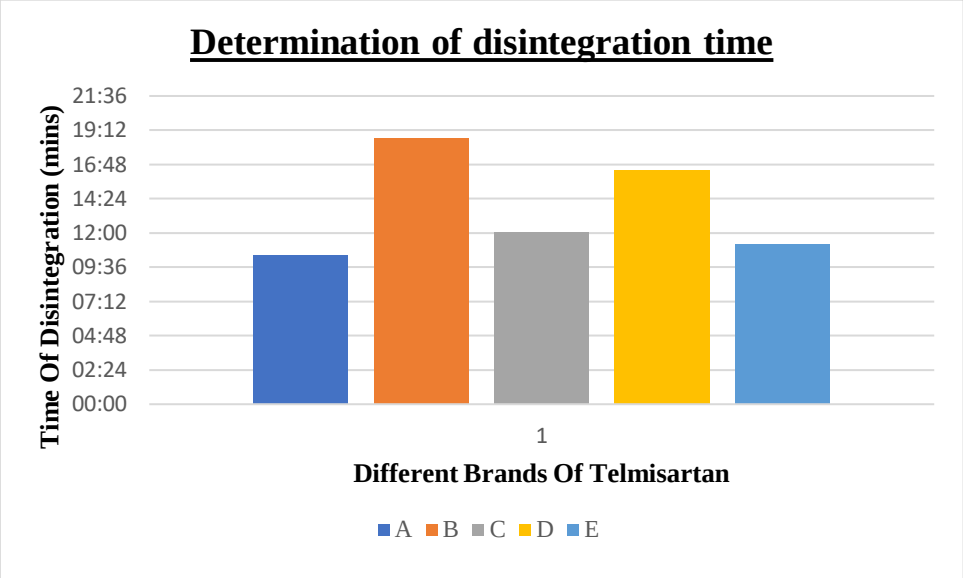
Disintegration Time Studies :

Methodology: Six tablets from each brand were tested using the disintegration instrument (Electrolab company). The time it took for the pill to completely disintegrate, leaving no palpable mass inside the instrument, was measured in seconds. The disintegration media employed was phosphate buffer maintained at 372°C. The experiment was done three times.[8]

Table 6: :Date of determination of disintegration of different brands of Telmisartan .

Brand name code	Time of disintegration (mins)
A	10:28
B	18:38
C	12:04
D	16:24
E	11:10

Fig 2:Determination of disintegration time of different brands of Telmisartan tablets.

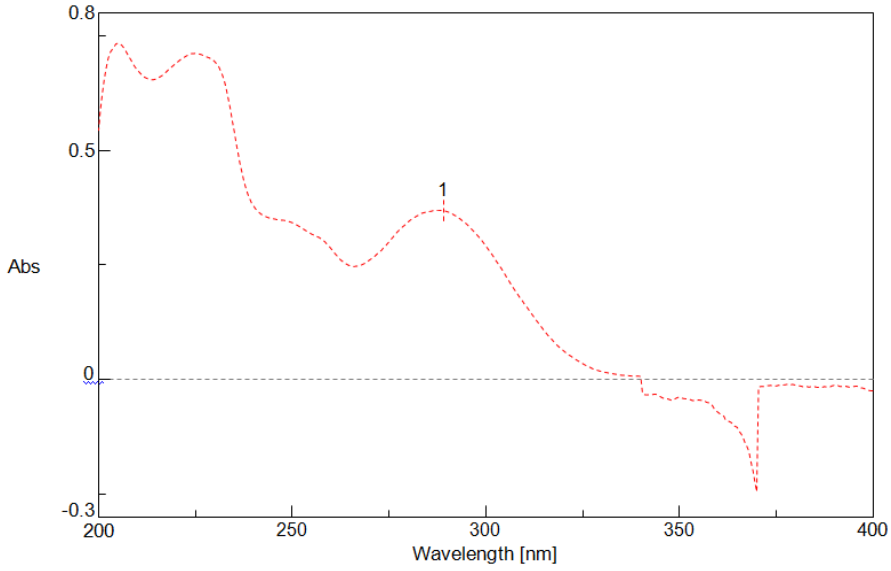


6. ASSAY OF TELMISARTAN:

Procedure for UV Assay:[9,10]

Using a glass mortar and pestle, weighed tablet (1) was ground into powder. Telmisartan 40 mg pill correctly weighed quantity is taken, dissolved in methanol, and added to 10ml volumetric flask. Pipette 1 ml of the aforementioned solution, then dilute it with 10 ml. To determine the drug content, 1 ml of the standard solution was pipette-out and diluted to 10 ml with 0.1 N HCl. The resultant solution was measured at 296 nm, and the drug concentration was calculated using 0.1 N HCl as a blank.

Fig 3: Assay of TELMISARTAN obtained by UV Spectrophotometer obtained by using Phosphate Buffer at pH 7.5



7. Dissolution Profile Study or In-vitro release studies:

Preparation of Standard Calibration Curve:

Methodology:

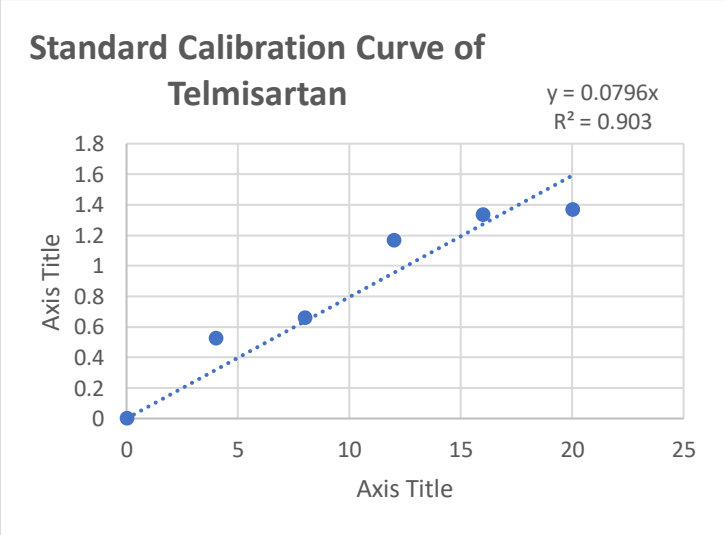
Preparation of standard drug solution:

40 mg of Telmisartan were precisely weighed and transferred to a 100 ml volumetric flask, where 1 ml of 0.1(M) sodium hydroxide (NaOH) solution was added in order to create the standard drug solution Telmisartan. Finally, 100 ml of methanol was added to create a transparent drug solution with a 0.40 mg/ml concentration.[8]

Table 7:Date of standard calibration curve of Telmisartan

CONC (µg/ml)	**ABS (nm)**
0	0
4	0.524
8	0.658
12	1.167
16	1.3326
20	1.366

FIG 4: Calibration curve of standard Telmisartan obtained by plotting concentration vs absorbance



Dissolution testing parameters:[8]

Dissolution Apparatus: **ELECTROLAB Dissolution Tester TDT-08L**

USP Type II (Paddle type)

Dissolution Medium Volume: 900ml of Phosphate Buffer (pH7.5)

Temperature: 37 ± 0.5 ℃

RPM: 75

Dissolution Time:60 min

Time interval for each sample: 5 mins up to 30 mins

15 mins up to 1 hour

Sample withdrawn: 3 ml each time point.

Dissolution Rate Determination:[8]

Using a **USP type II** apparatus, the dissolution test was performed on eight tablets of each brand. **ELECTROLAB DISSOLUTION TESTER TDT-08L** (paddle type). The dissolution medium utilised was 900 cc of freshly produced phosphate buffer with a pH of 7.5. The codes for the 5 tablet brands were **A, B, C, D,** and **E**. Using a heater, the medium's temperature was maintained at 37 0.5 C. For 60 minutes, the paddle was turned at 75 RPM. In the course of this procedure, 3 ml of the dissolving medium were regularly collected every 5 to 30 minutes.then 15 minutes to an hour later (5,10,15,20,25,30,45,60). Whatman filter paper was used to filter the withdrawn sample.A precise amount of the dissolution medium—900 ml—was refilled at the same time with freshly made phosphate buffer, which has a pH of 7.5. A 10 ml volumetric flask was filled with filtered phosphate buffer after 1 ml of the removed material was added. Using a **SHIMADZU CORP UV visible spectrophotometer (UV-1900i),** , the solution's absorbance was measured at a maximum of 296 nm against filtered phosphate buffer as a blank.

RESULT:

Table 8: Dissolulation profile of Telmisartan tablets coded by A in phosphate buffer

Tim Min	**Abs (nm)**	**Conc (µg/ml)**	**Conc * D.F**	**Drugs In Sample**	**Drugs 900ml**	**Cumm Drug Release**	**%Cumdrug Release**
5	0.123	2.321	23.207	0.928	20.886	20.88	52.216
10	0.147	2.773	27.736	1.109	24.962	25.890	64.726
15	0.156	2.943	29.434	1.177	26.499	27.6	69.000
20	0.164	3.094	30.943	1.237	27.849	29.026	72.566
25	0.17	3.207	32.075	1.283	28.867	30.106	75.264
30	0.173	3.264	32.641	1.305	29.377	30.660	76.650
45	0.173	3.264	32.642	1.305	29.377	30.683	76.707
60	0.175	3.3019	33.018	1.321	29.716	31.023	77.556

Table 9: Dissolulation profile of Telmisartan tablets coded by B in phosphate buffer

Time Min	Abs (nm)	Conc (µg/ml)	Conc* D.F	Drugs In Sample	Drug In 900 ml	Cumm Drug Release	%Cumu Drug Release
5	0.1181	2.228	22.283	0.891	20.054	20.054	50.137
10	0.1511	2.850	28.509	1.140	25.658	26.549	66.374
15	0.1705	3.217	32.169	1.286	28.952	30.093	75.233
20	0.1742	3.286	32.868	1.315	29.581	30.867	77.169
25	0.201	3.794	37.924	1.517	34.132	35.446	88.617
30	0.2103	3.967	39.679	1.587	35.711	37.228	93.071
45	0.2172	4.098	40.981	1.639	36.883	38.470	96.175
60	0.219	4.132	41.321	1.653	37.188	38.827	97.069

Table 10: Dissolulation profile of Telmisartan tablets coded by C in phosphate buffer.

Time Min	Abs (nm)	Conc (µg/ml)	Conc* D.F	Drugs In Sample	Drug In 900 ml	Cumm Drug Release	%Cumu Drug Release
5	0.167	3.151	31.509	1.260	28.358	28.358	70.896
10	0.178	3.358	33.585	1.343	30.226	31.486	78.717
15	0.1889	3.564	35.641	1.426	32.077	33.420	83.558
20	0.189	3.566	35.660	1.426	32.094	33.52	83.800
25	0.196	3.698	36.981	1.479	33.283	34.709	86.773
30	0.199	3.754	37.547	1.502	33.792	35.271	88.179
45	0.215	4.056	40.566	1.622	36.509	38.011	95.028
60	0.219	4.132	41.320	1.652	37.188	38.811	97.028

Table 11: Dissolulation profile of Telmisartan tablets coded by D in phosphate buffer

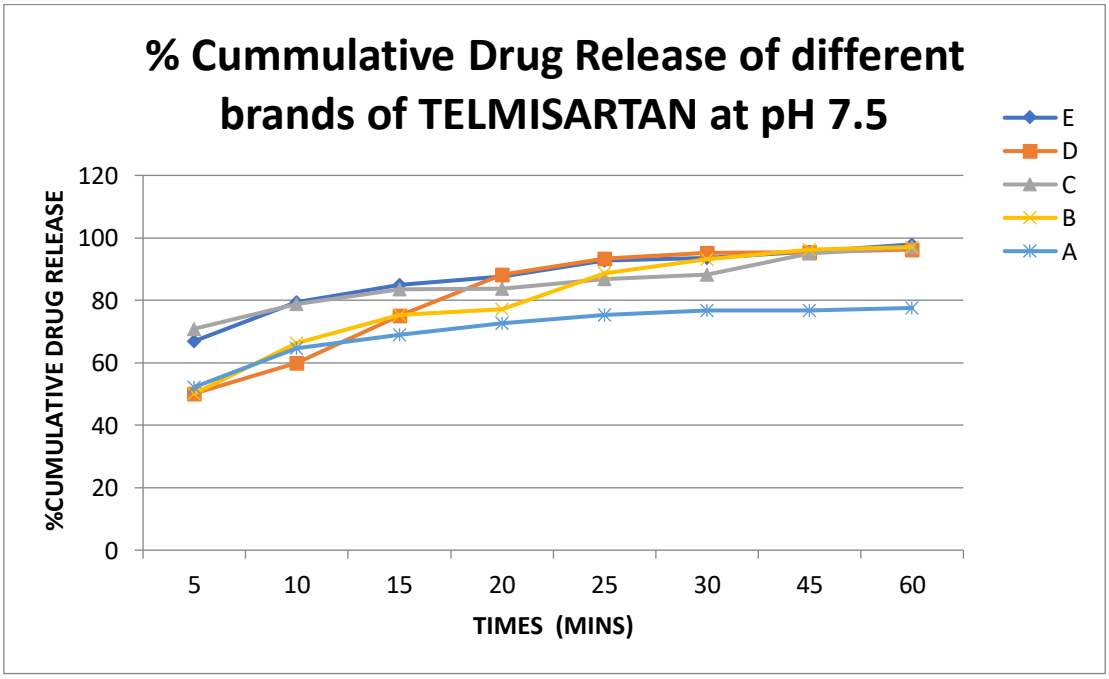
Time Min	Abs (nm)	Conc (µg/ml)	Conc* D.F	Drugs In Sample	Drug In 900 ml	Cumm Drug Release	%Cumu Drug Release
5	0.1182	2.230	22.301	0.892	20.071	20.0716	50.179
10	0.1361	2.567	25.679	1.027	23.111	24.003	60.008
15	0.171	3.226	32.264	1.290	29.037	30.064	75.162
20	0.2003	3.779	37.792	1.511	34.013	35.303	88.259

25	0.2108	3.977	39.773	1.590	35.796	37.307	93.269
30	0.2149	4.055	40.547	1.621	36.492	38.083	95.208
45	0.2151	4.058	40.584	1.623	36.526	38.148	95.370
60	0.2172	4.098	40.981	1.639	36.883	38.506	96.266

Table 12 : Dissolulation profile of Telmisartan tablets coded by E in phosphate buffer

Time Min	**Abs (nm)**	**Conc µg/ml**	**Conc* D.F**	**Drugs In Sample**	**Drug In 900 ml**	**Cumm Drug Release**	**%Cumu Drug Release**
5	0.1577	2.975	29.755	1.1901	26.779	26.779	66.948
10	0.18	3.396	33.962	1.358	30.566	31.756	79.390
15	0.1921	3.624	36.245	1.449	32.620	33.979	84.948
20	0.198	3.736	37.358	1.494	33.622	35.072	87.681
25	0.2096	3.955	39.547	1.582	35.592	37.086	92.716
30	0.211	3.981	39.811	1.592	35.830	37.412	93.530
45	0.216	4.075	40.754	1.630	36.679	38.272	95.679
60	0.221	4.169	41.698	1.667	37.528	39.1584	97.896

FIG 5: Comparison of dissolution profile of different brands of TELMISARTAN



The brands of **TELMISARTAN** as show in fig 5 and coded by A,B,C,D,E. After 20 minutes % Cumulative Drug Release of brand A is 72.56% and is less compared to brand B,C,D,E. At the end of 60 minutes % Cumulative Drug Release of brand A is 77.55% compared to brand B,C,D,E having % Cumulative Drug Release 97.06 %. Hence brand A has lesser % Cumulative Drug Release compared to brand B,C,D,E.

CONCLUSIONS:

From the quality control tests for telmisartan tablets like General appearance test, and hardness test, Friability test, Disintegration test, Dissolution test, weight variation test it is found that the different brands of telmisartan coded as brand A,B,C,D,E have taken compliance with Indian Pharmacopeial standards. From the hardness test it was found that brand E has a good average hardness value compared to other four brands. From the Friability Test it is found that the % Friability of brand C,D,E was better compared to that of brand A and B..From the weight variation test conducted it is found that the percentage weight variation of brand A, brand B and brand E was found to be more compared to other two tablets with brand E having highest Percentage weight variation. From the disintegration time of tablets it is found that all the five brands of telmisartan have undergone disintegration at specific time intervals and the disintegration time brand B and brand D was more whereas brands A,C,E have undergone dissolution at a faster rate. From the assay of telmisartan tablets it was found that peak of Telmisartan was at 288nm and the corresponding intensity was 0.199302.From the dissolution test of different brands of telmisartan tablets conducted it is found that after 20 minutes % cumulative drug release of brand A is 72.56% and is less compared to brand B,C,D,E. At the end of 60 minutes % cumulative Drug release of brand A is 77.55% compared to brand B,C,D,E having % cumulative drug release 97.06%.Hence brand A has lesser % cumulative drug release compared to brand B,C,D,E.

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