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Research Paper

Comparative Dissolution Study of Expired and Marketed Tablets

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ABSTRACT :-
The dissolution process is considered an important in vitro tool to evaluate product quality and drug release behavior. Single dissolution method for the analysis of combined dosage form are preferred to simplify quality control testing. The objective of the present work was to compare the dissolution profile of marketed and expired tablet.
In-vitro dissolution was carried out using USP dissolution apparatus type 2 by using different media for different tablets like 0.1N HCl, distilled water, phosphate buffer. Drug content of tablet was estimated by taking absorbance at particular wavelength with respect to drug by using UV spectrophotometer. In-vitro release profile of marketed and expired tablets was compared and results was found to be satisfactory.
Keywords:-*Clomifene citrate, Cilnidipine, Losartan potassium, dissolution.*

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I. INTRODUCTION :-

The main purpose of solid dosage form is to make a drug available to the human body at certain rate and define amount through the gastro intestinal tract so that the drug can producepharmacological effects. But studies on bioavailability of drugs from a given dosage form reveled that, in many situations, solid dosage forms did not give the same therapeutic effects. This ismainly due to the insufficient dissolution and subsequent absorption

of the drug from the GIT. So,dissolution analysis of pharmaceutical solid dosage forms is a very important test of productquality.

The rate and extent of dissolution of the drug from any solid dosage form determines the rate and extent of absorption of the drug. In case of poorly water soluble drug dissolution rate is rate limiting step in the process of absorption, potential bioavailability problem and relevant with extremely hydrophobic drug due to erratic and incomplete absorption from GIT.Dissolution testing is a requirement for all solid oral dosage forms and is used in all phases of development for product release and stability testing[1]. It is a key analytical test used for detecting physical changes in an active pharmaceutical ingredient (API) and in the formulated product.

At early stages of development, *in vitro* dissolution testing guides the optimization of drug release from formulations. Over the past 50 years, dissolution testing has also been employed as a quality control (QC) procedure, in R&D to detect the influence of critical manufacturing variables and in comparative studies for *in vitro-in vivo* correlation (IVIVC).The FDA guidance on dissolution testing for immediate release solid oral dosage forms[1] includes the use of the Biopharmaceutics Classification System (BCS) guidelines for biorelevant dissolution tests, which is based upon API solubility and permeability.[3] According to the BCS guidelines, *in vitro* dissolution testing may be a useful tool to forecast the *in vivo* performance of drug products and potentially reduce the number of bioavailability/bioequivalence studies required. The FDA guidance on scale-up and post-approval changes (SUPAC) for immediate release oral dosage forms recommends the use of *in vitro* dissolution to justify post-approval changes.

II. MATERIAL AND METHODS :-

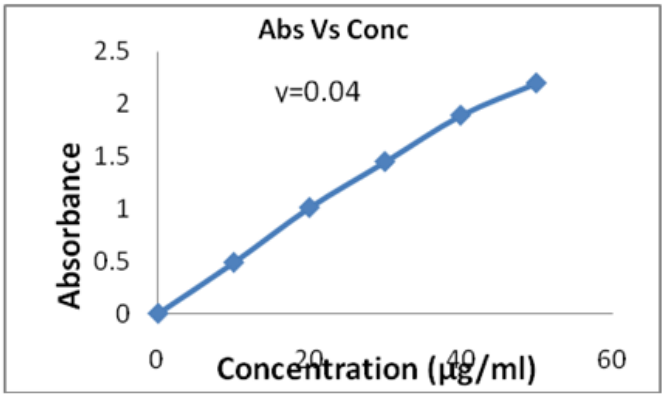
Clomifene citrate, Cilnidipine and Losartan potassium tablet wasb obtained from medical agencies, stores. Other chemicals required were 0.1 N HCl, sodium hydroxide, methanol, distilled water.

Methodolgy:-

1) Dissolution study of Clomifene Citrate tablet:-

Clomifene, also known as clomiphene, is a medication used to treat infertility in women who do not ovulate. This includes those who have polycystic ovary syndrome. Dissolution study was performed to conclude drug release profile in vitro conditions.

Standard calibration curve (0.1N HCl):-



Procedure:

Standard stock solution:

An accurately weighted quantity of Clomifene Citrate equivalent to 50 mg was taken in 50 ml volumetric flask and dissolved in 0.1 N HCl and volume was made upto mark with 0.1 N HCl. (1000µg/ml)

Working stock solution:-

The 1.0 ml portion of standard stock solution was diluted with 0.1 N HCl to get 100 µg/ml for Clomifene Citrate. The aliquot portion of working stock solution of Clomifene Citrate was further diluted with 0.1 N HCl to get series of concentrations range from 10-50µg/ml and absorbance was noted at 245 nm by UV Visible Spectrophotometry. Observations were shown in Table No.1.1

Table No. 1.1: Observation For Standard CalibrationCurveClomifene Citrate tablet :-

Clomifene citrate tablet(50mg)	Mfg. date	Expiry date
Marketed	Apr 2017	Mar 2020
Expired	Jan 2008	Dec 2010

Fig .Standard calibration curve of Clomifene Citrate

Concentration (µg/ml)	**Absorbance (At 245nm)**
0	0
10	0.487
20	1.012
30	1.451
40	1.894
50	2.203

***In vitro* Dissolution Test:-**

Release profiles were examined using dissolution test for marketed and expired tablet of Clomifene Citrate. It was performed using apparatus type 2, medium taken was 900 ml of 0.1 N HCl and speed and time was fixed at 100 rpm and 60 minutes, respectively.

The medium was maintained at 37±0.5°C. After the required amount of each sample had been placed into the dissolution medium, an aliquot portion of the solution was withdrawn at appropriate time intervals and diluted with 0.1N HCl then analyzed by spectrophotometer at 245 nm for the amount of dissolved drug. Tablet used are-

Observations were shown in Table No. 1.2, 1.3 for marketed and expired tablet.

Table No. 1.2 :Observation for release profile of marketed tablet

Time	Abs	Conc µg/ml	Conc µg/5ml	Conc µg/900ml	Conc mg/900ml	%CDR(M)
0	0	0	0	0	0	0
5	0.388	8.434	42.173	7590.6	7.5906	15.18
10	0.694	15.08	75.43	13572	13.572	27.14
15	0.892	19.39	96.95	17451	17.451	34.9
20	1.002	21.78	108.91	19602	19.602	39.2
30	1.324	28.78	143.91	25902	25.902	51.84
40	1.556	33.82	169.13	30438	30.438	60.87
60	1.872	40.96	203.47	36864	36.864	73.72

Table No. 1.3 : Observation table for release profile of Expired tablet

M = Marketed ; E = Expired

2) Dissolution study of Losartan potassium tablet:-

Time	Abs	Conc µg/ml	Conc µg/5ml	Conc µg/900ml	Conc mg/900ml	%CDR(E)
0	0	0	0	0	0	0
5	0.101	2.181	10.9	1963.28	1.963	3.92
10	0.205	4.42	22.13	3984.88	3.984	7.96
15	0.294	6.34	31.74	5714.9	5.714	11.42
20	0.384	8.29	41.46	7464.36	7.4643	14.92
30	0.425	9.17	45.89	8253	8.253	16.5
40	0.51	11.01	55.07	9913.6	9.913	19.82
60	0.621	13.41	67.06	12071	12.07	24.14

Introduction:-

Losartan potassium is a drug of the angiotensin- converting enzyme (ACE) inhibitor class primarily used in treatment of hypertension, congestive heart failure and heart attacks and also in preventing renal and retinal complications of diabetes. Its indications, contraindications and side effects are as those for all ACE inhibitors. It is designated chemically (2-butyl-4-chloro-1-{[2'- (1*H*-tetrazol-5 yl)biphenyl-4-yl]methyl}-1*H*-Imidazol-5-yl) methanol and It empirical formula is $C_{22}H_{22}ClKN_6O$.

Dissolution study was performed to concluded the release profile of tablet in vitro.

Standard calibration curve of losartan potassiumtablet :-

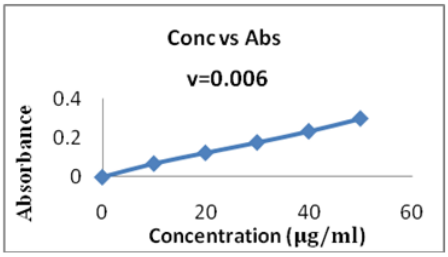
Losartan potassium tabletis weighted accurately equivalent to 50 mg of Losartan potassium in a 50 ml volumetric flask and volume up to 50 ml with methanol to dissolve.

Working stock solution:-

The 1.0 ml portion of standard stock solution was diluted with methanol to get 100 µg/ml for Losartanpotassium. The aliquot portion of working stock solution of Losartan potassium was further diluted with methanol to get series of concentrations range from 10-50µg/ml and absobance was noted at 240 nm by UV Visible Spectrophotometry. Observations were shown in Table No. 2.1

Table No. 2.1 :Standard calibration curve of losartan potassium tablet:-

Conc (µg/ml)	Abs
0	0
10	0.069
20	0.124
30	0.177
40	0.234
50	0.299



***In vitro*Dissolution test:-**

It was performed using dissolution apparatus type 2. One tablet in each basket was dissolved in 900 ml in distilled water media. An aliquot portion of filtered sample was collected for each time interval along with same volume of media replacement. The amount of Losartan potassium dissolved was determined by using UV absorption at the wavelength of maximum absorbance at about 240 nm.

Time	Abs	Conc µg/ml	Conc µg/5ml	Conc µg/900ml	Conc mg/900ml	%CDR(E)
0	0	0	0	0	0	0
5	0.013	2.16	10.83	1950	1.95	3.9
10	0.031	5.16	25.83	4650	4.65	9.3
15	0.051	8.5	42.5	7650	7.65	15.3
20	0.073	12.16	60.83	10950	10.95	21.9
30	0.092	15.33	76.66	13800	13.8	27.6
40	0.119	19.83	99.16	17850	17.85	35.7
60	0.128	21.33	106.66	19200	19.2	38.4

Following dissolution parameters were maintained.

1) Temperature :- 37± 0.5°C
2) Speed :- 50 rpm
3) Time :- 60 min.

Losartan K^+ (50mg)	Mfg. Date	Exp. Date
Marketed	Apr 2017	Mar 2019
Expired	Mar 2012	Feb 2014

Observations of dissolution study were shown in table 2.2, 2.3 .

Table No. 2.2 :Observational table for marketed tablet:-dissolution study of Losartan potassium

Time	Abs	Conc µg/ml	Conc µg/5ml	Conc µg/900ml	Conc mg/900ml	%CDR(M)
0	0	0	0	0	0	0
5	0.05	8.33	41.66	7500	7.5	15
10	0.092	15.33	76.66	13800	13.8	27.6
15	0.152	25.33	126.66	22800	22.8	45.6
20	0.215	35.83	179.16	32247	32.24	64.49
30	0.251	41.83	209.16	37650	37.65	75.3
40	0.296	49.33	246.66	44400	44.4	88.8
60	0.303	50.5	252.5	45450	45.45	90.9

Table No. 2.3 :Observational table for dissolution study of Losartan potassium expired tablet :-

3) Dissolution study of Cilnidipinetablet :-

Introduction :-

Cilnidipine is chemically, 1,4- Dihydro- 2,6-dimethyl- 4-(3-nitrophenyl)-3,5-pyridinecarboxylic acid 2-methoxyethyl(2E)-3-phenyl-propenyl ester.Cilnidipine is dual blocker of L-type voltage gated Ca^{2+} channels in vascular smooth muscle and N type Ca^{2+} channels in sympathetic nerve terminals that supply blood vessels. The inhibition of N type Ca^{2+} channels may provide a new strategy for the treatment of cardiovascular diseases. L-type Ca^{2+} channels are the main targets of the CCB. N type calcium channels are distributed along the nerve and brain, Cilnidipine is anticipated to exert specific action on nerve activity, such as inhibition of sympathetic activity. It inhibits the Ca^{2+} influx in both in vessel and in the nerve. So causes vasodilation and inhibits the release of nor epinephrine, which causes the vasodilation and decreases the heart rate and also decreases cardiac contraction in heart. So used in treatment of hypertension.

Standard calibration curve of Cilnidipinetablet :-

100 mg of Cilnidipine (pure) was accurately weighed and dissolved in 30 ml ethanol. The solution was filtered through Whatman filter Paper No. 41, volume of the filtrate was made up to 100 ml with ethanol (1 mg/ml).

Working stock solution:-

10 ml of the standard stock solution was diluted to 100ml with ethanol. Aliquots of the diluted solution was further diluted to 10 ml with ethanol to get series of concentrations range from 10-50µg/ml and the absorbance was measured at 240nm using ethanol as blank.

Table No. 3.1: Standard Calibration curve of Cilnidipinetablet :-

Conc	Abs
0	0
10	0.061
20	0.129
30	0.193
40	0.254
50	0.309

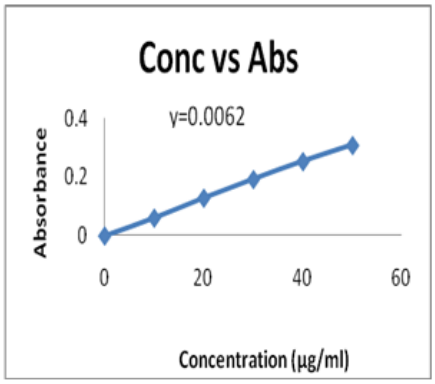


Fig. 3.1 Standard calibration curve of cilnidipine tablet

***In vitro* Dissolution test :-**

Dissolution test was performed in dissolution apparatus type II (USP). Tablet was placed in jar containing 900 ml of 0.1 N Hydrochloric acid for one hours and samples at different time interval 10 ml of aliquots were removed and filtered through whatmann filter paper at time interval specified (10-120 min) and 1 ml sample was further diluted to 10 ml using 0.1 N HCl and analyzed by UV- visible spectroscopy at 245 nm using 0.1 N HCl as blank.

Following dissolution parameters were maintained.

1) Temperature :- 37± 0.5°C
2) Speed :- 50 rpm
3) Time :- 60 min.

Cilnidipine (10mg)	Mfg. Date	Exp. Date
Marketed	May 2017	Apr 2019
Expired	Oct 2015	Sept 2017

Time	Abs	Conc µg/ml	Conc µg/5ml	Conc µg/900ml	Conc mg/900ml	%CDR
0	0	0	0	0	0	0
5	0.012	1.9354	9.677	1741.86	1.74186	17.41
10	0.019	3.06451	15.322	2758.05	2.75805	27.58
15	0.027	4.3548	21.774	3919.32	3.9193	39.91
20	0.032	5.1612	25.806	4645.08	4.64508	46.45
30	0.046	7.4193	37.096	6677.37	6.67737	66.77
40	0.052	8.387	41.934	7548.3	7.5483	75.48
60	0.061	9.8387	49.193	8854.83	8.85483	88.54

Observations were shown in table no. 3.2 , 3.3

Table No. 3.2 :Observation table of dissolution study for marketed tablet:-

Time	Abs	Conc µg/ml	Conc µg/5ml	Conc µg/900ml	Conc mg/900ml	%CDR
0	0	0	0	0	0	0
5	0.004	0.6451	3.22	580.64	0.5806	5.8
10	0.008	1.29	6.45	1161.29	1.161	11.61
15	0.019	3.064	15.32	2758.06	2.758	27.58
20	0.026	4.19	20.96	3774.19	3.774	37.74
30	0.038	6.129	30.64	5516.12	5.516	55.16
40	0.043	6.935	34.67	6241.93	6.2419	62.41
60	0.051	8.22	41.129	7403.22	7.4032	74.03

Table No. 3.3 Observation Table for dissolution study of expired tablet:-

III. RESULT AND DISCUSSION :-

Comparative dissolution profiles using a model independent approach were studied. Six tablets of marketed and expired tablet were tested by using dissolution apparatus with particular media, sampled at various time intervals and analyzed by UV spectrophotometer at particular wavelength with respect to drug.
Results were shown in table no. 6.1 forClomifene Citrate tablet, table no. 6.2 for Losartan potassium tablet and table no. 6.3 for Cilnidipine tablet.

Table no. 6.1 Comparative dissolution profile of the expired and marketed Clomifene Citrate tablet

Time	%CDR(M)	%CDR(E)
0	0	0
5	15.18	3.92
10	27.14	7.96
15	34.9	11.42
20	39.2	14.92
30	51.84	16.5
40	60.87	19.82

60	73.72	24.14

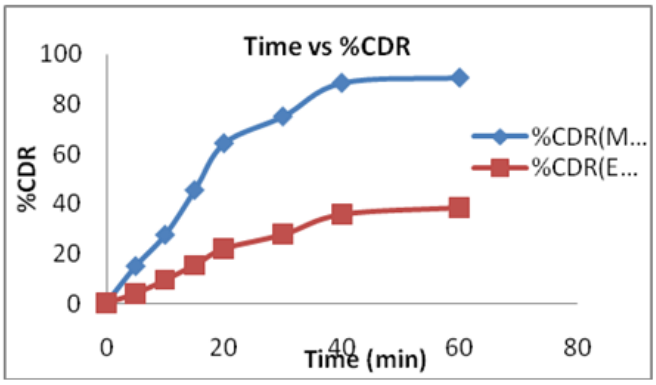


Fig. 6.1 Comparative dissolution profile of Clomifene Citrate tablet

Table no. 6.2 Comparative dissolution profile of the expired and marketed Losartan potassium tablet.

Time	%CDR(M)	%CDR(E)
0	0	0
5	15	3.9
10	27.6	9.3
15	45.6	15.3
20	64.49	21.9
30	75.3	27.6
40	88.8	35.7
60	90.9	38.4

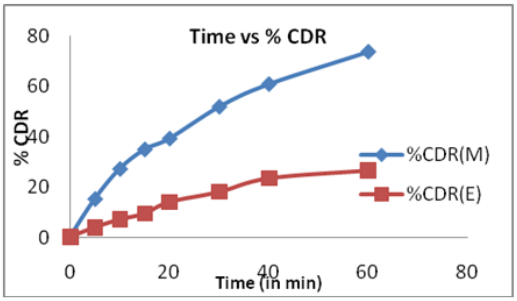


Fig. 6.2 Comparative dissolution profile of Losartan potassium tablet

Table no. 6.3 Comparative dissolution profile of the expired and marketed Cilnidipine tablet.

Time	%CDR (M)	%CDR (E)
0	0	0
5	17.41	5.8
10	27.58	11.61
15	39.91	27.58
20	46.45	37.74
30	66.77	55.16
40	75.48	62.41
60	88.54	74.03

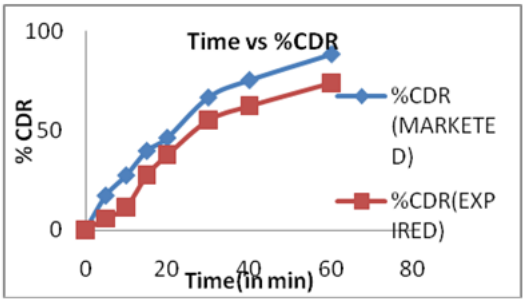


Fig .6.3 Comparative dissolution profile of Cilnidipine tablet

IV. CONCLUSION :-

In conclusion, the results indicate that the tablets used both marketed and expired for dissolution study showed differences in the dissolution rate and hence drug release from the formulations. From the result it is concluded that the dissolution rate of marketed tablet was found to be greater in comparision with expired tablet. As the dissolution rate of the tablet is rate limiting state it is important for study of absorption of drug. Study showed that the difference in dissolution rate of the marketed and recently expired tablet is about 30 % to 40 %. By studying various factors influencing the rate of dissolution, we can optimize the different properties of the formulation.

REFERENCES :-

[1]. Lachman Leon, Liberman Herbert A, Kanig Joseph L. The Theory and Practice of Indusstrial Pharmacy, 3rd edition, Varghese publishing house; 1987 Page no. 189, 301-303.

[2]. Indian Pharmacopoeia 2007; Government of India, Ministry of Health and Family Welfare, The Controller of Publication New Delhi, Vol-I

[3]. Page no. 950

[4]. " Enhancement of dissolution rate of slightly soluble drug Clomifene citrate by Solid dispersion" by DhingraDipti, Bhandari Anil, Sharma R.B. ,Gupta Ranjana, Gupta Sachin,Faculty of Pharmaceutical Sciences, Jodhpur National University, Jodhpur, Rajasthan, India.

[5]. "INTERNATIONAL JOURNAL OF UNIVERSAL PHARMACY AND BIO SCIENCES" "Enhancement of dissolution rate of Cilnidipine using liquisolid technique". Shalaka P. Rasal, Sheetal B. Gondkar, Nikhil P. Mahalpure, Ravindra B. Saudagar.

[6]. "Comparative in vitro dissolution study of Losartan Potassium Marketed Tablets in Four Different Dissolution media by Validated Analytical Method" TanzinaSharminNipun, DiptiDebnath, Md. Sium-UI HossainMiah, Muhammad Kamal Hossain, S.M. Hossen Department of pharmacy, University of Chittagong, Bangladesh.

[7]. 'Journal of Biomedical and Pharmaceutical Research 2(2) 2013, 25-30 "Formulation and In-vitro Evaluation of Immediate Release Tablets of Losartan Potassium Using Different Superdisintegrants" J. Vinod and A. Chenthilnathan'Department of Pharmaceutical Chemistry, ManonmaniamSundaranar University, Tiruneveli, Tamil Nadu, India'.

[8]. Online resources

[9]. www.pharmacopeia.cn/v29240/usp29nf24s0_m18490.html

[10]. https://en.m.wikipedia.org>wiki>dissolution_testing