Study of Post Compression Parameters of Various Marketed Paracetamol Tablets in India

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ABSTRACT

Paracetamol belongs to the class of antipyretic and analgesic. Various brands of some dosage forms are available in the market with a common claim that they are all bioequivalent. The main objective of the present experiment was to evaluate post compression parameters of various brands of paracetamol tablets containing 650 mg of drug and to determine whether all the formulations used were equivalent or significantly different. Paracetamol of 650 mg standard tablets from different manufacturers were selected in the studies. The post compression parameters like weight variation, friability, hardness, weight variation, disintegration, dissolution profiles were found to be varying but within the prescribed limit.

Keywords: Hardness, friability, weight variation, disintegration, In Vitro dissolution, Paracetamol, Phosphate buffer.

INTRODUCTION

Paracetamol is a non steroidal anti-inflammatory drug .It is prominently used as antipyretic and anodyne(analgesic), In treatment of fever, pain ,headache and such other discomfort. Its chemically familiar as acetaminophen i.e., (4- hydroxy acetanilide). It is also given in combination with many cold medications, also in cancer pains and to reduce the pain after surgery. It is predominantly safe in normal doses, higher doses causes hepatic disorders. (Nayak AK 2010)

Evaluations of different parameters like, hardness, friability, weight variation, disintegration time dissolution profile were performed. Therapeutic effectiveness and bioavailability of tablet depends on these parameters (Kar A et al.,2015; D.R.Jadge et al., 2014). Depending on this facts the present study was conducted to compare the quality standards of different commercially available paracetamol 650 mg tablets .

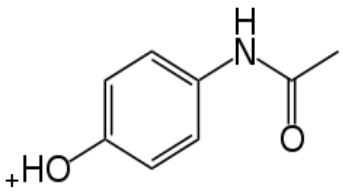

Fig No: 1- Chemical Structure of paracetamol

POST COMPRESSION EVALUATION PARAMETERS

WEIGHT VARIATION

This is an important in process quality control test, which has to be checked frequently (every half hour). Corrections are made during the punching of tablet if necessary. Any variation in the weight of tablet (for any reason) leads to either under medication or overdose .This is particularly true when the drugs are potent or low dose drugs. All tablet machines have provision to receive a known quantity (volume which is correlated to weight) of granules. Improper flow of granules from the hopper into the die is responsible for weight variation. The range of variation is 10 % for tablets weighing less than 80 mg, 7.5% for tablets weighing in the range of 80 to 250 mg, 5.0 % for tablets weighing above 250 mg. For paracetamol the deviation allowed is 5 %.

FRIABILITY

Friability is the loss of weight of tablet in the container/ package ,due to removal of the particles from the surface .This in process quality control test is performed to ensure the ability of tablets to withstand the shocks during processing (coating and strip.- packaging) handling ,transportation and shipment (Rahman Z U et al.,2013)(Binega G et

al.,2013). The friability of tablets is indicated by chipping, capping, breaking. The extent of friability is less than 0.8% .This limit is strictly adhered when the tablets are further processed for coating.

HARDNESS

Hardness is a force required to break a tablet across the diameter. The hardness of the tablet is an indication of its strength. This is a valuable test which might influence tablet disintegration and dissolution rate.

DISINTEGRATION

Disintegration is defined as that state in which any residue of tablet except fragments of insoluble coating, remaining on the screen of the test apparatus consisting of a soft mass having no palpably firm unmoistened core. Disintegration process involves the breaking of tablet into small particles .The quicker the disintegration the faster could be the action .disintegration roughly indicates the possible pattern of dissolution of active substance. Hence the experimental conditions closely mimic the situation that a tablet encounters in GI tract, in terms of temperature, pH and mechanics.

DISSOLUTION

Dissolution is defined as "the amount of drug substance that goes into solution per unit time under standardized conditions of liquid/solid interface, temperature and solvent composition". Dissolution is conducted to know the minimum time taken by the drug to dissolve itself in the systemic circulation and starts its action in the body.

There are 2 methods of to know the dissolution rate,

1. In vitro studies
2. In vivo studies

In the pharmaceutical industry, drug dissolution testing is routinely used to provide analytical in vitro drug release erudition for both quality control scheme, i.e., to compute batch-to-batch consistency of solid oral dosage forms such as tablets and drug reinforcement, i.e., to anticipate in vivo drug release profiles. It serves as are preventative factor for bioavailability and bioequivalence.

Hence comparative dissolution studies of various commercially marketed paracetamol products. paracetamol tablets of 650mg were selected .

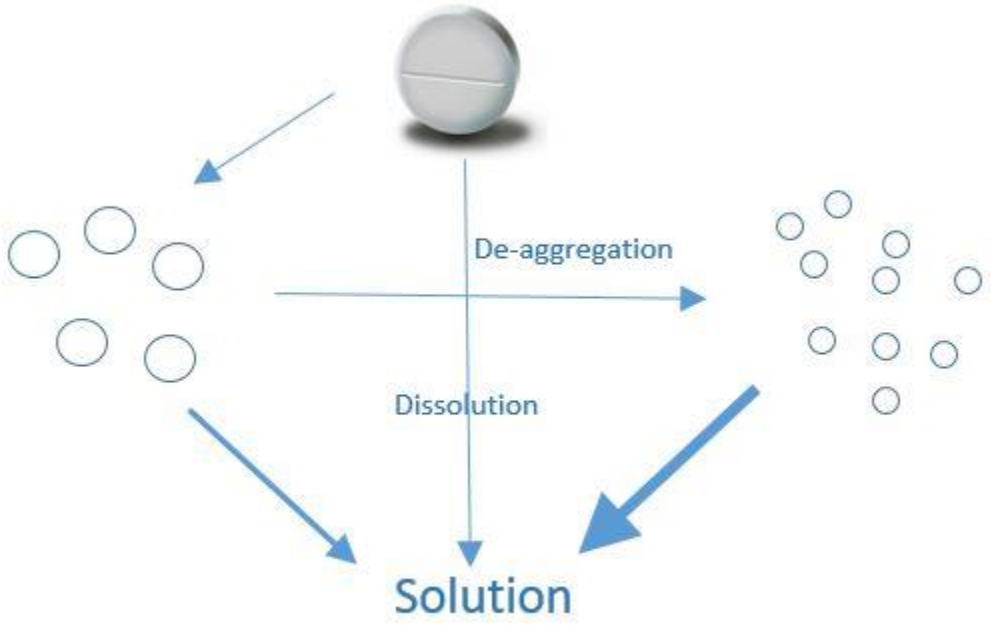

Fig No : 2 – Dissolution studies

Applications of dissolution

Dissolution test is used as a quality control tool to scrutinize habitually the uniformity and reproducibility of production batches. In case, a single point determination i.e., a certain percentage of the drug dissolved (released) in a given time interval is usually a sufficient control parameter. (Siew A 2016)

Dissolution test is used as a exploration tool for augment the parameters and ingredients in a new formulation. Commonly multi point determination is employed.

However *in vitro* and *in vivo* co-relations are surveyed, there the dissolution studies are used as means to surrogate the recurring studies of absorption .Normally multipoint determination is selected.

Factors influencing the dissolution

The important experimental factors that influence the dissolution of drugs are listed below :

- Temperature (body temperature)- 37°C (36.5° to 37.5°C)
- Agitation (hydrodynamics)- 25 to 150 rpm (normally 50 Revolutions per minute)
- Dissolution media (environment of GIT) - water ,0.1 N hydrochloroic acid, Simulated gastric fluids , Simulated intestinal fluids
- These are fixed in order to mimic the dissolution in the biological system. When the test is used as quality control tool ,a rapid method is desirable .Accordingly experimental conditions are fixed.

MATERIALS AND METHODS

The various marketed paracetamol tablet containing 650 mg (Medamol 650 mg, Paracip 650 mg,P-650 mg, Crocin 650 mg , paracetamol (janushad)650 mg and Dolo 650 mg.

WEIGHT VARAITION

Tablets of each brand were weighed individually using a analytical balance .20 tablets were weighed individually, average weight is calculated from the total weight .The percentage difference in the weight variation should be within the permissible limits.

FRIABILITY

Roche friability (D.R.Jadge et al.,2014) is used to measure the friability of the tablets. It rotates at rate of 25 rpm. 10 tablets are weighed collectively and placed in the chamber of the friability. In the friabilator the tablets are exposed to rolling, resulting from free fall of tablets within the chamber of the friabilator. After 100 rotation (4 minutes) the tablets are taken out from the friabilator and intact tablets are again weighed collectively. Percentage friability is determined by using this following formula.

Friability = (W1-W2/W1) *100

Where as W1= weight of the tablets before test

W2= weight of the tablet after test

HARDNESS

The hardness of tablet is tested using the Monsanto hardness tester. The tester is placed across the diameter in between the spindle and the anvil. The knob is adjusted to hold the tablet in position .The reading of the pointer is adjusted to zero. The pressure is increased slowly to break the tablet. “Hardness factor” - the average of the several determination is determined and reported

DISINTEGRATION

It was performed using Electro Lab Disintegration apparatus, 12 tablets were taken in disintegration test apparatus at 37± 2 °C containing simulated gastric fluid (0.1N HCl). Noted down the time taken for tablets to disintegration.

DISSOLUTION

Various marketed paracetamol tablets containing 650 mg of drug was purchased from local pharmacy in Davanagere. All the other ingredients are of analytical grade.

PREPARATION OF BUFFERS

Preparation of phosphate buffer solution, pH 7.8

Five hundred ml of 0.2M potassium dihydrogen is taken in 2000ml volumetric flask, to which 445.0ml of 0.2 N sodium hydroxide solution is added and the volumetric flask to which 445.0 ml of 0.2 N sodium hydroxide solution is added and the volume is made up to the mark with distilled water.

Potassium dihydrogen phosphate (0.2 M) solution

Potassium dihydrogen phosphate (13.609 gram)is added to 500 ml volumetric flask containing distilled water and the volume is made up to the mark with distilled water.

Sodium hydroxide (0.2N) solution :

Four gram of sodium hydroxide is taken in 500 ml volumetric flask containing distilled water and volume is made up to the mark with distilled water.

PROCEDURE

The dissolution method is a kinetic method .i.e., periodical samples are withdrawn for the determination

1)Phosphate buffer solution pH 7.8(900ml) is measured and transferred into the dissolution flask.

2)The temperature is maintained at 37±0.50 C.

3) Various marketed paracetamol tablet containing 650 mg drug is placed at the bottom of the jar.

4)The paddle is rotated at 50 rpm .

5)Five ml of sample is withdrawn at 0 min and transferred into the test tube appropriately labeled. Immediately 5ml of phosphate buffer solution pH 7.8 is replaced into the dissolution flask.

6)Similarly samples are collected at 1,2,3,4,5,6,7,8,9,10 min intervals. A 5 ml of fresh dissolution medium is replaced in the flask whenever the sample is withdrawn.

7)All samples are filtered using wattman filter paper .

8)The absorbance at 249 nm is measured in UV spectrophotometer using the phosphate buffer solution as a blank.

9)The absorbance are recorded in the table and further calculations are done

10)A graph is plotted by taking cumulative percent of drug dissolved on y-axis and time on x-axis .

Fig No:3 – Dissolution apparatus

RESULTS AND DISCUSSIONS

WEIGHT VARIATION : The weight variation of various brands of paracetamol are shown below in table no :1

Table No1- Weight variation studies of marketed paracetamol products

S.NO	BRAND	LABEL CLAIM	AVG OF 20 TABLES	% DIFFERENCE	CONCLUSION
1	Medamol 650 mg	650	0.774	1.0	Passes
2	Paracip 650 mg	650	0.748	0.6	Passes
3	P- 650 mg	650	0.843	0.7	Passes
4	Crocin- 650 mg	650	0.860	0.7	Passes
5	Paracetamol(janaushad) 650 mg	650	0.842	0.7	Passes
6	Dolo – 650 mg	650	0.822	0.4	passes

FRIABILITY: The friability of various brands of paracetamol are shown below in the table no 2

Table No 2- Friability data of marketed paracetamol products

SL.NO	BRANDS	FRIABILITY(%)
1	Medamol 650 mg	0.25
2	Paracip 650 mg	0.40
3	P- 650 mg	0.11
4	Crocin- 650 mg	0.23
5	Paracetamol(janaushad) – 650 mg	0.00
6	Dolo – 650 mg	0.36

DISINTEGRATION: The disintegration of various brands of paracetamol is shown below in table no :3

Table No 3- Disintegration data of studies of marketed paracetamol products

SL.NO	BRANDS	DISINTEGRATION TIME (mins)
1	Medamol 650 mg	1.31
2	Paracip 650 mg	1.13
3	P- 650 mg	0.15
4	Crocin- 650 mg	2.10
5	Paracetamol(janaushad) – 650 mg	1.00
6	Dolo – 650 mg	0.45

HARDNESS :

Hardness of various marketed brands of paracetamol are shown below in table no :4

Table No 4-Hardness studies of marketed paracetamol products

SL.NO	BRANDS	HARDNESS(kg/cm^2)
1	Medamol 650 mg	4.6
2	Paracip 650 mg	4.0
3	P- 650 mg	4.3
4	Crocin- 650 mg	4.3
5	Paracetamol(janaushad) – 650 mg	4.5
6	Dolo – 650 mg	4.2

DISSOLUTION

The dissolution profile of marketed tablets like Medomol 650, Paracip 650, P-650, Crocin 650 and Paracetamol 650 mg (Janaushad) are listed in the following table.

Table No :5 -Drug release profile of Medamol 650 mg tablet

Sl.no	Time (min)	Abs at 249nm	Conc (mg/ml)	Dilution factor	Conc (mg/ml)	Amount In 5 ml (mg)	Amount In 900ml (mg)	Cumulative amount	% Drug release
(1)	(2)	(3)	(4)	(5)	(6)=(4)*5	(7)=(6)*(5)	(8)=(6)* 900/1000	(9)#	(10)= (9)*100 /650
1	1	0.096	1.884	100	188	940	169.2	169.2	26.03
2	2	0.097	1.905	100	190	950	171	171.94	26.45
3	3	0.127	2.535	100	253	1265	227.7	230	35.38
4	4	0.172	3.48	100	348	1740	313.2	318.09	48.93
5	5	0.216	4.405	100	440	2200	396	403.09	62.01
6	6	0.292	6.002	100	600	3000	540	550.09	84.62
7	7	0.451	9.461	100	946.1	4730	851.4	866.34	133.24
8	8	0.349	7.291	100	729.1	3645	656.1	675.77	103.93
9	9	0.331	6.906	100	690.8	3454	621.7	644.13	99.0

Table No :6-Drug release profile of Paracip 650 mg tablet

Sl.no	Time (min)	Abs at 249 nm	Conc (mg/ml)	Dilution factor	Conc (mg/ml)	Amount in 5 ml (mg)	Amount in 900 ml (mg)	Cumulative amount	% Drug release
(1)	(2)	(3)	(4)	(5)	(6)=(4)*(5)	(7)=(6)*(5)	(8)=(6)* 900/1000	(9)#	(10)= (9)*100 /650

1	1	0.242	4.95	100	495	2475	445.5	445.5	68.53
2	2	0.300	5.75	100	575	2875	517.5	519.47	86.25
3	3	0.280	6.17	100	617	3085	555.3	560.65	79.91
4	4	0.329	6.77	100	677	3385	609.3	617.73	95.03
5	5	0.386	7.97	100	797	3985	717.3	729.12	112.17
6	6	0.336	6.92	100	692	3460	674.5	695.30	106.96

Table No :7- Drug release profile of P-650 mg tablet

Sl.no	Time (min)	Abs at 249nm	Conc (mg/ml)	Dilution factor	Conc (mg/ml)	Amount In 5 ml (mg)	Amount In 900ml (mg)	Cumulative amount	% Drug Release
(1)	(2)	(3)	(4)	(5)	(6)=(4)*(5)	(7)=(6)*(5)	(8)=(6)* 900/1000	(9)#	(10)= (9)*100 /650
1	1	0.064	1.212	100	121.2	606	109.08	109.08	16.78
2	2	0.165	3.334	100	333.4	1667	300.06	300.06	46.25
3	3	0.251	5.140	100	514	2570	462.6	464.87	71.51
4	4	0.281	5.771	100	577	2885	519.3	524.14	80.65
5	5	0.317	6.527	100	652.7	3263.5	587.43	599.15	92.17
6	6	0.387	7.997	100	799	3995	719.1	726.82	111.81

Table No :8-Drug release profile of Crocin 650 mg

Sl.no	Time (min)	Abs at 249nm	Conc (mg/ml)	Dilution factor	Conc (mg/ml)	Amount In 5 ml (mg)	Amount In 900ml (mg)	Cumulative amount	% Drug Release
(1)	(2)	(3)	(4)	(5)	(6)=(4)*(5)	(7)=(6)*(5)	(8)=(6)* 900/1000	(9)#	(10)= (9)*100 /650
1	1	0.039	0.686	100	68.6	34.3	61.74	61.74	9.49
2	2	0.146	2.934	100	293.4	1469.5	264.06	264.40	40.6
3	3	0.176	3.565	100	356.5	1782.5	320.8	325.49	50.07
4	4	0.204	4.153	100	415.3	2078	373.77	375.5	57.78
5	5	0.243	4.97	100	497	2485	447.3	453.7	69.50
6	6	0.301	6.191	100	619.1	3095.5	557.1	566.1	87.09
7	7	0.365	7.535	100	753.5	3767.5	678.15	696.41	102.14

Table No :9-Drug release profile of Paracetamol 650 mg (janaushad)

Sl.no	Time (min)	Abs at 249nm	Conc (mg/ml)	Dilution factor	Conc (mg/ml)	Amount In 5 ml (mg)	Amount In 900ml(mg)	Cumulative amount	% Drug Release
(1)	(2)	(3)	(4)	(5)	(6)=(4)*5	(7)=(6)*(5)	(8)=(6)* 900/1000	(9)#	(10)= (9)*100 /650
1	1	0.032	0.5468	100	54.68	273.4	49.14	49.14	7.6
2	2	0.240	4.972	100	497.2	2486	447.48	447.67	68.85
3	3	0.255	5.291	100	529.1	2645.7	476.19	496.45	73.58
4	4	0.286	5.951	100	595.1	2975.5	535.59	540.9	83.19
5	5	0.294	612.12	100	612.1	3060.6	550.8	559.17	86.00
6	6	0.336	701.48	100	701.4	3507.4	631.2	642.33	98.79

Table No :10– Drug release profile of Dolo 650 mg

Sl.no	Time (min)	Abs at 249nm	Conc (mg/ml)	Dilution factor	Conc (mg/ml)	Amount In 5 ml (mg)	Amount In 900ml(mg)	Cumulative amount	% Drug Release
(1)	(2)	(3)	(4)	(5)	(6)=(4)*(5)	(7)=(6)*(5)	(8)=(6)* 900/1000	(9)#	(10)= (9)*100 /650
1	1	0.227	4.636	100	463.6	2318	417.24	417.24	64.1
2	2	0.286	5.876	100	587.6	2938	528.84	531.15	81.71
3	3	0.374	7.724	100	772.4	3862	695.16	698.09	106.9
4	4	0.381	7.871	100	787.1	3935	708.39	712.25	109.57
5	5	0.417	8.628	100	862.8	4314	776.52	780.45	120.06

Table No :11-Comparative drug release profiles of Paracetamol tablet

Sl.no	Time	Medamol 650	Paracip 650	P-650	Crocin 650	Paracetamol 650(janaushad)	Dolo – 650
1	1	26.03	68.53	16.78	9.49	7.6	64.1
2	2	26.45	86.25	46.25	40.6	68.85	81.71
3	3	35.38	79.91	71.51	50.07	73.58	106.94
4	4	48.93	95.03	80.65	57.78	83.19	109.57
5	5	62.01	112.17	92.17	69.50	86.60	120.06
6	6	84.62	106.96	111.81	87.09	98.79	
7	7	133.24			102.14		
8	8	103.93					
9	9	99.0					

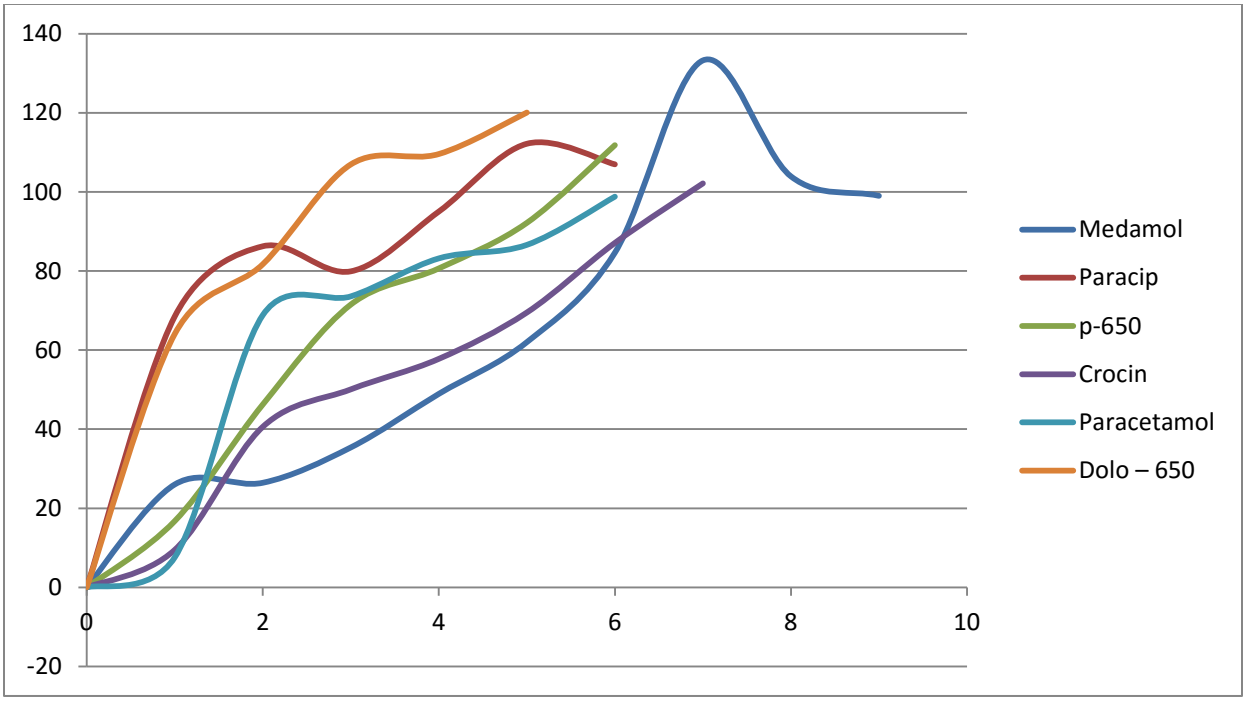

Fig No :4 -Dissolution profile of six different brands of paracetamol tablets

CONCLUSION

As a result of this study we have concluded that all the six brands of Paracetamol tablets meet the criteria laid in the official monographs and though they differ slightly in terms of various parameters like weight variation, hardness, friability, shows its complete release at in the range of 4 to 7 mins. All marketed paracetamol tablets of 650 mg were all under specified IP limits.

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Conflict of interest: None.

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