Exploring The Effect Of Light On Paracetamol Using Photostability Chamber

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ABSTRACT

This aims to compare intrinsic property of paracetamol. After 1.2million lux hrs light exposer and 200 watt per hr sq.meter a comprehensive analysis of various parameters to check efficacy, safety and adverse effects before expiry date and after manufacturing of tablet administration. Results indicate significant improvements in pain relief and reduction in fever post-administration, with minimal adverse effects observed, aiding healthcare professionals in making informed decisions regarding its usage. The effectiveness of drugs is directly related to the quality thus Quality evaluations of medications throughout the production process and Distribution are very essential. Paracetamol is a widely used Over-the-counter analgesic, antipyretic and a mild Anti inflammatory drug.The aim of the present experiment was to evaluate post compression parameters of paracetamol tablet. Evaluation of paracetamol tablet pharmaceutical and chemical equivalence in order to determine their interchangeability. The purpose of the study is to ensure the quality and safety of various brands of Paracetamol tablets available in market.

keywords- Dissolution, Disintegration, UV , Friability, weight variations, evaluations, pre compression and post compression.

INTRODUCTION

A common over-the-counter analgesic, antipyretic, and mild anti-inflammatory medication is paracetamol.[1,2] It works in a number of potential but unproven ways to provide its antipyretic and modest anti-inflammatory properties.[3,4].Acetaminophen has an oral bioavailability of 63.89% in adults, and it is readily absorbed from the proximal small bowel and does not undergo considerable first-pass metabolism in the liver.[5]

According to estimates, the oral route is used to provide at least 90% of medications designed to have a systemic effect[6]. This fact therefore emphasises the significance of tablets as a dose form in great detail. Standard uncoated tablets produced via compression are referred to as compressed tablets or standard compressed tablets. These tablets contain compressed drugs that are typically intended to have a systemic effect and have some aqueous solubility. The drug disintegrates in the GI contents and granular particles disaggregate, which in turn causes the particles to dissolve in the GI fluids and ultimately lead to aabsorption.[7]

Activities carried out to obtain more accurate information on a product being given marketing authorization and availability for community use are included in post-market qualitative research and evaluations. The information (qualitative and quantitative) gathered from this kind of post-market assessment could be applied to standards-compliant product development and quality enhancements. Since it is well known that regulatory

authorities grant market authorization for a product for use in the community based on limited data from clinical trials and scientific literature, post-market evaluations and the resulting data could be widely utilised to assess the approved products' quality, efficacy, and safety for end users in general. Thus, throughout the course of the product life cycle, post-market qualitative evaluation ought to be an ongoing endeavour. Post-market evaluation of a product has been defined as the following: public access to data collected and reported to drug regulatory authorities; assessment and investigation of product complaints that have been reported; process for production and review of label claims; and in vitro testing of the product to check for complaints in accordance with official specifications[8].A compressed tablet's medicinal efficacy depends on at least two things: its sufficient bioavailability and its uniform content, which is the label claim. An oral compressed tablet's primary goal is to provide the drug to the body through the

gastrointestinal tract (GIT) in a precise and defined quantity so that a therapeutic result can be achieved. As a result, a product's formulation directly affects quality parameters like weight variation, hardness, friability, and disintegration/dissolaffect[9]. Along with the manufacturing techniques, the physiochemical characteristics of the API and excipients are also crucial[10,11]. Moreover, quality control parameters are important instruments to take into consideration and should be carried out for each product in order to ensure a qualitative consistency in batch to batch production. Every quality control criterion is interconnected and affects the body's ability to absorb drugs and their availability[12].

Paracetamol's chemical makeup Acetaminophen, also known as paracetamol, is the active metabolite of phenacitin (fig -1). An OTC medication that is widely used is called paracetamol; its chemical formula is 4-hydroxy acetanilide[13].Non-opioid analgesic paracetamol is prescribed for headache, short-term musculoskeletal pain, and antipyretic purposes. There is no evidence that paracetamol has anti-inflammatory properties, and excessive dosages may harm the liver[14].

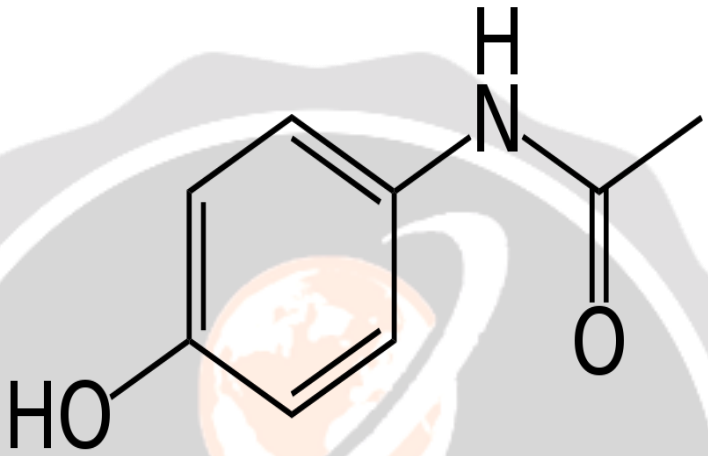

Fig 1: Paracetamol chemical structure

IUPAC Name: N-(4-hydroxy phenyl) ac4-hydroxyl Chemical formula: C8H9NO2 Molecular weight: 151.17.[15]

MATERIALS AND METHODS

MATERIALS

Factors influencing the dissolution

Body temperature: 36.50 to 37.50 °C

Hydrodynamic agitation: 50 revolutions per minute

Dissolution media (environment of GIT) - water ,0.1 N hydrochloroic acid, Simulated gastric fluids , Simulated intestinal fluids .

Phosphate buffer solution, pH 7.8

For dissolution testing instrument used: Dissolution apparatus II i.e. paddle apparatus DL-0708-CURIO.

UV-Spectrophotometer: model UV-1800 240V, CAT NO. 206-25400-38, Serial no. A11454600909CA 220-240V, Approx 50-60Hz-Shimadzu corporation Kyoto Japan.

For hardness: Monsanto Hardness Tester, Model: VMT With Frequency 50 Hz, ARGHC2202

• For friability: Roche Friabilator FB-0607-CURIO. And Electro Lab

• A disintegration tester : With Frequency 50 Hz, ARGHC2202

• Analytical balance (ADAM AFP 110L,india).

For thickness : Carbon fiber composites digital caliper.

Photosability chamber: Mack Pharma tech 14D. [16]

METHODS

Dissolution tests

For any medicine meant to be taken orally to be systemically effective, there must be sufficient medication access to the bodily fluids. The rate at which mass moves from the product to the bulk of the solution is known as dissolutiorat[16].

Fig 2: Dissolution apparatus

For dissolution testing instrument used: Dissolution apparatus II i.e. paddle apparatus DL-0708-CURIO.

Preparation

For every example Following the weighing of 20 tablets, 0.1g of powder was added to a 200 ml volumetric flask. After adding 100 millilitres of mobile phase to the volumetric flask, the mixture was shaken mechanically for ten minutes. The final solution was volume-diluted using a water:methanol (3:1) mobile phase. A volumetric flask holding 250 ml was filled with five millilitres of aliquot, which was then diluted to volume using mobile phase. After that, the solution was filtered and tested.[17]

Determination of Hardness

Twenty pills were chosen at random from each brand to determine the hardness, and the hardness was measured using the hardness tester described above.[16]

Determination of Friability

Following a random selection of ten tablets from each brand, the tablets were de-dusted and weighed using an analytical balance. They were then subjected to 100 rotations of the Roche Friabilator. The de-dusting and friability were then calculated as follows:

$$\%\ friability = \frac{difference\ in\ weight}{total\ obtain\ weight} \times 100$$

Determination of Disintegration test

Using the above-mentioned disintegration device, six tablets, randomly selected from each brand, were placed in a 900-milliliter Beaker filled with water at 37°C to measure the disintegration time.

Determination of weight variation

Using the previously indicated analytical balance and average weight, twenty pills of each of the three paracetamol brands were individually weighed, and the % deviation was calculated for each brand.[16]

Determination of UV Spectrophotometer test

One of the methods used in pharmaceutical analysis the most commonly is UV-visible spectrophotometry. It includes calculating how much visible or ultraviolet light is absorbed by a substance that is in solution. If any recorded data is available, a spectrophotometer can be used in qualitative analysis to identify organic substances. Quantitative spectrophotometric analysis is used to determine the number of molecular species that are absorbing the radiation. The spectrophotometric method is easy to use, quick, reasonably specific, and suitable for small amounts of substances. The Beer-Lambert law is the underlying principle that underpins quantitative spectrophotometric analysis.

Prepration of 0.1M sodium hydroxide Take about 100 ml of distilled water in clean and dry 1000ml volumetric flask. Add about 4gm of sodium hydroxide with continues stirring. Makeup the volume at 1000ml with distilled water.

Procedure :

1. Weigh and powder 20 tablets.
2. Weigh accurately a quantity of the powder equivalent to about 0.15 g of Paracetamol.
3. Take clean 200ml volumetric flask and place clean funnel on it.
4. Transfer carefully weighed quantity of powder into funnel.
5. Add 50 ml of 0.1M sodium hydroxide into funnel so as to all powder gets transferred to volumetric flask.
6. Dilute the resulting mixture with 100 ml of distilled water and shake for 15 minutes.
7. Finally add sufficient quantity of water to produce 200ml.
8. Filture resulting solution from whatman filter.
9. Take 10 mL of filtrate and dilute to 100 mL with water.
10. Take 10 mL resulting solution in 100 mL volumetric flask and add 0.1M sodium hydroxide.
11. Adjust the volume of solution using distilled water and mix.
12. Measure the absorbance of the resulting solution at the maximum at about 257 nm.
13. Calculate the content of, $C_8H_9NO_2$ taking 715 as the value of A(1%, 1 cm) at the maximum at about 257 nm.[18]

Photostability testing

The reaction of a medication or drug product to exposure to solar, UV, and visible light while it is in the solid, semisolid, or liquid state and causes a physical or chemical change is known as photostability.

The way a medicine reacts to light can be explained by two main mechanisms: either it undergoes photolysis, which produces free radicals, or it undergoes photosensitization, which involves the transfer of energy between molecules. The end products of these reactions are the result of primary (photochemical) and secondary (chemical) reactions.[19]

RESULTS AND DISCUSSION

In the study of Pre and Post Compression Parameters of Paracetamol , we conducted study over a brand name as Dolo 650 which is manufactured and available in India ; and standard books and Procedures were being used for this work Specially IP and USP.

The selected brand of tablet is Dolo 650 which contains Paracetamol as a content.

Summary of the test results of dissolution

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-1: Dissolution before manufacturing

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-2: Dissolution after manufacturing

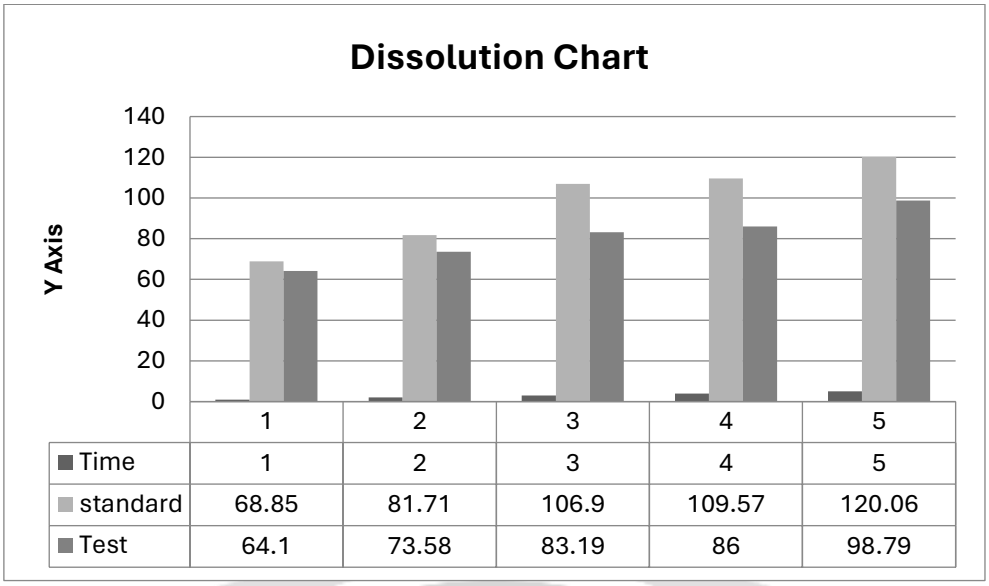

Chart-1: Dissolution before manufacturing and after manufacturing

Comparative study of all parameter using Photostability Chamber :

Parameters	Pre marketed	Post marketed
Hardness	4.2	4.0
Friability	0.48	0.36
Disintegration	0.45	1.00
Weight variation	0.8	0.4
Dissolution	106 (6min)	98.79 (6min)

Table- 3: Results for evaluation parameters of tablet.

Weight variation

For tablets weighing more than 325 mg, a weight variation test is performed to determine the relative fluctuations in the active ingredient and excipient.In this study, it was determined that no brand should stray from the average weight by more than 10%, and that no more than two tablets should differ from the average by more than 5%.

Every brand adheres to the BP guidelines, with not a single brand deviating by 5% from the average weight. Although weight variation is not a confirming test, it does provide a general idea of content consistency.

Hardness

The strength or resistance to endure mechanical shocks is known as hardness. Since hardness is not a recognised test, there isn't a compendial limit for hardness; however, a force of roughly 4 kg is thought to be the minimal required for satisfactory tablets. [20] Friability and disintegration are also influenced by hardness; that is, the less hard a tablet, the more friable it is and the faster it dissolves. With the exception of brand C, all the brands were determined to be good in terms of hardness.

Friability

The tablet's capacity to withstand coating, packaging, shipping, and other production operations is assessed by the friability test. As per BP guidelines, the overall reduction in weight must not surpass one percent. Furthermore, no tablet displays any kind of cracks or breaks.[21]

Disintegration

Since paracetamol pills in this study are conventional tablets and their disintegration time is less than 15 minutes, all of the brands used here meet the BP Specifications for the disintegration test. Disintegration and dissolution may be related, as is the drug's availability to the body (absorption) (FDA 2009), and lastly, the product's therapeutic efficacy.

Study type	Storage condition	Minimum time period covered
Long term	25°C +/- 2°C 60% RH +/- 5%	12 months
Intermediate	30°C +/- 2°C 65% RH +/- 5%	6 months
Accelerated	40°C +/- 2°C 75% RH +/- 5%	6 months

Table-4: Results for Photostability testing

Solution	Before exposure	After exposure	nm
1 ppm	0.0089	0.0063	254.0
	0.0056	0.0054	254.0
	0.0025	0.0039	254.0
2 ppm	0.0292	0.0105	254.0
	0.0274	0.0101	254.0
	0.0215	0.0104	254.0
3 ppm	0.0435	0.0352	254.0
	0.0421	0.0225	254.0
	0.0351	0.205	254.0

Table-5: Results for UV Spectrophotometer test

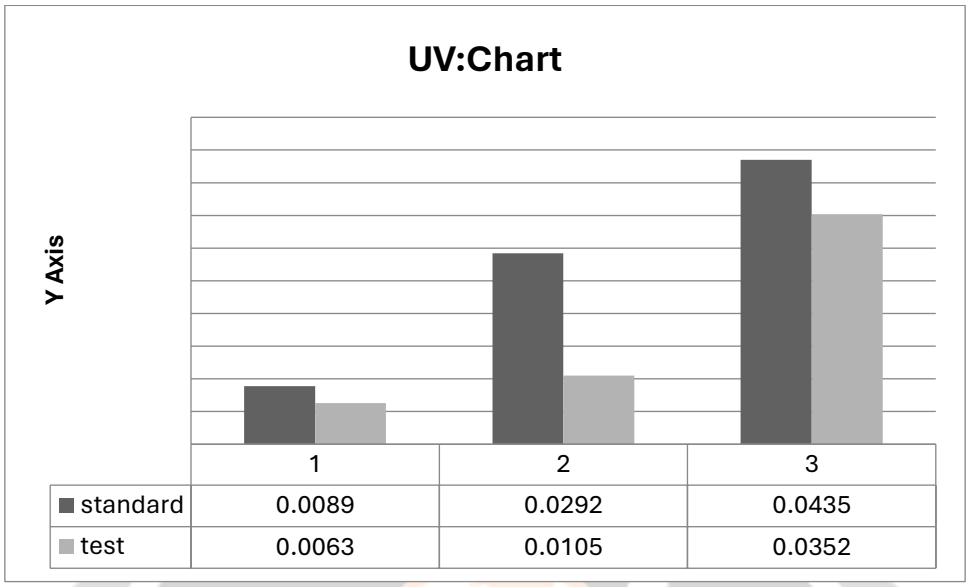

Chart-2: UV Spectrophotometer before manufacturing and after manufacturing

CONCLUSION

Paracetamol tablets were available, in different brands, in illegal markets located around the city All samples analyzed passed the weight variation And friability test. Some of the samples failed the Disintegration test while all samples were in Accordance to the standard set by the pharmacopeia For the dissolution test.Overall the quality evaluation results found in this Research are similar to the results observed from the Previous studies on quality evaluation studies of Paracetamol tablets obtained from legal drug Markets. Therefore the Pollen for the availability of paracetamol in the shops might not necessarily be from illegal drug outlets rather it may be sourced from the pharmacies, whole sales and other legal systems. Thus for the Drug regulatory authority to limit the presence of paracetamol in common shops, it might consider limiting the amount of paracetmol tablets to be dispensed to persons visiting pharmacies.

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