

Comparative Study on Commercially Available Samples Containing Paracetamol as API

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ABSTRACT

Antipyretics & Analgesics are widely used for the fever and different types of body aches. Paracetamol is one, which has antipyretic & analgesic properties. For the present study five brands of easily available samples from the market were compared for their physical and chemical properties and comparative study was made using various apparatus and instruments. To check the quality of paracetamol in different brand the sample were subjected to API test. A comparison was made between the claimed value of the different brand and the observed value. The comparative study results of various antipyretic analgesic samples are discussed in the paper.

Key-Words: Antipyretics & Analgesics, Paracetamol, Qualitative & Quantitative Analysis

INTRODUCTION

Antipyretics and Analgesics

An Antipyretic is a drug that is responsible for lowering the temperature of a feverish organism to normal but has no effect on normal temperature states. On the other hand, an analgesic may defined as agents that relieve pain by elevating the pain without disturbing consciousness or altering other sensory modalities [1]. It is widely recognized that analgesic-antipyretic drugs possess anti-inflammatory Properties [2]. A centre in the hypothalamus that ensures a balance between heat loss and production regulates normal body temperature. Fever occurs when there is a disturbance of this hypothalamic ' thermostat', which leads to the set-point of body temperature being raised. Once there has been a return to the normal set point, the temperature regulating mechanisms (dilatation of superficial blood vessels, sweating etc.) then operate to reduce temperature [3,4]. Most of the antipyretic drugs inhibit COX-2 expression to reduce the elevated body temperature by inhibiting PgE2 biosynthesis [5].

Analgesia is the inability to feel pain while still conscious. From the Greek an-, without + algesis, sense of pain [6].The main function of analgesics is to relieve decrease the sensation of pain. They act by increasing the threshold of pain, which may be defined as the lowest perceptible intensity of pain. The pain is induced by a stimulus and the amount of stimulus may be regarded as the measure of the threshold of pain. If more stimulus is required the threshold of pain increased and if less stimulus is required the threshold of pain is decreased. When analgesics are used the pain is not decreased but only the threshold of pain is increased. Therefore the patient does not feel the pain.[4]

Paracetamol

Paracetamol (acetaminophen, $C_8H_9O_2N$) is one of the most frequently prescribed anti-inflammatory, antipyretic, and analgesic drugs [8].It is a common analgesic & antipyretic drug that is used for the relief of fever, headache, & other minor aches & pains [6]. Its major ingredient is numerous cold & flu medications. The words ace amino Phenol & Paracetamol both come from the chemical name for the compound N-Acetyl Para- Amino phenol & Para acetyl amino phenol. Paracetamol has a characteristic of both antipyretic as well as analgesic [9]. Its effectiveness as an antipyretic agent has been attributed to its effect on the hypothalamic heat center, while its analgesic efficacy is due to its ability to raise the pain threshold [7].

MATERIAL AND METHODS

Easily available tablet samples in the market containing paracetamol as active pharma ingredient.

Description : White crystalline powder or white crystal.

Samples taken for the comparative study & analysis of Paracetamol

QUALITATIVE ANALYSIS OF DIFFERENT PARACETAMOL TABLET SAMPLE**1. Identification:**

- A.** 0.1 gm of sample was dissolved in 10ml of D.M. water to it 0.05ml of ferric chloride was added in test solution, a violet-blue color has appeared.
- B.** 0.1gm sample with 1ml of HCl for three minutes was added in 10ml of D.M. water, and cool; no ppt was produced . 0.05ml of 0.1N $K_2Cr_2O_7$ was added a Violet colour was slowly developed.[4]

2. pH :

The pH values conventionally represent the acidity or alkalinity of an aqueous solution. In the Pharmacopoeia, standards and limits of pH have been provided for those pharmacopoeia substances in which pH as a measure of the hydrogen ion activity is important from the standpoint of stability or physiological suitability. The determination is carried out at a temperature of 25°C, unless otherwise specified.

Procedure:

The pH value is determined in a suspension prepared by shaking 50 mg with 10 ml of *D.M.* water. In this suspension 2 drops of universal indicator was added the colour change of suspension was observed and by comparison with pH index of universal indicator was

S.No.	SAMPLE NAME	PARACETAMOL STRENGTH (in mg)
1	Antipyretic & Analgesic 1	500
2	Antipyretic & Analgesic 2	400
3	Antipyretic & Analgesic 3	500
4	Antipyretic & Analgesic 4	500
5	Antipyretic & Analgesic 5	500

observed.[4]

Range: The pH is Between 5.3 to 6.5

3. Melting Point

Instrument Used :- Melting Point Apparatus ,Capillary tubes

Melting range or temperature of a substance is defined as those points of temperature with in which, or the point at which, the substance begins to mentioned and is completely melted except as defined otherwise for certain substances. The following procedures are suitable for the various substances described in the Pharmacopoeia. Any other apparatus or method capable of the same accuracy may also be used. The accuracy should be checked frequently by using certified reference substances of declared melting point, such as those of the World Health Organization or other suitable substances, the reference substance selected being one that melts nearest to the melting range of the substance to be examined.

Procedure

The sample was crushed to a very fine powder and was Introduced into a capillary glass tube in sufficient quantity to form a compact column of 4 to 6 mm high. The bath was heated until the temperature was about 10⁰C below the expected melting temperature. The heating was continued and the temperature was noted at which the column of the sample collapsed against the side of the tube at any point, when melting may be considered to have begun as seen by the formation of a definite meniscus. [4]

Range;- Melts between 169^o and 172^o C

4. Heavy Metals Test

Preparation of std. solution

- 400 mg. of lead nitrate was dissolved in water which contained 2 ml of HNO₃ acid.than sufficient amount of water was added so 250 ml solution was produced.
- 1 vol. of this solution was added in 10 vol. of D.M. water.
- 1 vol. of solution (b) was added in 5 vol. of D.M. water.

Preparation of Test Solution

In 50 ml nessler cylinder 25 ml of 10% solution of paracetamol was added with 20 ml water and 5 ml dil. NaOH was also added to the solution.

Procedure

5 drops of sodium sulphide (10%) was added into cylinders containing standard and the test blank solution.The solutions in cylinders was allowed to stand for 5 min. The white colouration developed by the test solution indicate presence of heavy metals.[4]

Quantitative Analysis of Different Paracetamol Tablet Sample

1 Chemical Assay

Active matter (% of Paracetamol) in sample

Procedure

Accurately weighted 0.3 gms of sample was dissolved in a mixture of 10 ml of water & 50ml of 2N Sulphuric acid. The sample was boiled under reflux condenser for 1hour cooled and diluted to 100ml with water. To 20 ml of solution 40 ml of water in the form of ice was added .15 ml of 2N hydrochloric acid and 0.1 ml of ferroin solution was added and the solution was titrated with 0.1N ceric ammonium sulphate until a yellow colour appeared. A blank determination was also performed to make necessary correction. Each ml of 0.1 M ceric ammonium sulphate is equivalent to 0.00756 g of $C_8H_9NO_2$. [4]

Limit: Not less than 95% & not more than 105%

Preparation of solution:-

(1) 0.1N Standard Solution Of Ceric Ammonium Sulphate

65 g CAS was dissolved in 30 ml H_2SO_4 and 500ml of water was added into it and boiled then the solution was cooled and made it up to 1000ml.

2n Sulphuric Acid Solution

55.0 ml of conc. H_2SO_4 was added into 1-liter volumetric flask and made it up to the mark.

(2) 2n Hydro Chloric Acid

181 ml of 11N HCl was added into 1000 ml by D.M. water.

Calculation

$$\% \text{ of paracetamol} = \frac{F \times x}{y} \times 100$$

1. Amount of CAS consumed by unknown sample = x ml
2. Wt. of sample taken = y gm
3. Factor = F (0.00756g)

2. Loss On Drying

Instrument Used: - Hot Air Oven, L.O.D. Bottles

Loss on drying is the loss in weight in % w/w resulting from water and volatile matter of any kind that can be driven off under specified conditions. The test is carried out on a well-mixed sample of the substance. If the substance is in the form of large crystals, the size is reduced by rapid crushing to powder form.

Range: - Not more than 0.5%, determined on 1 g by drying in an oven at 105⁰C for 3 hours.

Procedure

A glass-Stoppered bottle of ml was dried and weighed , To the preweighed bottle approx 1 gm of sample was transferred and weighted . The sample was evenly distributed as practicable by gentle sidewise shaking to a depth not exceeding 10mm. The loaded bottle was placed in the drying chamber (oven or desiccators), the bottle was left in the chamber with stopper off. The sample was dried to constant weight or for the specified time 3 hours at specified temperature of 105⁰C. After drying is completed, the drying chamber was opened and the bottle was closed promptly and allowed to cool at room temperature (where applicable) in a desiccators before weighing. The bottle and the contents was weighed.[4]

Calculation

$$\text{L.O.D. \% W/W} = \frac{[W_2 - W_3]}{[W_2 - W_1]} \times 100$$

Wt. Of empty crucible = W1 gm

Wt. Of crucible + Sample (Before Drying) = W2 gm

Wt. Of crucible + Sample (After Drying) = W3 gm

3. Sulphated Ash Test

Procedure

Silica crucible was heated to redness for 10 minutes and allowed to cool in a desiccator and weighed. 1 g of sample was transferred to the crucible. The sample was ignited gently at first, until the substance is thoroughly charred. The residue was cooled and moistened with 1 ml of sulphuric acid, and heated gently until the white fumes no longer evolved. The residue was ignited at 800± 25⁰C until all black particles have disappeared. The ignition was conducted in a place protected from air currents and the crucible was allowed to cool. A few drops of sulphuric acid was added and the residue was heated. The residue was ignited as before, allowed to cool and weighed. The operation was repeated until two successive weightings do not differ by more than 0.5 mg.[4]

Reference Standards the Sulphated ash not more than 0.1%.

Calculation

$$\text{Sulphated Ash\% W/W} = \frac{[W_3 - W_1]}{[W_2 - W_1]} \times 100$$

Wt. Of empty Crucible = W₁ gm

Wt. Of crucible + Sample (Before ignition) = W₂ gm

Wt. Of crucible + Sample (After ignition) = W₃ gm

RESULTS & DISCUSSION

The present investigation on different samples which contain paracetamol was carried out to check the qualitative and quantitative analysis. The comparative results for qualitative analysis were shown in table 1. Comparative results demonstrated that all sample contain paracetamol as API. The results obtained after pH shows that samples are slightly acidic in nature and pH values of antipyretics and analgesic 2 and antipyretics and analgesic 4 is slightly above than expected value. M.P. and heavy metal test were also carried out and it is clearly shown by the results that melting point of the all samples were under range and they contain heavy metals which is also lesser than 10ppm.

The results of quantitative analysis are shown in Table 2. After the complete analysis of samples a comparison were made between percent values of chemical assay of different samples with each other and also with standard values which indicates that all these values are approximately similar. sulphated ash and loss on drying were also carried out in quantitative analysis to which sulphated ash was under ranged and LOD approximately similar, but it was observed that LOD of antipyretics analgesics 3 and antipyretics analgesics 4 were slightly above than limit value.

CONCLUSION

Qualitative and quantitative analysis were carried out to study the different samples of commercially available drug containing paracetamol as their active pharma ingredient. We concluded from the analysis of parameters studied that the total amount of API ,which present in the testing sample has sufficient quantity and amount is approximately similar to the company's recommended or claimed value.

S.No.	Sample Name	Identificatio	pH (5.3-6.5)	M.P. (169-172° C)	Heavy Metals Test (NMT 10 ppm)	
1.	Antipyretic & Analgesic 1	Identified	6.5	169° C	Positive	Pass
2.	Antipyretic & Analgesic 2	Identified	7.5	167° C	Positive	Pass
3.	Antipyretic & Analgesic 3	Identified	6.0	170° C	Positive	Pass
4.	Antipyretic & Analgesic 4	Identified	7.0	168° C	Positive	Pass

5.	Antipyretic & Analgesic 5	Identified	6.5	169° C	Positive	Pass
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Table:1 Comparative result chart for Qualitative analysis of different Paracetamol sample

S.No	SAMPLE NAME	Chemical assay (%) (Limit: 95-105% of label claimed)	Sulphated ash (%) (NMT 0.1%)	Loss on drying (%) (NMT 0.5%)
1	Antipyretic & Analgesic 1	95.50	0.107	0.33
2	Antipyretic & Analgesic 2	96.26	0.09	0.31
3	Antipyretic & Analgesic 3	99.79	0.089	0.98
4	Antipyretic & Analgesic 4	98.08	0.11	0.68
5	Antipyretic & Analgesic 5	60.98	0.06	0.58

Table : 2 Comparative result chart for Quantitative analysis of different Paracetamol sample**References:**

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