COMPARATIVE *IN VITRO* DISSOLUTION ASSESSMENT OF SOME COMMERCIALLY AVAILABLE PARACETAMOL TABLETS

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ABSTRACT

Various commercially available paracetamol tablets (500 mg) were evaluated comparatively for *in vitro* dissolution qualities along with drug content (assay). The assay results ascertain the presence and compendial quality of paracetamol in all these products. The *in vitro* dissolution profiles were found to be varying for each tablet, but within the prescribed limit. The dissolution at 15 minutes ($t_{15\ min}$, %) and 50 % of dissolution ($D_{50\ \%}$, min) were also determined. The paracetamol tablet, C exhibited highest dissolution (%) in 15 minutes (80.85 ± 1.84 %) and lowest value of 50 % dissolution (3.75 ± 0.18 min) along with comparatively highest drug content (99.78 ± 0.49). Statistical assessment of various *in vitro* dissolution parameters and assay results was also conducted to establish if there were any significant difference among them.

Keywords: Paracetamol tablets; Assay; Dissolution; *In vitro*.

Paracetamol is a non-steroidal anti-inflammatory drug (NSAID) and is prescribed most frequently. It is also commonly used as analgesic and antipyretic agent in the relief of fever, headaches, other minor aches and pains. Chemically, it is 4-hydroxy acetanilide (acetaminophen).[1] paracetamol is generally safe for human use at recommended doses. But, overdoses of paracetamol can cause potentially fatal liver damage and in rare individuals, a normal dose can do the same.[2]

The safety and efficacy of a pharmaceutical dosage form can be guaranteed when its quality is reliable.[3] The efficacy of pharmaceutical dosage forms generally depends on their formulation properties, and manufacturing methods, hence it is likely that the quality of dosage form may vary.[4-5] Dissolution test is one of the *in vitro* tests usually employed to assess the quality of oral pharmaceutical solid dosage forms such as tablets and capsules. *In vitro* dissolution tests can be used to guide formulation developments, identify critical manufacturing variables, monitor formulation quality from batch to batch, predict the *in vivo* performances and also serve as a surrogate for bioavailability and bioequivalence.[6-7] Therefore, it was decided to carry out the comparative evaluation of *in vitro* dissolution qualities of various commercially available paracetamol tablet samples. Paracetamol tablets of 500 mg were chosen for the study. Statistical assessment of various *in vitro* dissolution parameters was conducted to establish if there were any significant differences among them.

Paracetamol IP was obtained from Techno Remedies, Kolkata. The paracetamol tablets (500 mg) were purchased from local market and coded as A, B, C and D (Table 1). All commercial tablets were of same manufacturing year, and were recently manufactured.

Paracetamol tablets were weighed individually and powdered. Powdered paracetamol tablet materials equivalent to 0.15 gm of paracetamol was taken with 50 ml of 0.1 M NaOH in 250 ml volumetric flask and the volume was made with water. The flask is well shaken and the solution was filtered. 10 ml of filtrate was diluted to

100 ml by water. To 100 ml of the resulting solution, 10 ml of 0.1 M NaOH was added diluted to 50 ml with water and mixed thoroughly by shaking. The absorbance of the resulting solution was measured using a UV-VIS spectrophotometer (U. V. 2440 Double beam spectrophotometer, SHIMADZU Corporation, JAPAN) against a blank at 257 nm.[1]

In-vitro dissolution studies were carried out using a dissolution apparatus USP (Paddle type) at a paddle speed of 50 rpm. The dissolution medium was 900 ml of phosphate buffer, pH 7.8, which was maintained at 37 ± 0.5 °C.[8] In all dissolution experiments, 5 ml of dissolution samples were withdrawn and replaced with equal volume fresh phosphate buffer, pH 7.8 at regular intervals. Collected dissolution samples were used for determination of released paracetamol concentrations by using a UV-VIS spectrophotometer (U.V. 2440 Double beam spectrophotometer, SHIMADZU Corporation, JAPAN) at 249 nm wavelength against a blank.

The assay of paracetamol content in different paracetamol tablets, dissolution profiles at 15 minutes ($t_{15\ min}$, %) and 50 % of dissolution ($D_{50\ \%}$, min) were analyzed for significant differences by one-way analysis of variance (ANOVA) using a Student-Newman-Keuls test for all pair wise comparisons in this study. The statistical analysis was conducted using MedCalc software version 9.6.4.0.

All these paracetamol tablets contained paracetamol within 100 ± 10 % of the labeled claim. The USP[9] and IP[8] specifications for assay are that the Paracetamol content should be less than 90 % and not more than 110 % (Table 2). Therefore, the assay results ascertain the presence and compendial quality of paracetamol in all these products. But, the paracetamol content in paracetamol tablet, D is significantly less ($p < 0.05$) compared with paracetamol tablet, B and C. Whereas, the paracetamol content in paracetamol tablet, A possessed no significant difference ($p < 0.05$) in the assay results when compared with all other paracetamol tablets.

Table 1: Manufacturing date and expiry date of various paracetamol tablets used in the study.

Tablet code	Manufacturing date	Expiry date
A	July, 2009	June, 2012
B	April, 2009	March, 2012
C	October, 2009	September, 2012
D	June, 2009	May, 2011

Table 2: Assay results of paracetamol tablets.

Paracetamol Tablets	Assay (%)
A	98.76 ± 0.28*
B	99.67 ± 1.14
C	99.78 ± 0.49
D	97.47 ± 0.85¥

¥ Paracetamol content in paracetamol tablet, D was significantly less ($p < 0.05$) when compared with paracetamol tablet, B and C.

* Paracetamol content in paracetamol tablet, A possessed no significant difference ($p < 0.05$) in the assay results when compared with all paracetamol tablets.

Statistically significance ($p < 0.05$) compared with all paracetamol tablets determined by one-way ANOVA followed by using Student-Newman-Keuls test for all pair wise comparisons.

Table 3: Dissolution at 15 minutes ($t_{15\ min}$, %) and 50 % of dissolution ($D_{50\ \%}$, min) of paracetamol tablets.

Paracetamol tablets	$t_{15\ min}$ (%)	$D_{50\ \%}$ (min)
A	71.34 ± 2.03	4.02 ± 0.23
B	76.15 ± 0.31*	3.77 ± 0.03
C	80.85 ± 1.84¥	3.75 ± 0.18
D	71.23 ± 1.27	3.93 ± 0.20

* & ¥ The $t_{15\ min}$ values of paracetamol tablet, B and C were significantly different ($p < 0.05$) when compared with all other paracetamol tablets.

Statistically significance ($p < 0.05$) compared with all paracetamol tablets determined by one-way ANOVA followed by using Student-Newman-Keuls test for all pair wise comparisons.
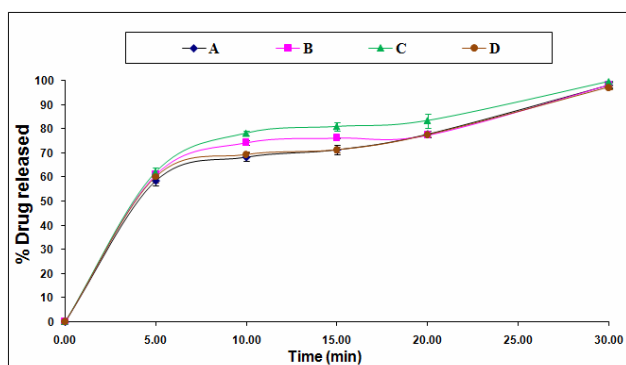
Figure 1: Comparative *in vitro* dissolution profiles of paracetamol tablets

Dissolution studies can give an idea of the amount of drug available absorption after oral administration. Drugs with poor dissolution profiles will not be available in the body system or target organ/tissues to elicit therapeutic effect.

The comparative *in vitro* dissolution profiles of various commercially available paracetamol tablets are shown in Figure 1. The *in vitro* dissolution profiles were found to be varying for each tablet, but within the prescribed limit. The dissolution at 15 minutes ($t_{15\ min}$, %) and 50 % of dissolution ($D_{50\ \%}$, min) were also determined (Table 3). The $t_{15\ min}$ values of paracetamol tablet, B and C were significantly different ($p < 0.05$) when compared with all other paracetamol tablets. But, there was no significant difference ($p < 0.05$) in the $D_{50\ \%}$ values of all these paracetamol tablets when compared with each other.

The paracetamol tablet, C exhibited highest dissolution (%) in 15 minutes (80.85 ± 1.84 %) and lowest value of 50 % dissolution (3.75 ± 0.18 min) along with comparatively highest drug content (99.78 ± 0.49). Therefore, the *in vitro* dissolution performance of paracetamol tablet, C was comparatively better than other paracetamol tablets used in this investigation.

REFERENCES

1. The Indian Pharmacopoeia, Government of India, Ministry of health and family welfare, Controller of publication, New Delhi, Volume I, 1996, 556.

2. Daly FF, Fountain JS, Murray L, Grandins A, Buckley NA, Guidelines for the management of paracetamol poisoning in Australia and New Zealand – explanation and elaboration. A consensus statement from clinical toxicologists consulting to the Australian poisons information centers, Med J Australia, 2008, 188(5), 296-301.

3. Chowdary KPR, Krishna Murty T, Quality evaluation of market sample of diclofenac SR products, The Eastern pharmacist, 2001, April, 111-113.

4. The Pharmaceutical Codex, Principle and practice of pharmaceutics, 12th edition, Pharmaceutical Press, London, 1994, 987-992.

5. Yogananda R, Nagaraja TS, Snehalatha, Jayadevaiah KV, Vijay Kumar MMJ, Comparative *in vitro* equivalence studies of designed, branded and generic tablets of ciprofloxacin-250, Int J Pharm Sci, 2009, 1(1), 28-34.

6. Olaniyi AA, Babilola CP, Oladende FO, Adegoke AO, Towards better quality assurance of drugs. In: Biopharmaceutical Methods in Drug Quality Assurance, Olaniyi AA, editors, University of Ibadan Press, Ibadan, 2001, 7-23.

7. Bamigbola EA, Ibrahim MA, Attama AA, Comparative *in-vitro* assessment of soluble and plain brands of aspirin tablets marketed in Nigeria, Sci Res Essays, 2009, 11(4), 1412-1414.

8. The Indian Pharmacopoeia, Government of India, Ministry of health and family welfare, Controller of publication, New Delhi, Volume II, 1996, A80-A84.

9. US Pharmacopoeia National Formulary, USP 23/NF 18, United States Pharmacopoeial Convention. Inc., Rockville, MD, 1995.

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