

Journal of Coastal Life Medicine

journal homepage: www.jclmm.com



Original article doi: 10.12980/jclm.4.2016J6-109

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Comparative *in-vitro* analysis of different brands of paracetamol tablets available in NepalGanesh Man Singh Thakuri^{1*}, Kailash Kumar Yadav², Rahul Rana Chhetri³¹Department of Pharmaceutical Chemistry, Doon (PG) Paramedical College and Hospital Dehradun, Hemavati Nandan Bahuguna Garhwal University, Pauri Garhwal, Uttarakhand, India²Department of Microbiology, Tribhuvan University, Kathmandu, Nepal³Department of Pharmacy, Pokhara University, Pokhara, Kaski, Nepal

ARTICLE INFO

Article history:

Received 20 Jun 2016

Received in revised form 7 Jul 2016

Accepted 20 Jul 2016

Available online 4 Aug 2016

Keywords:

Acetaminophen

Comparative study

In-vitro analysis

Paracetamol

Physico-chemical test

Quality control parameters

ABSTRACT

Objective: To examine the physico-chemical parameters of commercially available local and multinational brands of paracetamol tablets in Nepal.**Methods:** Different five paracetamol brands were explored by testing various parameters according to standard methods. The studied parameters included weight variation, friability, disintegration, dissolution and assay. The limits of the official test were referenced from official guidelines of Indian Pharmacopoeia (IP) and British Pharmacopoeia (BP). All brands were tested according to their pharmacopoeial claim and methods for these tests were successfully conducted to find out their qualities. Those methods were economic and authentic.**Results:** Requirements of weight variation and friability value were complied by all brands. Fifteen minutes of disintegration time were also complied by all the brands according to the BP/IP recommendation for uncoated tablets. All brands showed not less than 80% drug release in 45 min as per BP and not less than 85% in 30 min as per IP. Content of each brand was found to be within the range of 95%–105%. The present findings suggested that about every paracetamol brand which was accessible in Nepali market encountering the IP/BP requirements.**Conclusions:** Although the physico-chemical examinations such as weight variation, friability, disintegration, dissolution and assay were detected varying brand wise, but were found interior to defined limits. Being an over-the-counter drug, the consumption of paracetamol is too high. Therefore, it is important for each brand to be genuine, good manufactured and well marketed. So, additional exploration over the quality of paracetamol is compulsory for safe human consumption.

1. Introduction

Paracetamol or acetaminophen is a common analgesic and antipyretic drug used for the solace of fever, headaches and other minor aches[1]. It is a highly recommended medicine for several types of flu, cold and body pains. It is very applicable and secure drug for living being in adequate quantity but deliberate or accidental overdose is often observed due to its wide availability[2]. It is also a commonly used analgesic compound combined with centrally acting compounds such as caffeine, codeine and dextropropoxyphene as well as with oral decongestants in a variety of formulations for the relief of the symptoms of common cold, influenza and

sinusitis[3]. Besides headaches, minor aches and pains, it is also used in combination with opioids analgesics to control severe pains such as episiotomy pain, post-surgical pain and cancer pain[4]. It is considered that both names acetaminophen and paracetamol were derived from their chemical names N-acetyl-para-aminophenol and para-acetyl-aminophenol, respectively. Paracetamol is now globally accepted antipyretic and analgesic[5]. Paracetamol is a drug that comes under the category of aniline analgesic derived from coal tar. Paracetamol is a metabolite product of phenacetin. Being highly effective analgesic and antipyretic with less adverse effect and non carcinogenic at recommended dose, paracetamol has been replacing the phenacetin and its combination[6]. Even though paracetamol is said to be a safe drug, its overdose leads to liver toxicity and renal failure. Some researches suggest that paracetamol may alter the lipid profile by increasing the triglycerides and total cholesterol and decreasing high-density lipoprotein[7]. Several researches are being conducted to correlate the paracetamol with cancer. There are some attestations which infer that paracetamol may help to cause the

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The journal implements double-blind peer review practiced by specially invited international editorial board members.

urinary tract cancer but defend ovarian cancer[8].

Nepal is a developing country, especially in the pharmaceutical industry. Here, different local and multinational brands of drugs are available including paracetamol. Paracetamol tablets are widely used as analgesic and antipyretic drugs all over the world, especially in the developing countries like Nepal, India, Bhutan, Bangladesh, Pakistan and so on. In these countries, paracetamol tablets are frequently used to remove fever, aches and pains. In short, doctors in those places prescribe paracetamol for the treatment of fever and pain to others and also use it blindly by themselves. Nepal is one of them.

As we know that paracetamol is an over-the-counter drug easily available in market and the effect of such drugs is directly related to the public health[9]. That is the reason why every brand available in market should be genuine, good manufactured and well marketed. It is necessary that every available brand should pass its quality control and the parameters should range within the limits.

The effects of any pharmaceutical products are kindred on property of the dosage form. The quality of the same product may also vary brand wise depending on their formulation and manufacturing methods. To assure the safeness and efficaciousness of any dosage units, valuation tests are very necessary whether *in-vivo* or *in-vitro*. The *in-vitro* evaluations, which are easier and more economic, are normally used to assess the quality of dosage forms and vaticinate the *in-vivo* efficiency and it is also important for bioavailability and bioequivalence[10].

Hence, we have conducted this relative research work on paracetamol tablets of 500 mg obtained easily in Nepali markets for their quality assess. At a glance, the aim of this study was to investigate the physico-chemical parameters of five commercially available brands of paracetamol tablets in Nepal.

2. Materials and methods

According to the availability and consumption rate of commercial paracetamol tablets, five different brands of paracetamol tablets were collected randomly from pharmacies of Kathmandu, Nepal during the time of March–June 2015 and 500 mg of the five brand were named Np-1, Np-2, Np-3, Np-4 and Np-5. Among them, some were local brands and some were multinational. Tests of the parameters were conducted using the analytical reagents, potassium dihydrogen phosphate, sodium hydroxide and water.

Analytical glass wares included beaker, glass rod, dropper, volumetric flask, measuring cylinder and instruments, pH meter, weighing machine, friabilator, sonicator, disintegration tester, thermometer, dissolution apparatus and UV spectrophotometer.

2.1. Weight variation

Weight variation is the test which guesstimates the efficacy and persistency of dosage units during manufacturing and it is suggested that any deviation in the weight variation may affect the active ingredient of the product.

The average weight and weight variation of tablets were tested to adjudge whether each tablet was within the limit or not. The average weight was obtained after the total weight of the 20 tablets taken in

a tare weighing machine was divided by 20. Based on the average weight obtained, the individual tablet was measured whether each tablet was within the limit of percentage difference or not.

According to official guidelines, percentage difference of $\pm 10\%$ was taken for tablets of 80 mg or less, $\pm 7.5\%$ for tablets of 80–250 mg and $\pm 5\%$ for tablets above 250 mg. The product complied with the limit test, and there were not more than two tablets of the 20 tablets that were exterior to the official percentage limit and none of the tablets varied the official percentage limit by twice[11].

2.2. Friability

Friability is the test which is used to evaluate the competency of the tablets to withstand abrasion in packing, handling and transporting.

To conduct friability test, tablets equivalent to 6.5 gm were taken for weighing making sure that tablets were free from dusts and foreign particles. After taking the initial weight of tablets, they were placed in a friabilator for testing. According to the standard methods, the friabilator was rotated for a hundred times, *i.e.* 25 r/min. During the revolution, tablets fall from the distance of six inches each time. After the completion of 100 rotation, tablets were collected, dusted and reweighed. Now the difference of weights between the initial and final was the loss of tablets[11]. It was calculated in percentage by the following formula:

$$\text{Lose (\%)} = \frac{\text{Total initial weight} - \text{Total final weight}}{\text{Total initial weight}} \times 100$$

2.3. Disintegration

Disintegration suggests the effect of liquids on the tablets by breaking the internal bonds. However, there is no exact correlation between the disintegration and dissolution. It is inferred that the lower the disintegration time of tablets is, the higher the dissolution rate will be and vice versa. Simply, it gives the pre-idea regarding the bioavailability of dosages units. So, it is essential to break down of the tablets within the specified limits of 15 min for uncoated tablets and 30 min for most of the coated tablets[12].

The time of disintegration of six random tablets of each sample brand was resolved at $(37 \pm 2)^\circ\text{C}$ in 750 mL distilled water running disintegration apparatus in 30 r/min, according to Indian Pharmacopoeia (IP) specifications. Six tablets were randomly taken from each brand and put into the cylinders of the disintegration baskets with disc. The time for disintegration was reported when there was no any trace or pulp of tablets found in the mesh of the basket.

2.4. Dissolution

Dissolution is the method which is used to measure the rate of drug release from solid dosage forms. It also gives the knowledge of bioavailability of drugs by correlating the drug dissolving pattern in gastrointestinal track before reaching the systemic circulation.

According to IP, phosphate buffer with pH of 5.8 was used as the first dissolution medium. The apparatus was set with 900 mL

of buffer at $(37 \pm 0.5)^\circ\text{C}$ for 30 min at the speed of 50 r/min using paddle (apparatus 1). Second dilution was maintained with the same buffer solution and absorbance was reported at the wavelength of 243 nm in UV spectrophotometer[13].

According to British pharmacopeia (BP), phosphate buffer with pH of 5.8 was used as first dissolution medium at $(37 \pm 0.5)^\circ\text{C}$. The apparatus was set with 900 mL of buffer for 45 min at the speed of 50 r/min using paddle (apparatus 2). After the completion of running time, the second dilution was maintained with the 0.1 mol/L of sodium hydroxide to get the required concentration of sample solution and absorbance was reported at a wavelength of 257 nm in UV spectrophotometer[14].

During the test, buffer pH and volume were carefully noted. Besides these, the bath temperature, commanded revolutions per minute and sink of tablets were also important factors which could alter the test readings. Finally, the percentage of dissolved active ingredient of dosage units in the dissolution medium was calculated by the following formulas:

Calculation for dissolution percentage on as such basis was given:

$$\text{Dissolution} = \frac{\text{Absorbance of test sample}}{\text{Absorbance of standard sample}} \times \frac{\text{Standard dilution}}{\text{Test dilution}} \times \frac{\text{Potency of standard}}{100} \times 100$$

Calculation for dissolution percentage on dry basis is given:

$$\text{Dissolution} = \frac{\text{Absorbance of test sample}}{\text{Absorbance of standard sample}} \times \frac{\text{Standard dilution}}{\text{Test dilution}} \times \frac{\text{Potency of standard}}{100} \times \frac{100 - \text{water}}{100} \times 100$$

2.5. Assay

To quantitatively measure the presence or amount or the functional activity of a target entity, it is very essential to set a unbiased concentration of active pharmaceutical ingredient in each batch of medicament to their label claim. Twenty tablets were randomly taken and made into very fine powder with the help of pestle and mortar, and the weight of powder was equivalent to the standard one. Weights of the standard and samples were taken by considering the concentration of the final solution for UV spectrophotometer.

Weight powder was diluted with 0.1 mol/L of sodium hydroxide solutions and absorbance was measured in UV with the wavelength of 257 nm and the amount of paracetamol was calculated in mg.

Assay was calculated on as such basis:

$$\text{Assay} = \frac{\text{Absorbance of test sample}}{\text{Absorbance of standard sample}} \times \frac{\text{Standard dilution}}{\text{Test dilution}} \times \frac{\text{Potency of standard}}{100} \times \text{Average weight}$$

Assay was calculated on dry basis:

$$\text{Assay} = \frac{\text{Absorbance of test sample}}{\text{Absorbance of standard sample}} \times \frac{\text{Standard dilution}}{\text{Test dilution}} \times \frac{\text{Potency of standard}}{100} \times \frac{100 - \text{water}}{100} \times \text{Average weight}$$

3. Results

3.1. Weight variation

According to the BP and IP specifications, it was determined that all the tablets of each brand passed the test of weight variation with not more than $\pm 5\%$ deviation for tablets above 250 mg (Table 1).

Table 1

Observation for weight variation of different brands. (mg).

No.	Brand	Average weight	Upper limit	Lower limit
1	Np-1	595.915	612.800	583.800
2	Np-2	570.000	589.300	548.100
3	Np-3	595.625	620.900	572.700
4	Np-4	571.055	581.000	564.600
5	Np-5	576.490	583.300	568.400

3.2. Friability

In the official guidelines, it was noted that the percentage of weight loss must be not more than one percent and the brands of paracetamol tablets which were selected for our research work were found to be within the specified limits (Table 2).

Table 2

Observation for friability of different brands.

No.	Brand	Result (%)	IP/BP specification	Deviation from official limit
1	Np-1	0.41	Not more than 1%	Pass
2	Np-2	0.70		Pass
3	Np-3	0.34		Pass
4	Np-4	0.31		Pass
5	Np-5	0.33		Pass

From the above data, it was clear that brand Np-2 had the maximum friability result (0.70%), while brand Np-4 had the minimum (0.31%).

3.3. Disintegration time

As we discussed previously, it was the time when there was no any debris of tablets remaining on the mesh of the disintegration basket excluding some coated tablets which were insoluble in the used medium. It was found that every brand selected for the test passed the disintegration time evaluation that ranged within the pharmacopoeial specification (Table 3).

Table 3

Observation for disintegration time (min) of different brands.

No.	Brand	Result	IP/BP specification	Deviation from official limit
1	Np-1	9	Not more than 15 min	Pass
2	Np-2	1		Pass
3	Np-3	2		Pass
4	Np-4	10		Pass
5	Np-5	7		Pass

From the above data, brand Np-4 had the maximum disintegration time (10 min) while brand Np-2 had the minimum (1 min).

3.4. Dissolution

According to the standard limits of IP ($> 85\%$ in 30 min) and BP ($> 80\%$ in 45 min), all five brands complied with the dissolution rate test (Table 4).

Table 4

Observation for dissolution rate (%) of different brands.

No.	Brands	Minimum dissolution	Maximum dissolution	IP/BP specification	Deviation from official limit
1	Np-1	95.75	103.86	> 80	Pass
2	Np-2	97.11	105.38	> 80	Pass
3	Np-3	91.05	96.82	> 85	Pass
4	Np-4	96.29	103.60	> 85	Pass
5	Np-5	98.65	101.71	> 80	Pass

The maximum and minimum of dissolution of the five different paracetamol brands were evaluated in the above table where brand Np-2 had the maximum dissolution and brand Np-3 had the minimum dissolution but all brands were within the specified limit.

3.5. Assay

All brands which were evaluated for their amount of active ingredient passed the IP and BP specifications living within the limit of $(100 \pm 5)\%$ of labeled claim. Every selected brand was of 500 mg which meant the net content of paracetamol was found between 475.000 and 525.000 mg.

Table 5 shows that the brand Np-1 had the maximum content (493.995 mg/tablet), while brand Np-3 had the minimum (479.255 mg/tablet), but all of them were within the limit.

Table 5

Observation for content (mg/tablet) of different brands.

No.	Brands	Result	IP/BP specification	Deviation from official limit
1	Np-1	493.995		Pass
2	Np-2	493.000		Pass
3	Np-3	479.255	475.000–525.000	Pass
4	Np-4	485.705		Pass
5	Np-5	491.600		Pass

4. Discussion

The aim of this research was to examine the physico-chemical parameters of commercially available local and multinational brands of paracetamol tablets in Nepal. Five different brands which were easily and abundantly accessible in Nepali markets were assessed regarding their quality standards. All paracetamol tablet brands of 500 mg (uncoated) were estimated for their physical and chemical parameters comparatively. *In-vitro* examination like weight variation, friability, disintegration, dissolution and assay were performed.

All the paracetamol tablets of five brands were found not deviated by $\pm 5\%$ of the average tablet weight according to IP/BP specification. Even though brand Np-2 had greater friability than other four brands but testing results of all brands came under the specified limit, *i.e.* not more than 1%. According to pharmacopoeias, uncoated tablet should not cross 15 min duration during disintegration process and brand Np-2 took less time to disintegrate, *i.e.* 1 min, whereas brand Np-4 took more time, *i.e.* 10 min, as compared to other brands. The dissolved amount of all IP claimed brands were found not less than 85% of the labeled amount in 30 min and the dissolved amount of all BP claimed brands were found not less than 80% of the labeled amount in 45 min. The contents of all brands were found between the limit of 95%–105% of their labeled claim.

This study assured that all studied brands of paracetamol tablets which were available in Nepali markets were of good quality. Although the physico-chemical examinations such as weight variation, friability, disintegration, dissolution and assay were detected from varying brand wise, they were interior to the defined limits. Additional exploration over the quality of paracetamol is compulsory because it is an over-the-counter drug and the consumption of it is too high. Therefore, it is mandatory that each

brand should be genuine, good manufactured and well marketed for safe human consumption.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

We gratefully acknowledge Zest Laboratories Pvt. Ltd. for supporting this study and providing the laboratory to carry out this research work and we are also particularly grateful to all the staff members of Zest for their hospitality during the time of work.

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