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ASSESSMENT OF EFFECT OF FOOD ON DISSOLUTION PROFILE OF PARACETAMOL TABLET BY IN-VITRO METHOD

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ABSTRACT

Delivering the drugs by oral route is considered to be one of the most favored route of drug administration. People often consume oral solids, especially OTC drugs, at any time before or after breakfast with water or any other available hot or cold beverages. Crocin is one of the popular OTC brands of paracetamol, which is preferred in large number. Patient consumes this OTC tablet any time before or after meal or breakfast. However, breakfast interact with paracetamol, affecting the release of drug. Taking this into consideration, current study was planned to assess the effect of some most common Indian breakfasts on release of paracetamol (crocin tablet) tablet using USP type II dissolution apparatus. Dissolution media used was modified phosphate buffer (with pH 5.8), which was further added with breakfast and was analyzed by UV spectrophotometrically. Dissolution profile revealed the maximum drug release 97.03 ± 1.29 % in plain water was while minimum with dosa 28.87 ± 2.00 %. In conclusion, Paracetamol should be taken with water and should be taken after sufficient time interval of breakfast.

Keywords: Breakfast, crocin, paracetamol, tablet, dissolution

INTRODUCTION

Oral solid dosage types, such as tablets and hard-gelatin capsules, have been around since the nineteenth century and are still the most common today. Friability and hardness tests are used to determine whether a tablet can endure the pressures of subsequent packaging operations and reach to patient in a usable state. During the research and development stage, disintegration and dissolution of a tablet dosage type is studied in either water or simulated gastric medium, with simulated intestinal medium being used occasionally. Over-the-counter medications, such as tablets or pills, are commonly taken along with water. However, these drug types are often taken with other beverages to help with swallowing or to mask the taste of pharmaceuticals **[1]**. It is also being taken before or after breakfast/ meal. In India the breakfast varies a lot and some of the popular breakfast are **Upma**: It's a thick porridge made from coarse rice flour that's common in South India and Maharashtra for breakfast. Depending on personal preferences, various seasonings and/or vegetables are frequently added during the cooking process. Semolina (Rava), cooking oil, mustard seeds, cumin, asafoetida, curry leaves, garam masala, chopped onions are among the ingredients in Upma. season with salt to taste and grated coconut.

Idli: Idli is a savoury cake commonly eaten in India. The cakes are made with a batter of fermented rice that is steamed. The starches are broken down during the fermentation process, making them easier for the body to digest. It is eaten with sambar, a lentil-based vegetable stew with a tamarind. **Sheera:** In most parts of India, this simple sweet is made. Semolina, clarified Butter, water, Milk (liquid), Raisins, silvered cashews, silvered Almonds, Nutmeg grating, Cardamom pods are among the ingredients. **Poha**: Poha from India is typically spicy. Ingredients are big onion–finely chopped, teaspoon mustard seeds, tablespoon peanuts, curry leaves, green chill, chopped, tablespoon oil, salt, red or white beaten rice or flattened rice. **Masala Dosa**: Rice batter, black gramme, fenugreek seeds, salt, potatoes, cabbage, green chilies, curry leaves, mustard seeds, vegetable oil, and turmeric are among the ingredients.

Paracetamol, an anti-pyretic and analgesic, is the most frequently used drug for acute and mild-to-moderate painand fever, and it is available over the counter, without prescription **[2-5]**. Crocin tablet® is a well-known brand of paracetamol that can be taken before or after meals. The presence of meal in stomach changes the pH

as well as temperature of dissolution media which ultimately affects the release of drug. In addition to this, drug may interact with the content of the beverages **[1]** and meal which further affects the drug release. Thus, ultimately pharmacological action of drug is affected due to less absorption of drug. Literature survey suggests that viscosity of co-administered food plays a significant role in the release of drug from dosage forms. Also, any change in media viscosity can considerably impact the disintegration times of tablets via modification in liquid penetration rates **[6]**. In view of this, the current work was focused on study of the effect of various Indian breakfast such as upma, sheera (Halwa), Dosa, Idli sambar, Poha on release of paracetamol (crocin tablet) tablet using USP type II dissolution apparatus. Dissolution media used was modified phosphate buffer (with pH 5.8) which was further added with breakfast and was analyzed by UV spectrophotometrically. Thus, drug release profile of paracetamol tablet was focused in presence of various commonly consumed Indian breakfast.

MATERIALS AND METHODS

Materials

Paracetamol was obtained from Shri-Krishna Pharmaceuticals whereas Crocin tablets manufactured by GlaxoSmithKline Pharmaceuticals Ltd. was purchased from Sohit Medical Store Bavdhan (Batch No: R15185). Other beverages such as milk, tea, coffee, carbonated drink and buttermilk were purchased locally.

Methods

1) **Evaluation parameters of Tablet**

a) **Weight variation test**: Accurately, 20 individual tablets were weighed. The average weight of tablets and deviation were calculated using IP 2010.

b) **Friability test:** Friability test was carried out on 10 pre-weighed tablets by placing them in Roche friability apparatus at 100 rpm. Percent weight loss was calculated after reweighing the tablets.

c) **Disintegration test:** Time taken by individual tablet to fragment down into small particles was calculated by using disintegration apparatus (LAB India, DS-8000). A tablet was placed in each of 6 tubes containing distilled water at 37ºC ±1 as disintegrating medium. The basket ascended and descended through a distance of 5cm to 6cm at a frequency of 280 to 320 cycles per minute. Time at which all particles disintegrate was recorded.

d) **Hardness test:** Five tablets were subjected for hardness testing and crushing strength of tablet was measured using Monsanto hardness tester

2) **Preparation of phosphate buffer (having pH 5.8) solution**

Accurately weighed 27.1gm of potassium dihydrogen phosphate was added in 1000ml distilled water to make 0.2M solution (solution A). Likewise, 4gm of sodium hydroxide was dissolved in 500ml distilled water (solution B). Solution A (500 ml) and solution B (72 ml) were mixed and then volume was made up to 1000ml with distilled water to get pH5.8 buffer **[7]**.

3) **Calibration curve**

The standard stock solution was made by adding 25mg standard paracetamol in 25 ml distilled water. Further dilutions were prepared to obtain 5, 10, 15, 20 and 25ppm solutions. The calibration curve was prepared by recording absorbance of these solutions **[7]**.

4) **Dissolution study**

Dissolution study was performed using USP Type II apparatus **[7]** (LAB India, DS-8000) with 900ml media at37±0.5ºC, 50rpm. Crocin tablet (500mg of paracetamol) was introduced into vessel. The aliquots of samples were withdrawn periodically at 15min interval time and replaced with same volume of media which was maintained as blank medium. Filtering of samples was performed using Whatman filter paper (of 0.3µmpore size), using a vacuum filter pump. Later, the analysis was done after suitable dilution using UV spectrophotometer (Cary 100, Varian) at 243nm. Dissolution study was also performed with phosphate buffer and breakfasts such as upma, poha, dosa, idli sambar and sheera separately

One dish of poha was grinded in mixer and obtained coarse powder was added into dissolution vessel. The volume was madeup in dissolution vessel using 700 ml phosphate buffer. The temperature of the dissolution vessel was kept at 37 ±5 degree centigrade, and the rotations per minute of apparatus was fixed at 50rpm. 500 mg paracetamol (1 Crocin tablet each) was introduced in the three vessels and one vessel was maintained as blank. Sample volume up to 10ml was drawn from given three vessels at prescribed time intervals i.e. 15min, 30min, 45min, 60min, 90 min and 120min. After withdrawing the sample, same volume of sample was restored with fresh aliquot from the blank vessel. The samples so obtained were strained through whattman filter paper (0.3µpore size) using a vacuum filter pump. Dilution of the samples obtained from dissolution apparatus was done using mobile phase.1ml of filtered sample was taken, and it was diluted with 10ml of mobile phase, which consisted of water: methanol in the ratio of (3:1). Eventually, the diluted samples

were analyzed under UV at 243nm. Detector used in UV was photo Diode Array (PDA) type.

Dissolution studies were carried out for upma, dosa, idli sambar and sheera in the same way as of poha, where poha was replaced by other breakfast.

RESULT AND DISCUSSION

1) **Evaluation of tablets**

Weight variation is a valid indication of variation in drug content. According to USP, the weight variation should not be more than 5%. As it is shown in **Table 1**, crocin tablet comply with weight variation test. Disintegration time of Crocin tablet was 10mins which complies with USP. Disintegration, which is the first step in dissolution process, is actually the process of breaking down of tablet into particles. Friability results are shown in **Table 1**. The difference in weight of tablet before and after the test was 0.1% and it was within the acceptable limit. The Hardness test which measures the compression force required to break down the tablet was also recorded. Tablet hardness was found satisfactorily in the prescribed range. No significant deviation was observed in average thickness and diameter. The percent assay of crocin tablet was found to be 103% and complies with the requirement of USP.

2) **Calibration curve studies:**

Calibration curve was plotted using UV. Data of these studies is shown in **Figure 1**.

3) **Dissolution studies of paracetamol in solvents and breakfast**

Drug release using tea, coffee, milk, buttermilk, and carbonated drink as dissolution medium is shown in **Figure 2**. Drug release of paracetamol in phosphate buffer solution D0 was found to be 86.36 ± 2.30 % at 90 min and 93.43 ± 1.11% at 120min, while the release of drug in water DW was 95.7± 1.23 % at 90 min and 97.03 ± 1.29 % at 120min.

Drug release in breakfast:

Drug release of paracetamol in phosphate buffer + breakfast was found to be as follows.

Drug release in Phosphate buffer (700ml) + Sheera:

Drug release of Crocin in phosphate buffer and sheera was found to be 12.42± 1.8 % at 15min. At 30min the drug release was increased to 33.28± 1.9%. It was observed that at 45min drug release was to be 50.38± 1.9%. 54.96± 2 % of drug release was at 60min. At 90min the drug release obtained was 64.09± 1.6% and the maximum drug release was found to be 72.12± 2.1% at 120min. Sheera did not reduce the dissolution of the crocin tablet and results

were comparable with a media containing phosphate buffer-water. The dissolved sugar of sheera might be helping the crocin tablet to dissolve in the medium.

Drug release in Phosphate buffer (700ml) + Idli Sambhar:

Drug release of paracetamol in idli sambhar was found to be 6.19± 1.8 % at 15min. The drug release was enhanced at 30min i.e.12.77 ± 2.1%. At 45min the drug release was 14.4 ± 1.9%. The drug release was increased to 31.10 ± 1.8% at 60min. The release of paracetamol at 90min and 120min was observed to 34.00 ± 1.6% and 62.35 ± 2.1%.

It is reported that protein have little influence on paracetamol bioavailability, whilst carbohydrate-rich meals may reduce the absorption of the drug, possibly due to an interaction with pectin **[8]**. In addition, food intake as such seems to reduce the degree of paracetamol absorption, due to delayedgastric emptying **[9, 10]**. Parojcić J *et al*. studied decreaseddisintegration rate and dissolution rate of paracetamol tablets in viscous solutions of HPMC K4M. This effect was ascribedto the lesserwetting of the tablet surface and decreased hydrodynamic shear stress **[11]**. Kalantzi L *et al*. studied tablet disintegration in canine stomach in the fed state. They showed that tablet disintegration can be affected by formation of a film coat around the dosage form, amechanism which doesn't depend on viscosity **[12-13]**. Idli is carbohydrate breakfast and it might be adsorbing the paracetamol and retarding its dissolution. Sambhar also contains oil, which might be forming layer around the tablet and affecting its dissolution.

Drug release in Phosphate buffer (700ml) + Upma:

Drug release of Crocin in upma was found to be 15.31± 1.5 % at 15min. At 30min the drug release was increased to 22.87± 1.3%. It was observed that at 45min drug release was to be 30.20± 2.4%. 53.69± 1.8 % of drug release was at 60min. At 90min the drug release obtained was 84.40± 1.9 % and the maximum drug release was found to be 91.63± 1.7 % at 120min.this might be because of adsorption of paracetamol on upma particles. Upma also has lots of oil, which might be a reason of decrease in dissolution of the paracetamol in the medium.

Drug release in Phosphate buffer (700ml) + Poha:

Drug release of paracetamol in pohe was found to be 24.82± 1.3 % at 15min. At 30min the drug release was enhanced to 34.38± 2.1%. At 45min drug release was found to be 60.62± 1.9 %. 81.12± 1.8 % of drug release was at 60min. At 90min the drug release

observed was 87.87± 2.3 % and the maximum drug release was found to be 98.06± 2.0% at 120min. As compared to phosphate buffer and water, % drug release of paracetamol in pohe was found to be more and percent drug release of drug was found to be more in pohe as compared with sheera and upma.

The percent drug release of drug in phosphate pohe was found more as compared to phosphate buffer-water, phosphate buffer and phosphate buffer-idlisambhar medium. Pohe floats being light in weight floats on the surface, so its hindrance in paracetamol dissolution is very less, so the dissolution of paracetamol is good in medium containing pohe.

Drug release in Phosphate buffer (700ml) + Dosa:

Drug release of paracetamol in plain dosa was found to be 18.47±1.3% at 15min. At 30min the drug release was increased to 23.39±2.1%. At 45min drug release was observed 24.40±1.9%. 24.80±1.8 % drug release of crocin was found at 60min. At 90min the drug release observed was 26.26±2.3% and the maximum drug release was found to be 28.87±2.00% at 120min. As compared to phosphate buffer - water, % drug release of paracetamol in plain dosa was found to be less and % drug release was found to be less in plain dosa as compared with pohe, sheera, upma, and idli sambhar. Plain dosa contains fats, fibres, protein, sodium, potassium and sugars which Might be interacting with paracetamol release. Dosa contains carbohydrates and carbohydrates affect the drug release and dissolution **(Figure 1)**.

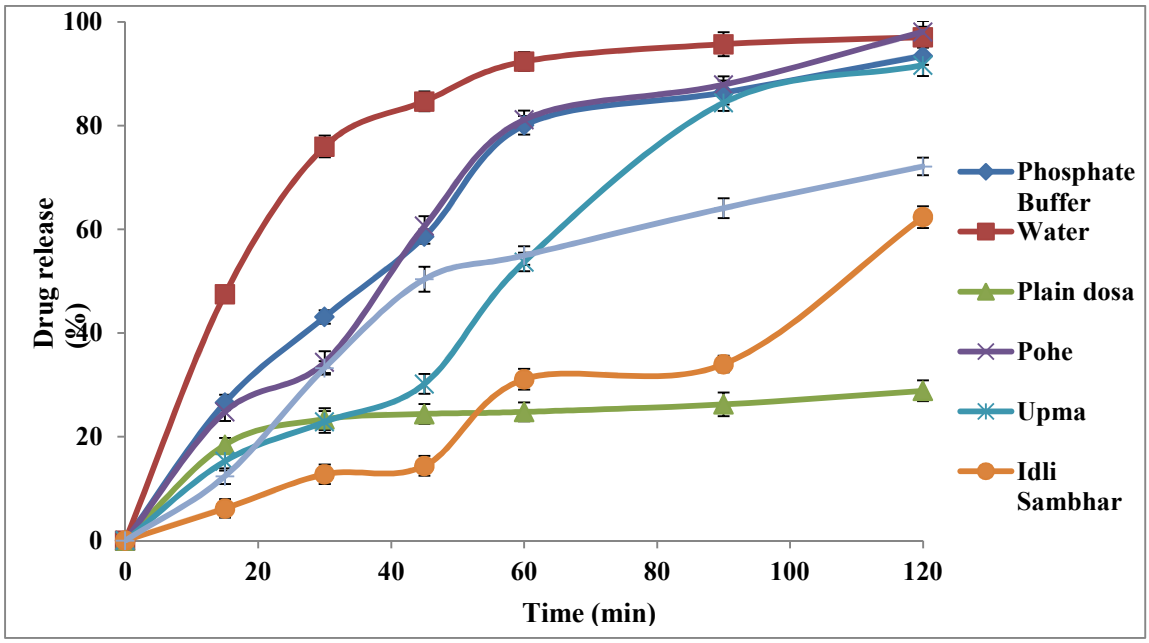

Figure 1: Dissolution profile of paracetamol in various breakfast by UV analysis

CONCLUSION

Paracetamol is one of the most common over-the-counter medicine used for fever and headache. Based on the experiments performed in this study, it was found that when paracetamol tablets are taken with water, drug dissolution takes place at maximum level as compared to when taken with comparator breakfasts. Hence, it can be concluded that paracetamol tablets should be administered with water **[14-15]** alone to get better therapeutic effect. The maximum amount of drug release was observed in pohe as compared to remaining four breakfasts, and lowest drug dissolution was found when comparator breakfast was dosa.

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CONFLICT OF INTEREST

Authors declare that no conflict of interest exist of any sort.

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