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Original Research Article

Investigation of the disintegration behaviour of paracetamol and metronidazole tablets in different beverages

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Abstract

Purpose: The aim of this study was to assess how different beverage media impact the disintegration times of some commonly used solid oral dosage formulations namely, paracetamol and metronidazole uncoated tablets.
Methods: Ten different types of media comprising non-alcoholic beverages (orange juice, sparkling fruit juice, cola and lemon/lime soft drinks), alcoholic beverages of 5, 11 and 18 %v/v alcohol, malt drink and 0.1 N hydrochloric acid were compared with distilled water at 37 ± 1 °C in their disintegration times of paracetamol and metronidazole tablets.
Results: Disintegration time of paracetamol tablets was significantly retarded by the beverages with times ranging from 4.4 - 8.6 min as against 3.5 min in distilled water. Orange juice gave the highest retardation while the malt drink facilitated disintegration with times of 8.6 and 2.8 min respectively. Metronidazole tablets disintegration time was not significantly retarded by the beverages against a time of 1.1 min in distilled water except orange juice with a disintegration time of 4.2 min.
Conclusion: Although the effect on the disintegration times of the tablets by the different beverages did not result in times above compendial requirement of 15 min, care should be taken when replacing water with any beverage in ingesting tablet drug products especially those that are slow in disintegration.

Keywords: Disintegration, beverages, retardation, paracetamol, metronidazole.

Indexing: Index Copernicus, African Index Medicus

Introduction

Disintegration can simply be defined as the process of breaking up of solid materials when in contact with a liquid medium. This usually involves the breaking of internal bonds of the solid material. Tablet disintegration is the disruption of internal bonds and a subsequent breakdown of tablets into granules as a result of the penetration of the tablets by an aqueous medium. The availability of a drug from a tablet depends on the tablet's ability to disintegrate fast enough in existing dissolution media [1]. Therefore, disintegration is the prerequisite for dissolution of active drug after oral administration of solid dosage forms. The disintegration time is often used to determine whether tablets or capsules would disintegrate within the desired time when placed in a liquid medium at given experimental conditions [2,3]. This test is a useful tool for quality control and can be a critical parameter for drug release in certain scenarios like highly soluble drugs [4,5].

A variety of excipients are usually employed by different manufacturers to ensure a final drug product with optimum physicochemical properties. Ultimately, these excipients will influence the disintegration behaviour of the drug products leading to different disintegration behaviours for a variety of different solid drug products. This may lead to differences in the bioavailability of the active ingredients. From a scientific point of view, it is clear that the contents of solid dosage forms can dissolve and become bioavailable only after disintegration. Therefore, disintegration is the most basic step to ensure bioavailability [6].

The general assumption is that an oral solid dosage form should be taken with a glass of water. Where this is not the case, the manufacturer usually gives further instructions as to the right liquid media to use. But the usual practice is that drugs are taken with different forms of liquid ranging from juices to alcoholic and non-alcoholic beverages. Different reasons behind the choice of liquid are easy swallowing, masking the taste of the drug or getting rid of the drug aftertaste, etc. Sufficient quantities of these liquids can influence the disintegration behaviour of a drug.

Several studies have shown that the presence of food in the stomach delays or retards disintegration times of drugs [7,8]. Zuo *et al* and Sreelesh *et al* studied the effect of some beverages on the disintegration time of four dietary supplements and three pain-relief tablets respectively and they observed that the disintegration times of the tablets were delayed by the beverages and in some cases quite significantly [6,9].

The aim of this study was to investigate the impact of beverages particularly fruit juices, soft drinks and alcoholic beverages on the disintegration times of paracetamol and metronidazole tablets.

Experimental

Materials

Paracetamol and metronidazole tablets were products of Emzor Pharmaceuticals, Lagos, Nigeria and were purchased from a local pharmacy in Benin City, Nigeria. Hydrochloric acid (BDH Chemicals. UK), Harp® lager beer and Malta® Guinness (Guinness Nigeria PLC, Ikeja, Lagos, Nigeria), Pure Heaven® sparkling juice and Bullet® caffeinated drink (Sun Mark Ltd, Middlesex, England), Coca Cola® and Sprite® (lemon/lime) soft drinks (Nigerian Bottling Company, Ebute-Metta, Lagos, Nigeria), Chivita orange juice (Chi Ltd, Lagos. Nigeria) and Baron de Valls red wine (Valencia, Spain) were all purchased locally from vendors. Water was double distilled.

Methods

Tablet weight and friability

Twenty tablets of each drug product were individually weighed using the electronic weighing balance (College B154, Mettler Toledo, Switzerland). The mean and standard deviation from the mean were calculated.

Ten tablets were weighed together and the friability was estimated by causing the selected tablets to cascade in the friabilator (Erweka GmbH, Germany) rotated at 25 rpm for 4 min. Percentage loss in weight was calculated to be the friability of the tablets.

Crushing strength

The mean crushing strength was determined by diametrial compression of each of 10 tablets per batch using a motorized hardness tester (Campbell Electronics, Model HT-30/50, India).

Disintegration time test

The time it took for each of six tablets to break up was determined in a BP disintegration tester (MK IV, Manesty Machines, UK). The disintegration medium was 750 ml of distilled water maintained at 37 ± 1 °C. The mean disintegration time was calculated. The time at which no particle remained in the tube, all having passed through the 2 mm diameter wire mesh, was recorded as the disintegration time for each tablet.

The above procedure was then repeated using the different beverages in their original purchased forms (without dilution) as the disintegration media in place of distilled water. Temperature was maintained at 37 ± 1 °C.

Statistical analysis

Individual disintegration times were noted and reported as the mean ± SD. Statistical analysis was carried out by one-way analysis of variance (ANOVA) at a significant level of $p < 0.05$ by Dunnett's multiple comparison tests using GraphPad InStat software version 3.10. The statistical tests were conducted between different beverage media.

Results

As observed from Table 1, the weight variations of 0.57 ± 0.02 g and 0.52 ± 0.01 g of paracetamol and metronidazole respectively were within acceptable range of pharmacopoeial standards. These variations are expected not to have a significant impact on the disintegration time of the tablets. Thus, the weight variations of the tablets will not have any effect on their disintegration time.

Table 1: Some physicochemical properties of paracetamol and metronidazole tablets

Tablets	Weight (g)	Friability (%)	Hardness (kp)
Paracetamol	0.57 ± 0.02	0.8 ± 0.02	9.612 ± 1.244
Metronidazole	0.52 ± 0.01	0.9 ± 0.04	4.070 ± 0.616

Values are mean ± standard deviation

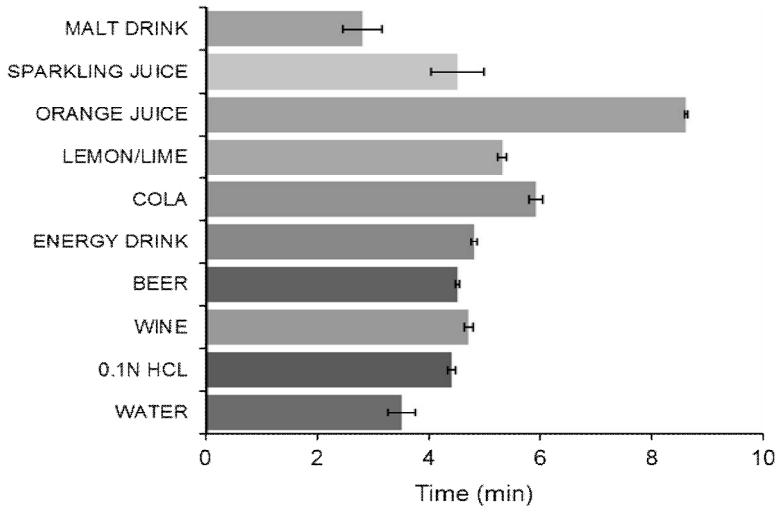

Figure 1: Disintegration times for paracetamol tablets in the different beverage media and water

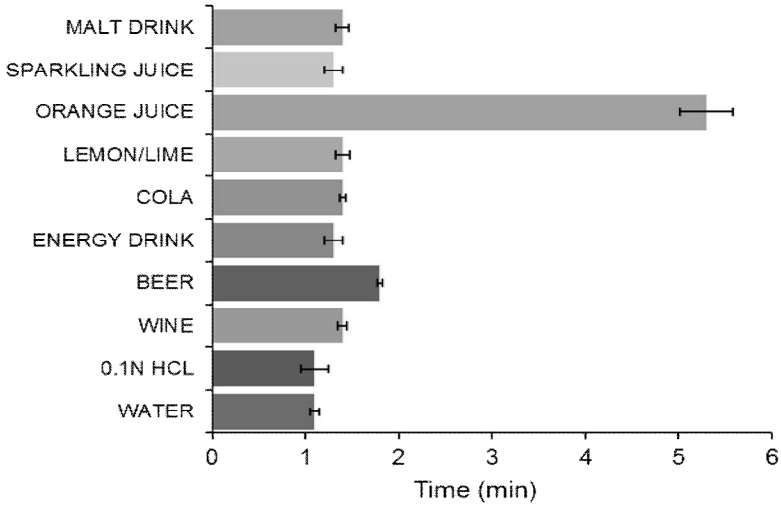

Figure 2: Disintegration times for metronidazole tablets in the different beverage media and water

The friability test evaluates the ability of a tablet to withstand chipping and abrasion in the process of packaging, handling and transportation. Both tablets showed acceptable friability values; 0.8 % loss for paracetamol tablets and 0.9 % loss of metronidazole tablets (Table 1). The British Pharmacopoeia specifies a range of 0.8 - 1 % loss in weight of the tested tablets without capping, lamination or breaking up in the course of the test [10].

The results of the crushing strength of the tablets gave a mean value of 9.612 kp for paracetamol and 4.070 kp for metronidazole (Table 1). Both tablets gave good hardness values above 4 kp since hardness values greater than or equal to 4 kp are considered optimal and acceptable [11].

The disintegration times of paracetamol tablets in the different beverages at 37 ± 1 °C are shown in Figure 1. The beverages increased the disintegration time of paracetamol tablets except the malt drink which reduced the disintegration time. The mean disintegration times of the paracetamol tablets in the different beverages ranged from 2.8 ± 0.4 min of the malt drink to 8.6 ± 0.03 min of the orange juice ($p < 0.05$) against 3.5 ± 0.3 min in water at 37 ± 1 °C ($p = 0.05$). The beverages significantly influenced the disintegration time of paracetamol tablet.

Figure 2 shows the disintegration times of metronidazole tablets in the different beverages at 37 ± 1 °C. The mean disintegration times of the metronidazole tablets ranged from 1.1 ± 0.2 min in 0.1 N HCl to 5.3 ± 0.3 min in orange juice compared with the 1.1 ± 0.1 min of water at 37 ± 1 °C. The disintegration times of the tablets in the beverages were not significantly increased ($p > 0.05$) except in the orange juice ($p = 0.0000143$). Therefore, almost all of the test beverages did not significantly influence the disintegration times of metronidazole tablets.

Discussion

The physicochemical properties of a tablet formulation play a great role in the availability of the drug in the tablet. The tablet must disintegrate for dissolution and absorption of the drug to take place. The faster the disintegration time of the tablet, the earlier will the drug undergo dissolution and absorption; therefore, the disintegration time test can be a valuable performance test for solid oral dosage forms [5]. Factors influencing the disintegration time of a tablet will ultimately affect the release and absorption of its drug component and eventually the onset of action of such drug. A tablet parameter that can affect disintegration time is the tablet hardness. An overly hard tablet would increase disintegration time. The major determinant of hardness is the binding activities of tablet excipients particularly the binder. The results of the crushing strength of paracetamol and metronidazole tablets showed that the binder used in the formulation of the tablets had acceptable binding properties. An implication of this is that the tablets would achieve proper wetting needed for the disintegration of the tablets to occur in time.

The mechanism of disintegration is that of liquid uptake or penetration of liquid into tablets to cause swelling and eventual rupture of the tablet. A liquid's viscosity, contact angle and surface tension have been shown to influence the penetration rate of the liquid into a tablet and consequently, the disintegration time of the tablet [12]. For example, it has been shown that disintegration is delayed in milk [13-15]. This is because, the penetration rates for milk are slow, which may be a reflection of its relatively high viscosity and low surface tension [16]. If the test media are grouped into low viscosity (water and 0.1 N HCl), medium viscosity (wine, beer, energy drink, cola, sprite, sparkling juice and malt drink) and high viscosity (orange juice) beverages, it would be expected that their penetration rate into the tablets will follow this order with the low viscosity beverages effecting faster disintegration times followed by the medium viscosity and high viscosity beverages, in that order. This was more or less the case except for the malt drink. There may be a component of the malt drink that led to a decrease in disintegration time rather than an increase.

Tablet disintegration is a combination of fluid penetration and swelling of the tablet culminating in the rupture of the tablet. Swelling results from tablet porosity or capillary action. A porous tablet will facilitate fluid penetration and swelling leading to faster disintegration times. Metronidazole tablets used in the study may have been more porous than the paracetamol tablets hence the faster disintegration times observed.

However, disintegration time increases with increase in porosity above a critical level. This is due to the fact that the swelling force generated in such cases is rendered ineffective as the inter-particulate distance becomes too large. The longer disintegration times of paracetamol tablets may be due to their relatively high tablet porosity.

Even though the delay in the disintegration times of paracetamol and metronidazole tablets in the test media were significant ($p < 0.05$), these results may not have a major clinical impact because their disintegration times were less than 15 min, which is the BP specified disintegration time limit for uncoated tablets and also the average gastric emptying time when fluid is taken with a dosage form in the absence of food [17]. However, for tablets that disintegrate slowly, the results may have clinical relevance because of a significant increase in disintegration time.

Conclusion

Disintegration is the most basic process that is required for the release of the content of a tablet or capsule dosage form into the body when administered orally. The results of this study suggest that water may be the best media to be used for the administration of solid oral dosage forms (e.g., paracetamol and metronidazole tablets), and that juices, soft drinks and alcoholic beverages should be avoided due to their impact on the disintegration of dosage forms especially those that undergo slow disintegration.

Declarations

Acknowledgement

The authors acknowledge the technical support received from the departmental laboratory staff.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them. Sylvester O. Eraga - supervision of laboratory works, collection, analysis of data and manuscript write-up. Matthew I. Arhewoh - analysis of data and manuscript write-up. Odera C. Unachukwu - carried out the laboratory work. Magnus A. Iwuagwu - conceived and designed the study.

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