PREDICTION OF RELATIVE IN VIVO BIOAVAILABILITY OF THREE COMMERCIAL BRANDS OF PEFLOXACIN FILM COATED TABLETS BASED ON IN VITRO DISSOLUTION EFFICIENCY PARAMETER.

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SUMMARY

The in vitro dissolution efficiencies (DE) of three commercial brands of pefloxacin film coated tablets were assessed in O.IN acetic acid (pH 2.8) and phosphate buffer (pH 7.4). Results obtained indicate that one of the brands (Abaktal) exhibited the highest dissolution efficiency in the two dissolution media tested. Peflacine and peflotab had very close D. E. values in the two media and may exhibit close bioavailability in vivo. The relative ranking of the D. E. of these brands are in the order of Abaktal, peflotab peflacine. This may represent their relative in vivo bioavailability since D. E. ranking usually correlate with in vivo bioavailability.

INTRODUCTION

Due to the concern about drug availability, there have been published within the last three decades literatures concerning dissolution rates (1-4). The goal of most investigators in this area has been to device tests which in vitro, could predict quantitatively or at least predict ranks of performance in vivo.

Pefloxacin mesylate is a fluoroquinolone antibacterial agent with actions and uses similar to those of ciprofloxacin. Unlike ciprofloxacin, it has a plasma half life of about 8 - 13hr and is extensively metabolized, the primary metabolite being N-desmethylpefloxacin, otherwise known as norfloxacin (5). In addition to the uses described for ciprofloxacin, pefloxacin has bactericidal activity against Mycobacterium leprae and has been tried in the treatment of leprosy (5). There are presently about three most popular commercial brands of pefloxacin film coated tablets available in the market. The dissolution efficiencies (DE) of these three brands (Peflacine, Peflotab and Abaktal) were evaluated in vitro and used as the basis for in vivo ranking of their likely relative bioavailability. This concept (DE) was employed in estimating the in vivo bioavailability of some commercial brands of ciprofloxacin tablets in a recent study (6).

EXPERIMENTAL

Materials and Method: The following materials and chemicals were used as procured from their manufacturers without further purification: sodium hydroxide, glacial acetic acid, pefloxacin mesylate (May and Baker, England), potassium dihydrogen orthophosphate, disodium hydrogen phosphate (Sigma Chem. Co., U. S. A.). Three brands of pefloxacin mesylate film coated tablets (peflacine, May and Baker, England, peflotab, V. S Int., India and Abaktal, Lek, Yugoslavia) were purchased from a retail Pharmacy shop in Nsukka, Nigeria.

Dissolution profile studies: The dissolution profiles of the tablets were evaluated according to the BP 1993 method with paddle of an Erweka dissolution apparatus (DT-D model) Operated at 50 ± 1 rpm. The dissolution medium was 1000ml of 0.1 N acetic acid. or phosphate buffer (pH 7.4) maintained at 37 + 1°C. 0.1 N acetic acid instead of 0.1N HCl was used purely based on excellent solubility of pefloxacin in it. More so, the pH of 0.1 N acetic acid (~ 2.8) is within the pH range of the stomach. Samples were withdrawn at predetermined time intervals and analysed spectrophotometrically at 277 nm in a UV/VIS Spectrophotometer. The dissolution data obtained were fitted into normal dissolution curve and the dissolution efficiencies of the different brands were calculated using a method previously reported (6). All analysis were carried out before the expiration date of the tablets.

RESULTS AND DISCUSSION

Peflacine and Abaktal had almost equivalent crushing strength value of 33.30 ± 0.09 N and 33.14 ± 0.46 N respectively. Peflotab had the least value of crushing strength (27.69 ± 3.90 N). The tablet brands were non friable after 100 rpm in an Erweka friabilator probably because of the polymer film coats around them.

From the dissolution profiles shown in Figure 1, pefloxacin release was fastest from Abaktal and least from peflacine. All the brands, however, released upto 90% of the drug within 1h in 0.1 N acetic acid. In phosphate buffer, Abaktal released upto 90% of its drug content within 30 min. (Figure 2). There was an initial fast release of the drug from peflacine and peflotab upto 45 and 50% cumulative drug release respectively within the first 5 min. The release profile remained almost constant resulting in plateaus within the next 5 min. While Abaktal behaved like a normal release formulation in phosphate buffer, Peflacine and Peflotab behaved like sustained release formulations in this media. The D.E - (dissolution efficacy calculated at the 60- minute) values of the tablets are presented in Table 1. Abaktal had the highest D.E- of 68% in acetic acid and 71.6% in phosphate buffer. It is evident from Table 1 that the D. E- of Peflacine and Peflotab decreased in phosphate buffer while that of Abaktal increased slightly.

The three pefloxacin tablet brands that were tested are film coated. In the film coating of solid dosage forms a variety of hydrophilic and hydrophobic polymers are normally employed. Different manufactures may adopt different polymer and method to coat their solid dosage forms. Factors such as polymer type and film thickness may affect the rate and extent of drug release from a film coated dosage form. In addition the type of dissolution media used may affect the solubility and/or the behaviour of a given film coat. It may be that polymers used in coating Peflacine and Peflotab are similar and may have interacted with the components of the phosphate buffer resulting in the formation of gel network around the core tablet. This may have retarded the rate and extent of pefloxacin released from the two brands. Visual observation on the two brands during the dissolution studies revealed the presence of gel network around the tablets.

The calculated values of $D.E^{60}$ for the three brands of pefloxacin show that Abaktal had the highest value of $D.E.^{60}$ in 0.1 N acetic acid and in phosphate buffer. Dissolution efficiency is a comparative parameter and it offers the advantage of allowing comparison to be made between a large number of formulations. In addition, it can be theoretically related to in vivo data. This is based in the assumption that the degree of absorption of a drug in vivo is proportional to the concentration of the drug in solution and the time this solution is in contact with a suitable absorption region of the GIT (7). Pefloxacin is weakly acidic and is most likely to be absorbed in the acidic region of the gastrointestinal track (GIT). Based on the above theoretical relationship, the likely ranking of the in vivo bioavailability of the three formulations would likely follow their relative in vivo ranking in 0.1 N acetic acid, that is, Abaktal > Peflotab > Peflacine. It may therefore be concluded that Peflacine and Peflotab may likely exhibit close bioavailability in vivo while Abaktal may exhibit the highest bioavailability.

The present study does not replace the need for in vivo study on the formulations. This is because, whereas it is possible to mimic in vivo some of the parameters (such as temperature, pH, viscosity and surface tension of GIT fluid), the type and intensity of mixing and interaction of drug with food or food residues cannot be reproduced. However, data available in literature on testing of the same formulations in dissolution test and bioavailability studies over the past 25 years have shown that formulations that have poor release characteristics in vivo often have low bioavailability in clinical studies (8). Consequently, in vivo dissolution tests provide valuable data for the development of pharmaceutical products, an

indication of relative potential in vivo performance and means for quality control (8). Pefloxacin is a strong antibacterial agent used in the treatment of many serious infections. It is therefore suggested that excipients and other processes involved in its formulation as a tablet dosage form be specified in the official compendia to reduce any variability in its bioavailability from different formulations.

CONCLUSION

The concept of dissolution efficiency (D.E.), could be employed in the estimation of relative in vivo bioavailability of different brands of pefloxacin film coated tablets.

Table 1: Dissolution Efficiency of Pefloxacin Tablets.

Dissolution Medium	Dissolution Efficiency (D. E.)%		
	Peflacine	Peflotab	Abaktal
0.1 N acetic acid (pH 2.8)	47.0	53.5	68.0
Phosphate buffer (pH 7.4)	17.7	19.3	71.6

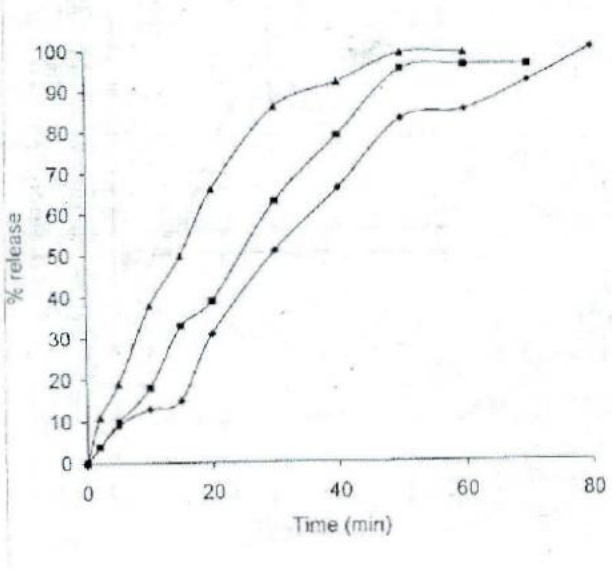

Fig. 1 Release profiles of brands of Pefloxacine tablets in 0.1 N acetic acid (pH 2.8). Peflacine (◆), Peflotab (■), Abaktal (▲).

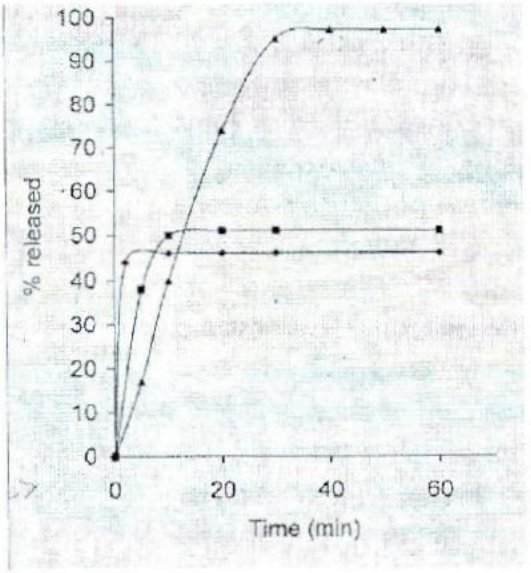

Fig 2 Release profiles of brands of pefloxacine tablets in phosphate buffer (7.4). Peflacine (◆), Peflotab (■), Abaktal (▲)

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