Class experiment with student volunteers illustrating the influence of formulation on absorption of aspirin

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The influence of formulation on the absorption of drugs is an important aspect of clinical pharmacology. However, such a topic is not readily demonstrated to students since undergraduate practical classes generally operate with constraints such as limited duration of laboratory period, lack of sophisticated equipment and varying technical ability of the students themselves. Nevertheless, we have devised a number of volunteer experiments which can be performed satisfactorily within such constraints and one of these is described below. It is simple to carry out and requires a minimum of practical expertise and equipment. The experiment demonstrates the influence of formulation on the absorption of aspirin using urinary excretion of salicylate over a 2 h period as the index of absorption.

Three different tablet formulations each containing 325 mg aspirin have been employed. Each healthy student volunteer swallows two tablets of one of the formulations with water (150 ml), at least 2 h after a light meal. The bladder is emptied immediately prior to dosing and at 0.5, 1.0, 1.5 and 2.0 hours. The volume of urine at each time is measured and, after alkaline hydrolysis, salicylate content determined colorimetrically using Trinder's reagent (Staff of Department of Pharmacology 1970). Students with a history of gastric disorders, known sensitivity to aspirin or who have not previously taken aspirin, are excluded from the experiment.

With the following fomulations: (A) aspirin with 10% wheat starch (10 s disintegration time, by standard B.P. 1973 test), (B) aspirin with 2% wheat starch (60 min disintegration time) and (C) enteric coated aspirin tablets B.P., typical results (accumulative totals of urinary salicylate, mg mean $\pm$ s.e. at 0.5, 1.0, 1.5 and 2.0 h) for groups of eight students are, for A, 5.2 ± 3.0, 15.6 ± 6.3, 25.5 ± 6.8, 39.1 ± 5.4; for B, 0.7 ± 0.2, 2.6 ± 0.7, 6.5 ± 1.2, 12.1 ± 2.4; for C, zero, zero, 0.8 ± 0.3 and 2.1 ± 0.9.

This basic study may be modified to investigate the influence of a variety of orally administered medicines such as antacids, kaolin, iron preparations and antispasmodics on the absorption of salicylate.

We are grateful to Dr N.A. Armstrong for supplying the aspirin tablets.

Reference

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Intersubject variability of sulphadimidine acetylation in student volunteers

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An acetylation polymorphism affects the metabolism of several drugs such as isoniazid and sulphadimidine. Rao, Mitchison, Nair, Prema & Tripathy (1970) have proposed that classification of individuals into slow and rapid inactivators of isoniazid may be made on the basis of the degree of acetylation of a test dose of sulphadimidine.

We have modified the procedure of Rao *et al.* (1970) for teaching purposes to illustrate the inter-subject variation in the acetylation of this sulphonamide. The drug is taken by healthy student volunteers at least 2 h after a light meal and urine is collected between 1 and 3 h after dosing for determination of sulphonamide.

The bladder is voided 1 h before the practical class, a sample of the urine (control) being retained for assay. Each volunteer then swallows four tablets of sulphadimidine B.P. (2 g) with water (150 ml). One hour later, at the commencement of the class, the bladder is again voided, the urine being discarded and a further 150 ml water taken. All urine passed between 1 and 3 h after dosing is collected in a combined volume and assayed colorimetrically for free and total sulphonamide by the method of Bratton & Marshall (1939). Using absorbance values (corrected for control readings) only, the proportion of acetylated sulphadimidine in the urine sample is calculated. This makes it unnecessary to measure volume of urine collected or to run standards through the assay procedure. It is important to thoroughly mix the reagents at each step and to use the coupling reagent

freshly prepared. Urine samples seeded with sulphadimidine and its acetylated conjugate are made available for 'practice runs' during the early part of the practical class.

A bimodal distribution for the acetylation of this sulphonamide is evident from the results of the class experiment. Thus, in a group of 57 students the frequency distribution pattern was 10 (0–9% acetylation), 3 (10–19%), 4 (20–29%), 0 (30–39%), 5 (40–49%), 14 (50–59%), 11 (60–69%), 5 (70–79%), 5 (80–89%) and 0 (90–100%). Data obtained from class experiments over the past three years has indicated that even with small groups (i.e. 22 students) this bimodal distribution pattern is obtained. On the basis of these results it would appear that the good acetylators are above the 40% value whereas the poor acetylators are below this figure. If large enough numbers of students participate it may be possible to analyse the data in terms of ethnic groupings.

During the class it is also possible to examine urine samples for the presence of free and acetylated sulphadimidine by thin layer chromatography using silica gel plates containing a fluorescent indicator (Merck F254). Control and test urines (2–3 μl) together with the two pure sulphonamides are applied as separate spots to the plate which is then developed in benzene: acetone (3:1, v/v) for 20 minutes. Sulphadimidine and its acetylated metabolite are then detected as quenching spots (under light at 254 nm) with Rf values of 0.42 and 0.23 respectively.

References

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Films in pharmacology teaching

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Film loops and full length films, especially those in colour, are used in pharmacology courses to supplement lectures, practicals, and other audio-visual material. Selected film material may thereby increase the scope and interest of courses as well as adding variety to their content.

The film loop, lasting from 2 to 15 min, may be projected on to a conventional screen or displayed on small portable desk-top monitors, and may thus be shown to small groups or to whole classes. It is particularly useful for the demonstration of simple practical techniques, as it can be allowed to run and repeat itself until the student is familiar with the experimental technique. The use of close-up and colour enables the clear visualization of detail which may not always be possible during live demonstrations. In addition, film loops provide economies in demonstrator time and permit students to learn independently at their own rate. The production of film loops is well within the capabilities and budget of many university audio-visual departments.

The expense and time involved in making a first class full-length film puts film-making outside the scope of all but the largest organizations. However, there are many excellent films on pharmacological topics which are available from the pharmaceutical industry and from other sources. In many cases these are not orientated towards commercial promotion, and may be hired free or at nominal cost. Such films cover many aspects of drug actions and their therapeutic uses, as well as relevant physiological and clinical topics. Obvious benefits of the use of films include the convenient access to material which would otherwise be unavailable to the student, and the juxtaposition of basic theory with experimental and clinical material. Imaginative use of animated diagrams, colour, cinemicrophotography, slow motion sequences, and other techniques, contribute to the powerful impact and teaching effectiveness of films.

The intention of this demonstration is (a) to show examples of films and film loops which illustrate some of the points discussed above, and which demonstrate the potential value of films in pharmacology teaching programmes; and (b) to provide catalogued information and basic details about film material which is now available, both from academic and commercial sources. Much of the information concerning films made by pharmaceutical companies has been obtained from a recent questionnaire (April–May 1976) which shows that many companies have a lively interest in pharmacology teaching.

I wish to acknowledge the kind co-operation of many pharmaceutical companies in providing information, and especially to those who have generously loaned films for this demonstration.